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JOURNAL OF BANGLADESH COLLEGE OF PHYSICIANS AND SURGEONS

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EDITORIAL

Acute Glumerulonephritis in Children : Bangladesh Perspective

Acute glumerulonephritis (AGN) is characterized by sudden, often explosive, onset of symptoms of glumerular injury which include haematuria, hypertension, oedema, oliguria and a varying degree of renal insufficiency. In children, the majority of cases of acute glumerulonephritis are post-infections, most commonly (80%) following infection with Group A - haemolytic Streptococci. A small proportion of cases are caused by drugs, toxins or as a part of a systemic disease.

Although the incidence of post-streptococcal acute glumerulonephritis (PSAGN) has decreased dramatically in the west, probably because of better nutrition and primary care and appropriate use of antibiotics for upper respiratory tract infections, it is not so in the developing countries. Three papers have so for been published on the disease in Bangladesh[1,2,3]. Acute glumerulonephritis comprises of 22% of the total admissions in the Paediatric Renal Unit of the Institute of Post-graduate Medicine and Research, Dhaka. In China, it is the most common cause for hospital admissions for kidney disease in children.

Though we have no population based study it is suspected that approximately 1.5 million children in Bangladesh suffer from AGN each year. The true incidence cannot be assessed with accuracy because of the wide range of clinical manifestations. Asymptomatic GN may be more common than is realized.

Although PSAGN following pharyngitis is more common in the west and even in some Asian countries[5,6], our experience shows that 90% of children with AGN had healed or active lesions of infected scabies on admission. Most of them have come from a poor socio- economic background having little or no idea about primary health care.

Diagnostic facilities such as urinanalysis, serological and immunological tests, and other investigations to exclude systemic diseases causing nephritis are available in Bangladesh. Few children having atypical presentations of the disease, persistence of hamaturia, proteinuria, hypertension, low C_3 level and impaired renal function need kidney biopsy to see the underlying histopathological changes. In children, light microscopy (LM) is not frequently diagnostic and a precise identification depends on immuno-flour-escence (IF) and electron microscopy (EM). We are, at this moment, lacking the EM facility in Bangladesh though IF is available in a limited scale.

Management of the child with acute glumerulonephritis in children centres on supportive and symptomatic care. There is little that can be done to alter the course of the disease once it becomes symptomatic. Often the physicians may find that the main task is reassuring anxious parents that conservative measures and watchful waiting are all that is required. Complications like hypertensive encephalopathy, acute pulmonary oedema and acute renal failure need immediate intensive treatment. Physicians often face difficulty in managing children with mixed features of AGN and nephrotic syydrome. It is better not to institute steroid and cytotoxic drug therapy until the underlying histopath-ological variety is detemined by renal biopsy.

The acute phase of the illness in AGN, in general, lasts 2-3 weeks. Urinary findings may take much longer to resolve. Microscopic haematuria may persist for upto 12 months often accompanied by proteinuria for six

months. C_3 level is expected to return to normal by eight weeks.

It is generally agreed that the outcome is more favourable in children than in adults with this disease. Follow-up studies report an incidence of impaired renal function that ranges from less than 1% to as high as 20%[2,7,8]. Of Children with PSAGN, a small minority of those hospitalized, 0.5-2% may have a rapid progression to end stage renal disease within weeks to months having extensive crescent formation in their kidneys. It is not clear whether early aggressive treatment of these children with corticosteroids, cytotoxic agents and anticoagulants offer any advantage over supportive care alone in altering the long term prognosis.

There is no doubt that a considerable number of children in Bangladesh are suffering from AGN causing significant morbidity and mortality, school failure and anxiety to the parents. Some of these children would probably go into end stage renal failure and some forms of renal replacement therapy like CAPD, haemodialysis and transplantation would be required for their normal growth and activity. This type of therapy is too costly and highly technical. Emphasis should be given on prevention of the disease through mass health education, providing primary health care and early recognition and treatment of scabies infections and respiratory tract infection. Extensive research works have been going on in developed countries to find out the mechanism of glumerular injury in PSAGN and the determinants of reversibility, so that permanent damage in more severe proliferative GN can be prevented.

MD. MOAZZAM HOSSAIN, MBBS, FCPS
Professor of Paediatric Nephrology
Institute of Post- graduate Medicine and Research, Dhaka

(J Bangladesh Coll Phys Surg 1995; 13: 87–88)

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Juvenile Nasopharyngeal Angiofibroma-A Review of 135 Cases

M ALAUDDIN, FRCS[a], M ABDULLAH, FCPS[b], K AHMED, FCPS[c]

Summary :

One hundred and thirty five cases of juvenile nasopharyngeal angiofibroma (JNA) seen at ENT department of Dhaka Medical College Hospital during July 1979 to June 1993 were reviewed. Majority of them were between 11 and 20 years of age and were from low socio–economic class. Most of the patients presented with recurrent epistaxis, nasal obstruction, nasal discharge and tumour arising from the roof of the nasopharynx and adjacent part of the choana. All the patients were treated surgically and 90% of the patients who came for regular follow-up became asymptomatic. External carotids were ligated in 30 cases to avoid excessive haemorrhage during surgery but there was no noticeable benefit over those who had surgery without carotid ligation. The usefulness and versatility of the surgical treatment is emphasized in reference to high cure rates, low recurrene rates, minimal chances of residual tumour and decreased length of hospital stay. The usefulness of different surgical approaches is also briefly summarised.

(J Bangladesh Coll Phys Surg 1995; 13: 89–94)

Introduction :

Juvenile nasopharyngeal angiofibroma (JNA) is a benign but biologically aggressive tumour. It originates almost exclusively from the posterior nasal and nasopharyngeal region in adolescent males[1,2]. Thus it has been known as juvenile angiofibroma, although cases have been reported in females and adults as well[2]. It is a rare tumour accounting for 0.05% of all head and neck tumours[3] and the reported incidence ranges from one in 5,000 to one in 50,000 of otolaryngological admissions in different countries[4]. It behaves like a locally malignant tumour because of it's tendency to erode the surrounding vital structures and tendency to recur if not completely removed. The main presenting symptoms are recurrent nose bleeding, nasal obstruction, swelling in and around the face and/ or eyes and occasionally dysphagia, earache and deafness. Besides, nasal speech, headache, anosmia, pansinusitis, even blindness and death due to extension into the cranial cavity were reported[5].

Various types of treatment of JNA have been advocated which includes surgery, radiotherapy, cryotherapy, electrocoagulation, hormonal therapy, embolization and injection of sclerosing agents but surgery is recommended as the treatement of choice[1]. The surgical procedure selected should be determined by the location and extent of the tumour[6].

The purpose of this study was to review the various clinical aspects of JNA and to share the experience of 135 cases of JNA managed surgically and also to review the available literature.

Materials and method :

One hundred and thirty five male patients treated surgically at ENT department of Dhaka Medical College Hospital between July 1979 and June 1993 with diagnosis of JNA were reviewed. Diagnosis was made mainly on the basis of clinical features and radiological examination of nasopharynx and paranasal sinuses.

a. Prof. M Alauddin, Professor and Head of the Department of Otolaryngology, Dhaka Medical College and Hospital (DMCH), Dhaka
b. Md. Abdullah, Asst. Professor, ENTD, DMCH, Dhaka
c. Dr. Khabiruddin Ahmed, Resident Surgeon, ENTD, DMCH, Dhaka
Correspondence to: Prof. M Alauddin, Professor and Head of the Department of Otolaryngology, DMCH, Dhaka
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Histopathological examination of all the specimens of tumours were done following surgery to confirm the diagnosis. CT scan was also done in few cases.

In addition, all patients had otorhinolaryngological assessment, head and neck examination and laboratory studies consisting of a haemogramme, urine analysis and X-ray chest.

Results :

The subjects were between eight and 26 years of age with predominance in the second decade (80%) (Fig.-1).

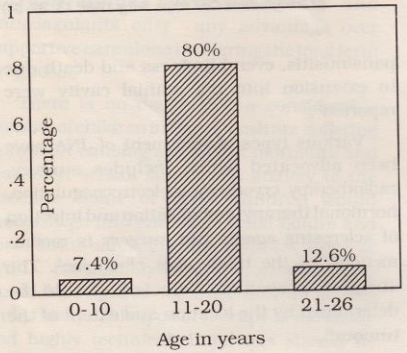

Fig-1: *Age Incidence (n=135)*

Majority of the patients (85.19%) came from low socio-economic group and from rural areas. No patient was from affluent class background (Table-I).

Table–I

Socio-economic condition (n=135)

Socio–economic condition	Number	%
Lower class	115	85.19
Middle class	20	14.81
Affluent class	00	00

All 135 cases had recurrent epistaxis followed by nasal obstruction, nasal discharge, facial swelling, proptosis, headache and ear symptoms (Table-II).

Table-II

Presenting features (n=135)

Features	Number	%
Recurrent epistxis	135	100.00
Nasal obstruction	122	90.37
Nasal discharge	125	88.00
Facial swelling	30	22.22
Protrusion of the eyeball	20	14.80
Dysphagia	15	11.11
Aural symptoms	15	11.11
Headache	05	3.70

All of them had nasopharyngeal and nasal mass, cheek swelling, palatal bulging, proptosis and oropharyngeal mass (Table-III) (Fig.-2 and 3).

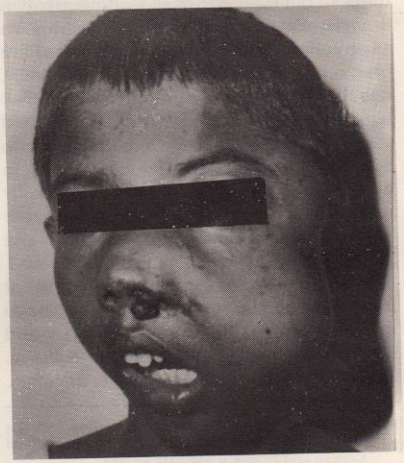

Fig-2: *Photograph of a patient of recurrent JNA showing nasal mass hanging through the left nostril with left sided facial and temporal swelling with scar mark of previous left lateral rhinotomy incision.*

Table—III

Clinical examination findings (n=135)

Signs	Number	%
Nasopharyngeal mass	135	100
Nasal mass	128	94.81
Swelling of the cheek	32	23.70
Palatal bulging	30	22.22
Proptosis	20	14.80

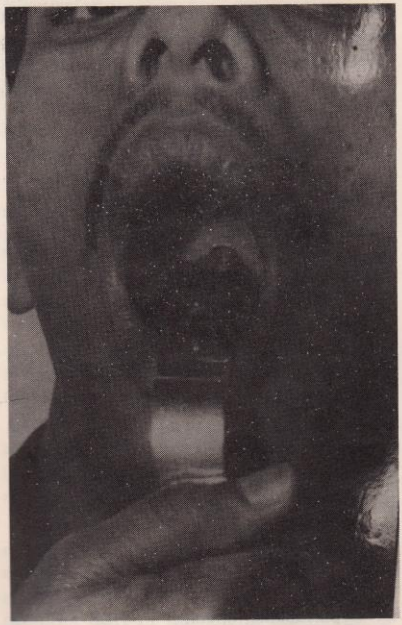

Fig-3: *Photograph of a patient of JNA showing oropharyngeal mass hanging from the nasopharynx.*

Out of 135 cases, 130 (96.29%) had their tumour originating from the roof of the nasopharynx and posterior margin of the choana and the rest five (3.70%) from the posterior part of the lateral nasal wall. (Table-IV).

Table—IV

Site of origin (N=135)

Site of origin	Number	%
Roof of the nasopharynx and posterior margin of choana	130	96.29
Posterior part of the lateral nasal wall	5	3.70

Majority (96.29%) had their extension into the nasal cavity and then into pterygopalatine fossa, infratemporal fossa, maxillary antrum, orbit and oropharynx (Table-V).

Table—V

Extension of tumour observed during surgery (n=135)

Sites	Number	%
Nasal cavity	130	96.29
Pterygopalatine fossa	60	44.40
Infratemporal fossa	32	23.68
Orbit	20	14.80
Oropharynx	15	11.11
Maxillary antrum	12	08.88
Intracranial extension	00	00

All the 135 cases were treated surgically. Majority (55.56%) had undergone transpalatal approach. Other approaches followed were transpalatal with lateral rhinotomy, transpalatal with sublabial extension, transpalatal with sublabial and temporal incision, and lateral rhinotomy approach (Table-VI). Recurrent cases were also treated with surgery. None was treated by radiotherapy, hormonal or cryotherapy. In 30 cases, external carotid was ligated prior to surgery to minimize excessive bleeding during surgery, but the result was discouraging. All the specimens of tumours were sent for histopathological examinations (Fig. - 4).

Table—VI

Surgical approaches (n=135)

Approach	Number	%
Transpalatal only	75	55.56
Transpalatal with lateral rhinotomy	25	18.52
Transpalatal with sub-labial extension	18	13.33
Transpalatal with sub-labial extension with temporal incision	12	08.89
Lateral rhinotomy	05	3.70

Fig-4: *Photomicrograph of JNA showing fibrous connective tissue interspersed with variable proportions of endothelium lined vascular spaces.*

Blood transfusion was required in all the cases during surgery and the quantity varied between 800 and 2,000 ml.

During surgery, 15 (11.11%) patients developed cardiac arrest of which 12 (8.89%) patients died due to irreversible cardiac arrest and the rest were managed by conservative measures. Two (1.48%) patients developed avulsion of the soft palate. Amongst the post-operative complications, highest incidence (14.8%) was of crusting in the nose with atrophic change. The crusting was probably due to roamy nasal cavity due to tumour removal. They were treated with regular nasal douching and crust removal. Post-operative haemorrhage, both reactionary and secondary, was recorded in 10 (7.4%) cases and was controlled by postnasal packing. Palatal perforation developed in 12 (8.89%) cases which was probably due to lack of bony support underneath the suture line. Eight of them healed spontaneously and the rest required secondary suture to close the perforation. Nasal voice developed in eight (5.92%) cases which was probably due to larger nasopharyngeal and nasal space and fibrosis of the soft palate causing restricted movement of the soft palate (Table -VII).

Table—VII

Complications (n=135)

Type	Number	%
Per-operative:		
i. Cardiac arrest	15	11.11
reversible 03		
irreversible 12		
ii. Avulsion of the soft palate	2	1.48
Post-operative:		
i. Haemorrhage	10	7.40
reactionary -3		
secondary -7		
ii. Palatal perforation	12	8.89
iii. Crusting in the nose with atrophic change	20	14.80
iv. Hypernasality of voice	08	05.92
v. Death	12	8.89

Out of 135 cases, 86 cases reported for follow up at regular interval. Out of those, 78 (90.70%) were found free of recurrence and eight cases presented with recurrence. Six cases developed palatal perforation without recurrence (Table VIII).

Table—VIII

Follow-up findings (n=86)

Findings	Number	%
No recurrence	78	90.70
Recurrence	08	9.30
Palatal perforation without recurrence	06	6.98

Discussion :

All the cases in this series were male, although the diseases has been reported in females also[2]. The age range was between eight and 26 years with predominance of second decade (80%) which coincides with the findings of Amin et al[1], Sharma et al[7] and Briant et al[8].

The triad of recurrent epistaxis (100%), nasal obstruction (90.37%) and nasal discharge (88%) was the most common combination of symptoms which agrees with the findings of Sharma et al[7]. Although facial swelling and proptosis are uncommon symptoms of JNA but many of these patients presented with those symptoms probably due to late presentation.

The commonest findings were nasopharyngeal mass (100%), nasal mass (94.81%), cheek swelling (23.70%), palatal swelling (22.22%) and proptosis (14.80%).

Regarding the site of origin, 130 (96.29%) cases had their origin from the nasopharynx and the adjacent part of the posterior choana and the rest five (3.70%) originated from the posterior part of the lateral nasal wall, a finding different from that of Amin et al[1] but nearly agrees with that of Sharma et al[7].

Majority (96.29%) had their extension into the nasal cavity later encroaching upon pterygopalatine fossa, infratemporal fossa, orbit, oropharynx and maxillary antrum. The incidence of extranasopharyngeal extension was much higher in this series than that of Sharma et al[7]. No case in this series had intracranial extension.

The treatment of choice of JNA is surgery[1,7] and all the cases in our series were treated surgically. Majority of the cases had transpalatal approach. Transpalatal approach was prefered because it gives wide exposure of the nasopharynx and can be extended as required for the removal of the extranasopharyngeal extension of the tumour. Extension into the temporal fossa was removed by giving separate incision into the temporal region. For a large lesion, combination of transpalatal and lateral rhinotomy incision was used. Infratemporal pterygomaxillary extensions were dealt with by transpalatal-sublabial approaches. Lateral rhinotomy incision was used only in five (3.70%) cases where the tumour was intranasal and arose from the posterior part of the lateral nasal wall. Surgical excision is the ideal method of treatment because of it's high cure and low recurrence rate. The reduction of haemorrhage is desirable during surgery, but difficult to achieve. To avoid excessive haemorrhage during surgery, ligation of the external carotids or their branches has been practised for a long time. So, external carotid ligation was done prior to surgery in 30 cases, but the result was very discouraging which agrees with Conley and Healey[9] and Ramanjaneyulu[10]. In our opinion, the source of bleeding in these lesions were from wide connecting veins and not from the arterioles of the nasopharyngeal mucosa supplied by the carotid system. Dibble and King[11] found rather the venous pterygoid plexuses responsible for bleeding. Carotid ligation is reported only in the older literature and was rarely found to be an efficient procedure[12].

Blood transfuion during the surgery of JNA is the commonest requirement, but the quantity varies from patient to patient and centre to centre also[1]. All of our patients required blood transfuion during surgery amount varying between 800 and 2,000 ml and majority of them required 1,000 to 1,200 ml of blood. Regarding complications of surgery, 15 (11.11%) patients developed

cardiac arrest of which 12 (8.89%) patients died during the post-operative period. Amongst the deceased, nine had extensive recurrent diseases and the rest three had large tumour with extranasopharyngeal extensions. The mortality rate in this series was higher than those of Amin et al[1] and Chatterji et al [13], who showed mortality rate of 5% and 2% respectively. The higher mortality rate in this series was probably due to extensive recurrent diseases, large tumour with extensions and severe anaemia due to recurrent epistaxis. Majority of the complications other than cardiac arrest and death were minor in nature and most of the patients became symptom free within few weeks.

Out of 135 cases, only 86 came for follow-up and most of them were free from recurrence. Only eight patients had recurrence and were treated successully with surgery.

It may thus be concluded from this study that an adolescent male presenting with the triad of epistaxis, nasal obstruction and nasal discharge should raise the suspicion of JNA; all extracranial JNA can be treated by surgery; transpalatal approach is recommended because it gives wide exposure of the nasopharynx and it can be extended as required and facial scar can be avoided; external carotid ligation during surgery does not give any benefit over cases without ligation; surgery should be the treatment of choice because it gives high cure rates, low recurrence, minimal chances of residual tumour and decreased length of hospital stay.

Acknowledgement:

We are indebted to the Director of Dhaka Medical Collegte Hospital for allowing us to publish this study. We are also grateful to the doctors of ENT department of this hospital for their active co-operation in preparing this paper.

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Nasopharyngeal Carcinoma—A Report of 62 Cases

PK GHOSH, M.Phil[a], M KAMAL, Ph.D[b], KMN ISLAM, M.Phil[c]

Summary :

Nasopharyngeal cacinoma (NPC) is the most common cancer of nasopharynx. In Bangladesh, this cancer is not uncommon. During the year 1991 and 1992, we have examined a total of 18,275 surgical pathology specimens. Among those, the number of nasopharyngeal biopsy samples were 338. Of these, 20 cases were diagnosed as NPC (5.9% of nasopharyngeal biopsies). Out of total 2,120 cases of lymphnode samples examined, 444 cases were diagnosed as metastatic carcinoma (20.9%) among which 42 cases were compatible with metastatic NPC (9.4% of metastatic carcinoma). The average age of patients with primary NPC was 46±3 years. On the other hand, the mean age of those of metastatic NPC was 15±2.2 years. Most of the patients were male. The tumour cells were undifferentiated and non-keratinizing having a similar appearance to those seen in other South-East Asian countries.

(J Bangladesh Coll Phys Surg 1995; 13: 95—98)

Introduction :

Nasopharyngeal carcinoma (NPC) is one of the important malignant tumours of the nasopharynx. It has a distinctive epidemiological pattern, showing an increased incidence among the Chinese and other South-East Asian people[1]. The highest incidence was reported from Southern China, Hongkong, South-East Asian Chinese and emigrant Chinese elsewhere[1]. It is not uncommon in African countries also[1].

In Bangladesh, the true incidence of NPC is unknown and often we tend to miss the diagnosis. In order to institute appropriate therapy it is very important to diagnose NPC in its early stage. Often it is very difficult to diagnose the disease as the primary tumour does not produce clinical manifestation unless it metastasizes to the lymphnodes[2,3,4]. This behaviour of the tumour is more common among the young people[4]. When lymphnodes are involved the diagnosis is possible from the lymphnode biopsy.

a. Dr. Paritosh K Ghosh, Assistant Professor, Pathology, Bangladesh Medical College, Dhaka
b. Dr. Mohammad Kamal, Associate Professor, Pathology, IPGMR, Dhaka
c. Prof. K M Nazrul Islam, Professor of Pathology (Rtd.), IPGMR, Dhaka
Correspondence to: Dr. Paritosh K Ghosh, Assistant Professor, Pathology, Bangladesh Medical College, Dhanmondi, Dhaka
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The present paper reports mostly the frequency of metastatic NPC in the lymphnode biopsy samples we examind during a period of two years.

Materials and method :

During the year 1991 and 1992 we have examined a total of 18,275 surgical pathology specimens in a private histopathological laboratory (The Laboratory, 39, New Elephant Road, Dhaka). From those specimens we have selected lymphnode and nasopharyngeal biopsy samples as study materials. The lymphnode specimens were examined to find out the numbers of metastatic NPC. From the nasopharyngeal specimens we have selected the cases of non-keratinizing poorly diferentiated or unifferentiated carcinomas.

The biopsy samples were processed for paraffin embedding and stained with Haematoxylin and Eosin (H and E). In addition to histological examination of the samples, clinical features of the patients including age and sex were also noted.

The diagnosis was made according to the following standard morphological criteria[5]. In case of primary tumour, the cells are undifferentiated and non-keratinizing. The cells have large vesicular nuclei and single prominent eosinophilic nucleoli. The cells are disposed in sheets and have a syncytial

appearance. Dense lymphocytic infiltration is present in the tumour. The histological appearance in the lymphnode metastasis is always indentical to the very characteristics of primary lesion[2]. In lymphnodes, the tumour cells are arranged in closely packed tight clusters or packets invading the lymphnodes[6].

Results :

During the year 1991 and 1992 the total number of samples sent for histopathological examination were 19,275. Among these, total number of lymphnode biopsy samples were 2,120 (11.6%). Out of those lymphonode samples, 444 cases (20.9%) were diagnosed as metastatic carcinoma among which 42 cases were suggestive of metastatic NPC (9.45%) (Fig.–1 and 2). Out of the total nasopharyngeal biopsies, 20 cases were diagnosed as undifferentiated carcinoma (5.91%) (Table–I). Among the total cases, three showed presence of primary undifferentiated carcinoma in the nasopharynx with metastasis in the cervical lymphnodes.

The age range of the patients suffering from primary NPC was from 37 to 55 years (mean age 46±3 years). Among those only two

Fig-1: *Sections of lymphnode showing metastatic nasopharyngeal carcinoma (H&E x 150).*

Fig-2: *Metastatic nasopharyngeal carcinoma in lymphnode (H&E x 350).*

Table—I

Distribution of NPC in nasopharynx and metastatic NPC in the lymphnodes

Sample	No. of cases	Neoplastic	Non-neoplastic	Metastatic carcinoma	Primary or metastatic NPC	% of NPC
Lymphnodes	2,120	1,042	1,078	444	42	9.45
Nasopharyngeal biopsy	338	248	90	00	20	5.91

Table—II

Age and sexwise ditribution of the patients with NPC

	Male	Female	Age range	Mean age ±SE
Metastatic NPC	42	0	12-21 years	15±2.2
Primary NPC	16	4	37-55 years	46±3

* SE (standard error)

were females (Table–II). On the contrary, metastatic NPC in the lymphnodes were found mostly among the young people. Their age varied from 12 to 21 years (mean age 15±2.2 years). All of the patients were male (Table—II).

Discussion :

Nasopharyngeal carcinoma is common in South–East Asian countries[7]. In Bangladesh, the incidence of this disease is not known. In our two years study we have diagnosed a total of twenty cases of primary NPC and 42 cases of metastatic NPC in the lymphnode biopsy samples. Among these two groups, three cases were found to present both primary NPC as well as metastasis in the cervical lymphnodes.

Most of the primary tumours were either poorly differentiated or undifferentiated. In the lymphnode samples, the metastatic NPC were also poorly differentiated. Both in the primary and in the metastatic group, the tumour cells were large with vesicular nuclei showing prominent nucleoli. These appearances support previous observations[6]. It is remarkable that young children are also common victims and present with cervical lymphadenopathy without having clinical manifestation in the primary site. We have diagnosed those cases only from the lymphnode biopsy samples (Fig.–1 and 2).

Our observation of metastatic NPC in cervical lymphnodes coroborate with previous observations[7], where subsequent biopsy from the fossa of Rosenmuller confirmed the existence of primary NPC.

The aetiology of NPC is not clear. A susceptible genetic constitution clearly plays an important role in the aetiology[8]. Marked variation in incidence of the disease has been noted among different ethnic groups in countries with multiracial population such as Singapore and Hawaii[8]. So racial influence is considered to be an important aetiological factor[1]. In undifferentiated NPC, irrespective of race or geographical location, Epstein Barr viral nuclear antigen is found in the genome of tumour cells[9]. Epstein Barr virus related antibodies are also noted in the serum of the patients of NPC[10].

Environmental factors, household smoke and cigarette smoking may play a role in the genesis of NPC. Consumption of salted fish has been suggested as an aetiological factor[11].

In this study we have observed that NPC is not uncommon in Bangladesh. In the younger patients the primary tumour remains asymptomatic in most of the cases but frequently metastasizes to the cervical lymphnodes and becomes the main presenting feature. Diagnosis has to be confirmed by lymphnode biopsy. It is more common among the males. It has a bimodal age distribution showing its presence below 16 years and also around fourth decade[8].

We have diagnosed the cases by examining the H and E stained slides only from the morphological appearance of tumour cells. This two year study reports that the NPC is not uncommon in Bangladesh. The histological appearance of the tumour and the biological behaviour regarding metastasis are essentially similar to that of other South–East Asian countries.

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Analysis of HLA-DRB1 in Vogt–Koyanagi-Harada's Disease

SMM ISLAM, MBBS[a], Y KONNO, MD[a], J NUMAGA, MD[a], Y FUJINO, MD[a], R HIRATA, MD[b], K MATSUKI, MD[b], H MAEDA, MD[b], K MASUDA, MD[a]

Summary:

Vogt-Koyanagi-Harada's disease (VKH) is an autoimmune disorder of melanocyte containing tissues. The disease has a strong relationship with HLA-DR4, a specificity originally determined by serology comprising at least 12 different genotypes. Since it is not well established which genotype is associated with VKH, we analyzed the HLA-DR of Japanese patients with VKH serologically and by the techniques of molecular biology. Ninety three percent of the patients had HLA-DR4. The frequency of DRB1 * 0405 was 76% among the patients and was only 27% among the controls ($Pc<9.7 \times 10^{-10}$). When we considered only the DR4 positive subjects, the frequencies were 78% and 63% in the patients and in the controls respectively. This difference was not statistically signifiant. Our data confirms the previous observation that VKH is associated with HLA-DR4, but does not support the hypothesis that certain DR4 genotype(s) is preferentially associated with VKH.

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Introduction :

Vogt-Koyanagi-Harada's disease (VKH) is a systemic disorder causing a bilateral diffuse granulomatous uveitis associated with vitiligo, poliosis, tinnitus, dysacousis and meningeal symptoms[1,2]. The disease is characterized by an acute inflammation and eventual depigmentation of the melanocyte containing tissues and is especially prevalent among the pigmented races[3]. Though the exact cause of the disease is not certain, it is suggested that some autoimmune mechanisms may play roles in the pathogenesis of the disease[4].

One of the important features of the disease is its strong relationship with HLA-DR4,[5-7] a specificity originally determined by serology. HLA–DR4 is subdivided into 12 different genotypes till to date[8]. We investigated the HLA of Japanese patients with VKH upto the genetic level to demonstrate whether any specific genotype is particularly responsible for the pathogenesis of the disease.

a. SM Monowarul Islam, Yasuhiro Konno, Jero Numaga, Yujiro Fujino, Kanjiro Masuda, Department of Ophthalmology, University of Tokyo School of Medicine, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113, Japan
b. Ranko Hirata, Kazumasa Matsuki, Hiroo Maeda, Blood Transfusion Service, Saitama Medical Center, Saitama Medical School, 1981 Kamoda, Kawagoe, Saitama 350, Japan
Correspondence : SM Monowarul Islam, Department of Ophthalmology, University of Tokyo School of Medicine, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113, Japan
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Materials and method :

Fifty four (26 male and 28 female) Japanese patients with VKH were randomly selected for this study while 461 apparently healthy Japanese blood donors served as controls. All patients underwent complete ophthalmological and related examinations and the diagnosis was made according to the criteria proposed by Sugiura et al.[9]

Of 54 patients, we have typed 42 serologically, 51 at the DNA level and 39 by both methods, and of 461 serologically typed controls we typed the DNA of 218 subjects.

HLA analysis :

Serological typing was done by standard complement dependent microcytotoxicity method[10].

Genomic DNA was extracted from the peripheral white blood cells by the previously described method[6]. After extraction, DNA was subjected to group specific polymerase chain reaction (PCR) amplification. The primers used for DR4 specific amplification were DR4-AMPA (5'- GTTTCTTGGAGCAGGTTAAAC) and DR4-AMPB (5'–CCGCTGCACTGTGAAGCTCT), which were used at the Eleventh International Histocompatibility Workshop. PCR was carried

out at 94°C 30 sec, 61°C 30 sec and 74°C 45 sec for 30 cycles with DNA Thermal Cycler (Perkin Elmer). After PCR single strand conformation, polymorphism (SSCP) analysis was performed according to Orita et al[11] with modification: 2μl of PCR product was mixed with 14μl loading buffer (95% formamide, 20 mM EDTA/ pH 8.0, 0.05% bromphenol blue, 0.05% xylene cyanol) and heated-denatured at 95°C for five minutes. An aliquot of this mixture (3 μl per lane) was run in a 8% polyacrylamide gel (acrylamide: bis=49 : 1 with 5% glycerol) for 3.5 to four hours at 30 mAmp constant current and at a controlled temperature of 30°C in 45 mM Tris/pH 7.6, 45 mM boric acid, 1 mM EDTA (0.5x TBE). The gel was stained with the silver staining kit (Bio-Rad) after electrophoresis. When necessary, PCR-restriction fragment length polymorphism (RFLP)[12] was employed in addition to the SSCP analysis to confirm the HLA—DNA typing.

Statistical analysis:

Fisher's exact test or *chi-square* analysis was done to compare parameters between patients and controls. *P* values were corrected for multiple comparisons.

Results:

As for class I antigens, only the increased frequency of HLA-B54 antigen was significant (38.0%) in the patients as compared to 16.3% in the controls (corrected P (Pc)<0.01). As for class II antigens, we observed a significant increase in DR53, HLA-DR4, and DQ4 frequencies, and a significant decrease in HLA-DR13, DR52, DQ1 and DQ3 frequencies (Table-I). Relative risk was highest for DR53 (25.6) followed by DR4 (16.5) and DQ4 (3.8).

At the genomic level, the frequency of DRB1*0405 was significantly greater in 51 DNA-typed patients than in DNA controls (76% in the patients as cmpared to 27% in the controls; $P<1.0 \times 10^{-10}$) (Table-II). No deviation in any other genotype was observed. Relative risk for DRB1*0405 was 8.9.

Table-I

The frequencies of HLA antigens

Antigen	Patients		Controls		Relative
	N	%	N	%	Risk
	(n=42)		(n=461)		
B54	16	38.0	75	16.3*	
	(n=54)		(n=461)		
DR1	5	9.0	40	8.7	
DR2	13	23.0	158	34.3	
DR3	0		1	0.2	
DR4	50	92.5	199	43.2	16.5‡
DR7	0		4	0.9	
DR8	6	11.0	110	23.9	
DR9	9	16.0	132	28.6	
DR10	0		5	1.1	
DR11	0		13	2.8	
DR12	2	4.0	40	8.7	
DR13	0		79	17.1	
DR14	5	9.0	67	14.5	
DR52	7	12.0	186	40.3	0.2§
DR53	53	98.0	311	67.5	25.6§
DQ1	4	7.0	330	71.6	0.0‡
DQ2	0		5	1.1	
DQ3	15	27.0	276	59.9	0.2§
DQ4	36	64.0	148	32.1	3.8§
DQ7	3	5.0	84	18.2	

*Pc < 0.01, §Pc< 0.001, ‡Pc< 1.0×10^{-10}; Pc : Corrected P.

Discussion:

The increased frequency of HLA-B54 can be explained by the linkage disequilibrium between HLA-B54 and DR4 antigens in Japanese population. The DR53 frequency was the highest among the patients with the highest relative risk of 25.6. Though the relative risk was highest for DR53, it is unlikely that DR53 itself primarily confers the susceptibility

Table–II

The frequencies of HLA–DRB1 genotypes

Genotype	Total				DR4-Positives			
	Patients		Controls		Patients		Controls	
DRB1*	N=54		N=218		N=50		N=94	
	N	%	N	%	N	%	N	%
0401	0		4	2	0		4	4
0403	4	7	13	6	4	8	13	14
0404	0		1	0.5	0		1	1
0405	39‡	76	59	27	39	78	59	63
0406	5	9	11	5	5	10	11	5
0407	0		5	2	0		5	5
0410	4	7	10	5	4	8	10	11

Relative risk 8.9; ‡ $Pc < 1.0 \times 10^{-10}$

to VKH. DR53 and three other DR locus antigens (DR4, DR7 and DR9) are known to be correlated very tightly but in VKH patients the frequencies of DR7 and DR9 were not increased. The high association of DR53 with VKH is atributable to a linkage disequilibrium between DR 4 and DR53. This is similar to the previous observation[5-7]. Deviations in the DQ specificities need further investigation that is now being on progress.

At the genetic level, the frequency of DRB1*0405 was significantly higher in 51 DNA–typed patients than in DNA controls (76% as compared to 27% in the controls, $Pc< 1.0x10^{-10}$). Relative risk for DRB1*0405 was 8.9, definitely much lower than that of DR4.

The greater frequency of DRB1* 0405 was observed among the patients when all the patients and all the controls were considered in general. When only the DR4 positive subjects were considered both in the patients and in the controls, still the frequency of *0405 was slightly higher (78% in the patients as compared to 63% among the DR4–positive controls). This increase was insignificant on statistical analysis. The other genotypes did not show any deviation among the patients. These indicate that HLA-DR4 is the primary antigen for the disease development but do not support the hypothesis that a certain DR4 genotype(s) is preferentially associated with VKH.

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Acute Glomerulonephritis in Children : Clinical Profile and Immediate Prognosis—A Study of 100 Cases

M N ABSAR, FCPS[a], M A H SHEIKH, DCH[b]

Summary :

One hundred cases of acute glomerulonephritis (AGN) in children under 12 years of age were studied. Mean age of the subjects (±SD) was 8.22 ±2.07 years. Male female ratio was 1:1.08. Scanty urine (98%), puffy face (72%), hypertension (55%), swelling of whole body (31%), nacked eye haematuria (28%), heart failure (28%), convulsion (7%) and anuria (2%) were the presenting features. Albuminuria was present in 95% of cases, of which 58% had mild, 29% moderate and 8% severe albuminuria. Fifty four percent of both complicated and uncomplicated patients were discharged from the hospital with full recovery within 10 days of admission. One patient died of hypertension and heart failure. One patient showed persistent hypertension even after three weeks of treatment. History of skin infection was present in 56% of the cases and 33% patients had active scabies at the time of presentation. Two had the history of mumps. It was observed that skin infection was the commonest cause of acute glomerulonephritis. Nephritic presentation (scanty urine, oedema, haematuria, hypertension and heart failure) was the commonest mode of presentation. Immediate prognosis was excellent. Long term follow-up is recommended.

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Introduction :

Acute glomerulonephritis (AGN) is a disease of multiple aetiology. Streptococcal infection is by far the commonest cause of the disease[1,2,3]. Other possible causes are staphylococceus aureus, pneumococcus, mumps and hepatitis-B virus infection. Acute post-streptococcal glomerulonephritis is the prototype disease of acute glomerulonephritis[4]. Post-streptococcal glomerulonephritis is principally a disease of the children[5]. Skin infection and scabies are very common in Bangladesh[6,7]. Skin infection is the main source of streptococcal infection and many of them subsequently develop AGN especially in developing countries[1,2,8,9]. Throat infection by streptococcus also plays an important role in the pathogenesis of acute glomerulonephritis[1,2].

AGN causes acute reduction of urine output and occasionally complicated by hypertension, heartfailure and acute renal failure (ARF). The duration of oliguria may be variable[1,10,11]. But short term prognosis has been described to be good even if there is anuria, hypertension or heart failure[1,2]. However, AGN may present with no symptom at all (asymtomatic AGN) and some patients (both children and adult) may go into chronicity[10,12].

This study was conducted to see the aetiological relationship, possible presentations and immediate outcome of AGN in children. No long–term follow-up was done.

Materials and method :

This study was done in Khulna hospital during the period of January '91 to January '92. All patients admitted with AGN, with or without complications, were included in this study. Diagnostic criteria were scanty urine (infrequent and less than normal in amount as stated by the parents), swelling of the face (or whole body starting form face), high coloured urine with or without albuminuria, no past history of similar attack (recurrence) and microscopic or nacked eye haematuria. Blood urea, creatinine, urine total protein, ASO, anti–DNaseB and C_3 estimation could not be done. Eight patients with massive

a. Md. Nurul Absar, Assistant Professor, Paediatrics, Institute of Postgraduate Medicine and Research (IPGMR), Dhaka
b. M A Hamid Sheikh, Assistant Professor, Paediatrics, Sher–E–Bangla Medical College and Hospital, Barisal
Correspondence to : Dr. Md. Nurul Absar, Asstt. Professor Paediatrics, IPGMR, Dhaka
Received : October 9, 1994, Accepted : May 16, 1995

albuminuria who were treated as AGN and became symptom free with disappearence of albuminuria spontaneously were also included in this study.

Treatment schedule was Inj. Procain penicillin 4 lac unit im daily for 10 days, salt and proteint free diet till the onset of diuresis, and potassium free diet until diuresis started. Fluid requirement was calculated according to obligatory loss (400 ml/sq meter body surface area) which was added with previous day's output. Intake-output chart was strictly maintained so that no fluid overload could occur.

Patients with heart failure were treated with diuretic (frusemide) and digitalis. All hypertensive patients were given methyledopa. Those with hypertensive encephalopathy were given nifidipine in addition, and frusemide. Diazepam was given to those who had seizure. Hypertension was defined as a diastolic pressure more than 80 mm Hg.

Criteria of discharge from the hospital were absence of puffyness and oedema, adequate urine formation, completion of penicillin course and absence of heart failure and hypertensive encephalopathy. These together were taken as clinical recovery. No long term follow-up was done.

Results :

Age range of studied children was two to 12 years with a mean of 8.22±2.07 years. More were in higher age groups (Table-I). The modal age group was between eight and 11 years. Male to female ratio was 1:1.08. Incidence of AGN was found to be more in children coming from urban areas than rural areas. Seventy patients were from urban areas and rest from rural areas. Presenting features are shown in Table-II. Ninety eight percent patients presented with scanty urine. Two patients presented with 24 hours anuria. The duration of hospital stay in simple cases and those complicated with either hypertension or heart failure or both is shown in Table - III.

Table–I

Age and sexwise distribution of patients (N=100)

Age in years	Male	Female	Total
02-05	05	08	13(13%)
05-08	12	13	25(25%)
08-11	21	21	42(42%)
11-12	10	10	20(20%)
Total	48(48%)	52(52%)	100(100%)

Mean age in years	8.22±2.07
Lowest age	2 years
Age range	2 to 12 years.

Table–II

Presenting features at the time of admission (n=100)

Presenting features	No. of patients
Scanty Urine	98 (98%)
Puffy face	72 (72%)
Hypertension	55(55%)
Swelling of whole body	31(31%)
Macroscopic haematuria (dark urine)	28(28%)
Heart failure	28(28%)
Fever	16(16%)
Convulsion	7(7%)
Headache	3(3%)
Loss of visual acuity	2(2%)
Anuria (24 hours)	2(2%)
Associated conditions:	
H/O recent skin infection	56(56%)
Scabies	33(33%)
H/O mumps in preceding days	2(2%)
Albuminuria :	
Mild (+)	58(58%)
Moderate (++)	29(29%)
Severe (+++)	8(8%)
Nil	5(5%)

It has been observed that heart failure responded promptly to treatment. Two patients with 24 hours anuria responded well with usual conservative management.

Table–III

*Duration of hospital stay in days (N=99)**

Days	No. of patients	
	Simple	Complicated **
10	23	31
10-14	08	09
>14	06	22

* One patient died.

** Complicated with hypertension and / or heart failue.

Despite adequate diuresis hypertension was persistent in a good number of patients even after adequate doses of antihypertensives. One patient had persistent hypertension even after two weeks of treatment. This patient was given methyldopa and nifidipine without appreciable effect.

Hypertensive encephalopathy was not directly related to the severity of hypertension. In some patients it was noted only with diastolic blood pressure around 90 mm of Hg, while in others even at 120 mm of Hg diasftolic pressure no encephalopathy developed. All patients except one recovered well clinically. One patient who had hypertension and heart failure died.

Discussion :

It was observed in this country that AGN was a common disease in the paediatric admissions[13]. Similar trend was also observed during the study period. In a 20 bed capacity paediatric unit 100 patients were treated in one year time. According to Leung et al, post-streptococcal glomerulonephritis is not an uncommon problem of developing countries[8]. So, it can be concluded that AGN is a common kidney problem in children in Bangladesh. It is well known that AGN is uncommon below the age of three years[1,4]. The lowest age in our series was two years. In different studies in Bangladesh lowest age of AGN in children was reported to be between two and three years[2,6,13].

The mean age in our series (8.22±2.07 yrs) is consistant with the study of Rashid et al[2]. Increasing number of patients were observed in five to 12 years age group in our series which contradicts the observation of Nahar and Salim[13]. They have noted highest incidence among under six children. But our observation correlates well with that of Islam et al[6]. We did not get any significant difference in sex incidence. But in other studies a male-female ratio of 2:1 was noted. It is however well recognized that for reasons unknown, the prevalence of AGN is more in male children[2,4,6,13]. Our study revealed that more patients were coming form urban areas than from rural areas. Nahar and Salim has reported more patients from rural areas[13]. Different studies have shown that streptococcal infection is one of the most important causes of AGN in children in Bangladesh and part of South–East Asia[8,9]. Moreover, AGN is known to be influenced by socio-economic and environmental factors and common in communities of low socioeconomic status with poor hygienic condition and crowded home[2,4,13]. So, urban slum might be a very ideal place for streptococcal infection and AGN. Our study children were mostly form urban areas (mostly urban slum), because the study place was an urban hospital and the attendence of rural people in general was less in the hospital, may be due to distance.

Skin infection and scabies were found to be the commonest cause in our study children. In Bangladesh and in other parts of the world, post-streptococcal glomerulonephritis has been recognized as the commonest cause of AGN[2,3,4,6,13,14,15]. Rashid et al has shown that

post-streptococcal AGN presents with nephritic illness characterized by puffy face, scanty urine, with or without ankle oedma and hypertension in 96.07% cases. Our study findings are also comparable with this study and the studies of Nahar et al and Islam et al as well[2,6,13]. Other findings like, generalized oedema, macroscopic haematuria and varying degrees of proteinuria are comparable with other studies [1,2,4,6,13,16]. We have seen 8% patients presenting with massive proteinuria. In the study of Nahar et al and Rashid et al massive proteinuria was present in 3% and 28% cases respectively. In general 10% cases of AGN shows nephrotic range of proteinuria[2,4,6,13,16].

Hypertension, heart failure, encephalopathy and ARF were found to be the immediate complications. These are the recognized complications of AGN[1,4]. We had 55% patients with hypertension, and encephalopathy was present in 7% cases. Rashid et al observed hypertension in about 35% cases while Nahar et al in 96% cases and Islam et al in 26% cases. So the observed incidence of hypertension in AGN in children in our country varies from 26% to 96%[2,6,13]. Leung et al has suggested that irrespective of age 80% AGN patients may have elevated BP[8].

Mortality rate in childhood AGN has been reported to be 1% in acute stage[4]. We had similar finding but in Nahar's study it was 13.33%[13].

Period of recovery (hospital stay) varies from seven days to three weeks in different studies in Bangladesh. In our series, 54% patients recovered completely clinically within 10 days of admission. In Islam's series 96% recovered within 10 days and in Nahar's series 80% recovered within 10 days. Maximum duration for recovery was two weeks in Nahar's series and three weeks in Islam's series[6,13]. In our study 28 patients had to stay in hospital for more than two weeks and were having persistent hypertension during this period despite adequate diuresis. However, within three weeks their blood pressure returned to normal. One patient had persistent hypertension even after three weeks treatment. So, it is obvious that overall immediate prognosis of AGN in children is excellent. But all patients of AGN should have long term follow-up. It has been observed that in both symptomatic and asymptomatic post-streptococcal AGN some patients go into chronicity, even to end stage renal failure[10,12] Rashid et al in their two years follow-up study of children patients of post-streptococcal AGN in Bangladesh observed that 7.18% cases showed deterioration of renal function[2].

In conclusion, it can be presumed that though mostly recoverable, AGN in children should not be taken as a benign condition. Timely and proper intervention is necessary and long term follow-up should be done in every patient. Measures should also be taken to prevent skin infection and scabies in the community. Becauses once infection with strepto-beta-haemolyticus occurs, treatment of infection does not decrease the chance of AGN[1].

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Effect of Indomethacin on Induction and Growth of Rat Mammary Tumours

A ROUF[a], B ISLAM[b], BR KHAN[c], KMN ISLAM[d]

Summary :

Female virgin 58 day old Sprague Dawley rats were treated intragastrically with a single dose of 20 mg of 7,12 - dimethylbenz (a) anthreacene (DMBA) dissolved in one ml of seasame oil. Soon after carcinogen treatment, one group of rats were put on to indomethacin (IND) supplemented drinking water with a concentration of 20 mg/litre continuously for a period of eight weeks. Another group of DMBA treated rats were supplied with plain tap water for the same duration. Rats receiving IND showed delay in the appearance of mammary tumour, lower tumour incidence and significant reduction in tumour multiplicity and its mean diameter/ weight in comparison to those in control rats. Tomour suppressive effect of IND was also investigated by putting rats onto IND supplemented drinking water eight weeks after DMBA treatment. At the end of twelfth week, rats receiving IND for the last four weeks showed a significant reduction in tumour multiplicity and mean tumour diameter/ weight compared to those of the rats who did not receive IND.

It was concluded that IND has a significant protective and suppressive activity on DMBA induced mammary carcinogenesis in Sprague Dawley rats.

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Introduction:

Enzymatic oxidation of arachidonic acid (AA) leads to a multitude of biochemically important products. Among these are prostaglandins (PG), thromboxane, prostacyclin and leukotrienes (LT). These substances, referred to collectively as eicosanoids, constitute what has become known as the arachidonic acid cascade. There is mounting evidence in experimental systems that the products of AA cascade are involved in mechanism for initiation and promotion of tumours [1,2,3]. Tumour tissue, both naturally occuring as well as experimentally induced, contains a high level of prostaglandins[4,5].

On the basis of these findings, researchers have investigated the effect of blockade of AA cascade on experimentally induced colonic and hepatic tumours by chemical carcinogens[5,6,7,8] and influence of dietary fat and indomethacin (IND) on the growth of transplantable mammary tumours in rats[9].

IND is a nonsteroidal anti-inflammatory drug. The primary pharmacological activity of IND is to inhibit cycloxygenase pathway of arachidonic acid cascade, i.e. PG synthesis and also of immune functions [6,10].

Experimentally induced tumours are a major way of studying the different aspect of tumour, like initiation, growth, progress and the role of drug in the prevention of induction and growth. Taking all the above information in account, the present study was designed to evaluate anti-tumour effect of IND on induction and growth of experimentally induced mammary tumours in rats.

Materials and method:

Animals : a total of 60 Sprague Dawley female rats of 50 days age and having an average weight of 250 gm were used in the experiment.

Chemicals : a) 7,12 Dimethylbenz (a) anthreacene (DMBA), b) indomethacin (IND),

a. Dr. Abdur Rouf, Asstt. Professor, Department of Pathology and Microbiology, Dhaka Dental College, Dhaka
b. Dr. Badrul Islam, Associate Professor, Department of Pathology, IPGMR, Dhaka
c. Dr. B R Khan, Professor and Head, Department of Pathology, IPGMR, Dhaka
d. Dr. KMN Islam, Retd. Professor of Pathology, IPGMR, Dhaka
Correspondence to : Dr. Abdur Rouf, Asstt. Professor, Department of Pathology and Microbiology, Dhaka Dental College, Dhaka
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c) sesame oil and d) absolute ethanol.

DMBA, the chemical carcinogen (sigma) administered orally as single dose of 20 mg/rat dissolved in 1 ml of sesame oil.

IND was dissolved in ebsolute ethanol at a concentration of 10 mg/ml. Of this solution, 2 ml was added to one litre of tap water to reach a final concentration of 20 mg/L.

Fresh IND was provided three times a week in light protected bottle and the rats consumed about 3 mg of IND /Kg /day.

The animals were separated into five groups and kept in different cages at room temperature in 12 hours light / 12 hours dark cycle. The rats were weighed weekly and given basal laboratory diet.

Table–I

Groups and number of rats with treatment protocol

Groups Number	DMBA in seasame oil	DMBA and IND	Seasame oil (vehicle of DMBA)	Ethanol (vehicle of IND)
Group A (n=26)	+	-	-	-
Group B (n=16)	-	+	-	-
Group C (n=6)	-	-	+	-
Group D (n=6)	-	-	-	+
Group E (n=6)	(untreated control) received basal laboratory diet and plain tap water			

The rats were grouped as follows:

Group A, chemical carcinogen treated rats.

Group B, rats treated with chemical carcinogen but concomitently with IND in drinking water.

Group C, received seasame oil, the vehicle of DMBA, to see whether the vehicle itself can produce any pathological effect.

Group D, received ethanol in drinking water at a concentration of 2 ml per liter (same as present in IND solution) to exclude any effect produced by ethanol.

Group E, untreated control, fed normal laboratory diet and plain tap water, served as a normal control of this experiment.

The animals in all groups were palpated carefully for tumour bi-weekly. During the first eight weeks of experiment, palpable tumours in all DMBA treated and DMBA+IND treated rats were compared to assess the preventive role of IND in tumour induction.

During 8-12 weeks of experiment, to note the role of IND after the formation of tumour, the rats of DMBA treated group (Group-A) having palpable tumours were divided into two groups (Table–II) and treated as follows:

Table–II

Showing eight to 12 weeks treatment schedule

Group	Number	Treatment
A_1	10	No treatment
A_2	10	IND

Group A_2 received IND with drinking water to see whether IND could influence the growth of tumour when it would have already formed.

Group A_1 received no treatment and served as a control of group A_2.

All animals were examined weekly to see the appearance of new tumour, disappearance or regression of previous tumours or continued growth of the tumours in different groups and ultimately establishing the role of IND in tumourogenesis.

Sacrifice schedule : At the end of eighth weeks of experiment, six rats randomly selected from group-A and all the rats of

group-B were sacrificed. At autopsy, tumours from each rat were resected. At the end of twelfth week of study, all animals were sacrificed and resected tumours were processed for histological examination. Liver, spleen, kidney and stomach were also examined.

Results :

During the first eight weeks of experiment, palpable mammary tumour nodule first appeared at 21 days after DMBA administration in three rats of group-A (DMBA treated). Majority of the rats of group-A developed palpable tumour nodule by the end of the fifth wek. At the end of eight weeks all rats of group-A (100%) had one or more easily palpable tumour nodules. In group-B rats (DMBA and subsequently IND in drinking water), first palpable tumour nodule was found at the end of 45 days in two rats. At the end of eight weeks, seven of the 16 rats (43.75%) of group-B had tumour nodule (Table-III).

Table–III

Tumourogenesis during the first eight weeks of experiment

Group	No. of animals	Appearance of first tumour	Animals with tumour at the end of eighth week	Incidence of tumour at the end eighth week
A	26	21 days	26/26	100%
B	16	45 days	7/16	43.75%

At autopsy at the end of eighth week, a total of 11 tumour nodules of various sizes were resected from six rats of group-A. From 16 rats of group-B, a total of seven tumour nodules were excised. No mammary tumour nodule was found in nine rats of group-B on meticulous gross examination of mammary areas.

It was observed that the time for the appearance of first tumour and development of subsequent tumours (tumour latency period) in group-B rats (IND treated) were markedly delayed than that of group-A rats. Continuous post-carcinogen administration of IND in drinking water to the group-B rats significantly ($p<0.001$) inhibited the incidence of tumour in this group at the end of eighth week. Indomethacin administration to group-B rats significantly ($P<0.001$) inhibited tumour multiplicity (number of tumours/ rat) in comparison to group-A rats. Mean diameter of the tumours of group-B rats was significantly ($p<0.001$) lower in comparison to group-A rats which was also reflected by tumour weight (Table–IV).

Table–IV

Morphological comparison of the tumours resected from six rats of group-A and all rats of group-B at the end of eighth week of experiment

Group	No of Animals	Total no. resected tumours	Cancer per rat	Tumour size in diameter mean (cm)±SD	Tumour weight mean (gm)±SD
A	6	11	1.83	0.87±34	1.00±35
B	16	7	<1	0.42±22	0.52±23

During the second part of the experiment, progressive growth of the existing tumours were noticed in all rats of group-A_1. All the rats of group A_1 developed two or more new tumour nodules during this period. At the end of twelfth week the previous tumours were markedly enlarged. On the other hand, the growth rate of most of the existing tumours were substantially slowed in group-A_2 rats (IND treated). Seven rats were found to have developed new tumour nodules (one in each rat). The growth of the new tumour nodules was also markedly slow in comparison to new tumour nodules of group A_1.

At the end of twelfth week, all the rats of five groups were sacrificed. At autopsy, all tumours of group-A_1 and group-A_2 were excised and kept separately. From group-A_1 rats a total of 44 tumours were resected. Twenty eight tumours were resected from the 10 rats of group-A_2 (Table–V).

Table–V

Morphological analysis of the tumours at the end of twelfth week

Group	No. of Rats	Total no. resected tumours	Cancer per rat	Tumour size in diameter mean (cm)±SD	Tumour weight mean (gm)±SD
A_1	10	44	4.4	1.34±46	1.95±1.60
A_2	10	26	2.6	0.98±47	1.21±1.05
C	6	0	0	-	-
D	6	0	0	-	-
E	6	0	0	-	-

In group C, D and E no tumour nodule or any other symptoms of illness were found.

Tumour nodules were fixed in 10% formalin and subsequently processed for parraffin embedding. H and E stained sections of each tumour were examined. All were histologically confirmed as mammary carcinoma.

Stomach particularly of IND treated rats, were examined grossly. No ulceration was seen. All other internal viscera of each rat of all groups were examined. No gross abnormality or pathological change was observed.

It was observed that continuous administration of IND in drinking water to group-A_2 rats beginning from the end of eighth week significantly ($p<0.01$) inhibited the tumour multiplicity (tumour per rat) in comparison to group-A_1 rats (not receiving IND) at the end of twelfth week (Table–V). Mean tumour diameter of the tumours resected from group-A_2 rats was significantly ($p<0.01$) lower than that of tumours of group-A_1 rats, which was also reflected by tumour weight.

Discussion:

The anti-tumour activity of IND in both early as well as late stage of rat mammary carcinogenesis suggests a variety of possible mechanisms. Many researchers showed the direct evidence that application of 12-0-tetradecanoylphorbol-13-acetate (TPA), a tumour promoter to mouse skin *in vivo* resulted in a pronounced increase in the prostaglandin content (mainly of PGE_2) after 60 minutes of application[11,12,13]. The increase in epidermal prostaglandin E content was dependent on the dose of TPA and was associated with induction of epidermal ornithine decarboxylase (ODC) activity, a functional change essential for skin tumour promotion[12]. So, the result suggests that early increase in epidermal prostaglandin E is an obligatory event in the course of induction of epidermal cell proliferation by TPA[12]. Pretreatment of mouse skin with prostaglandin synthesis inhibitor IND prevents the accumulation of prostaglandin E and subsequent cellular proliferation induced by TPA[12]. Prostaglandin E_2 and F_{2a} and prostaglandin synthetase activities have been reported to be higher in experimentally induced mammary carcinoma than in nonneoplastic rat mammae[14]. Hence, IND may inhibit the DMBA induced mammary carcinogesis in a similar way, i.e. by inhibiting prostaglandin synthesis and prevention of induction of ornithine decarboxylase.

Ornithine decarboxylase catalyses the decarboxylation of ornithine to form putrescine, a key enzyme in the biosynthesis of polyamines. Accumulation of the polyamines appears essential for noplastic growth[15]. Very recently, by a specific inhibitor of orithine decarboxylase namely DL-2–difluoromethy-lornithine (DFMO) has also been found to have significant inhibitory effect on experimentally induced rat mammary carcinogenesis[16] which strongly supports earlier observations[12,13].

IND has been claimed to possess a number of immunopotentiating activities as well. These include enhancement of natural and antibody dependent cell mediated cytotoxicity [16,17] and also the modulation of suppressor cell activity[18,19]. Biological response modifier (such as bacillus Calmette–Guerin) is known to have a significant activity as inhibitors of experimentally induced mammary carcinogenesis in rats[20], suggesting that modulation of immune response can be a mechanism through which tumour iduction/ growth may be suppressed.

Some earlier postulations[1,21] stated that immunodepression described in some cancer patients as well as in experimental animals results from the influence of high level of prostaglandins on the immune system. It can therefore be speculated that the inhibition of prostaglanding production by IND may be associated with restoration of depressed immune system to healthy functional state or it may enhance immune response expression followed by tumour growth inhibition.

There are also many reports that IND reversibly inhibited cell proliferation in a variety of mammalian tissue *in vitro*[22,28,24]. So inhibition of cell proliferation may be an important mechanism of prevention of tumour induction and growth.

To sum up, data from the present study indicate that IND has significant activity against the early stage as well as late stage of experimentally induced mammary carcinogenesis.

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REVIEW ARTICLE (J Bangladesh Coll Phys Surg 1995; 13: 114–122)

Subependymal/Intraventricular Haemorrhage in the Neonates : A Review

ASM IQBAL, FCPS

Introduction :

Perinatal stress like birth asphyxia, hypotension or trauma can result in a spectrum of cerebral injury outcome of which may depend on type and degree of insult, gestational age and any other underlying factor. The problem is important both because of its incidence as well as later sequelae like handicap.

Kowitz in 1974[1] was the first to report on intraventricular haemorrhage (IVH) in new born. Since then advances in imaging technique like CT scan providing more *in vivo* information[2] and real time ultrasound had made the investigation convenient and safe[3]. Dramatic improvement in neonatal care has resulted in survival of more preterm newborn with resultant increase in intracranial incidence to an epidemic level[4]. Portable ultrasonogram has helped in serial examination and early diagnosis[5] without causing any harm[6].

In the following discussion, a brief review of grading system, pathogenesis, risk factors, clinical features, diagnosis, prevention and outcome of subependymal / Intraventricular haemorrhage (SEH / IVH) will be presented.

Grading of subependymal/ intraventricular haemorrhage : Two major groups of lesions are recognised–SEH/IVH complex and periventricular leukomalacia (PVL) :

Subependymal/intracranial haemorrhage: There are different grading systems of IVH. Papile et al[7] has classified the IVH into four grades :

Grade I : Isolated germinal matrix haemorrhage.

Grade II : IVH with normal ventricular size.

Grade III : IVH with ventricular dilatation.

Grade IV : IVH with parenchymal haemorrhage.

The reported incidence of SEH/ IVH in preterm infants is ranged from 32%[8] to 90%[9]. Mortality is clearly higher in infants with SEH/ IVH than in neonates without haemorrhage matched for birth weight or gestational age[9,10]. Although the long-term neurodevelopmental outcome in those infants with lesser grades of SEH/ IVH remains unresolved, most oberservers agree that the more severe grades of IVH are associated with a higher incidence of neurodevelopmental handicaps[7,11].

Periventricular leukomalacia :

The term periventricular leukomalacia (PVL) was originally coined by Banker and Larroche[12] to describe a specific but subtle macroscopic appearance of brain in infants dying after a complicated perinatal course. High resolution real time ultrasound enables a diagnosis of PVL to be made in the living infants[13,14]. Periventricular leukomalacia are non- haemorhagic lesions and characterised by coarse, triangular areas of increased echogenicity localised in the region of the periventricular white matter at the superolateral angle of the lateral ventricles[15].

Dr. ASM Iqbal, FCPS, Consultant, Paediatrics, Sadar Hospital, Feni, Bangladesh
Correspondence to : Dr. ASM Iqbal, Consultant, Paediatrics, Sadar Hospital, Feni, Bangladesh
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PVL may or may not be associated with SEH/IVH[16, 17]. Trounce et al [18] proposed that although the aetiology of PVL may be border zone infarction, more than one aetiological factors are probably involved. They recognised three forms of PVL :

a. *Pre-cystic:* An echodense triangle with its apex lying at the lateral border of the lateral ventricle. In many cases intraventricular clot accompanies this parenchymal appearance.

b. *Cystic :* In surviving infants, the precystic stage of echodensity resolves to discrete echo free cavities representing cyst formation. The cysts are small, and often multiple and separate from the lateral ventricles. The ependyma of the lateral ventricles remains intact in most cases.

c. *Prolonged flare:* An appearance of relative increased echodensity in the periventricular region persisting for two weeks or more but not undergoing cystic degeneration.

The reported incidence of PVL ranges from 7.5 to 26% of low birth weight population[13,18]. Unlike SEH/ IVH, which commonly appear on ultrasonograms within the first week, the cystic lesions of PVL are manifested more commonly after the first month[19] and the prognosis in babies who survive with extensive cystic lesions may be very poor[13,14].

Pathogenesis of subependymal/ intraventricular haemorrhage :

The primary lesion in IVH involves bleeding into the germinal layer beneath the ependyma of the lateral ventricle with subsequent rupture of the haematoma into the ventricular system[20,21,22]. SEH/IVH is attributable to the vulnerability of the germinal matrix to haemorrhage. The germinal matrix consists of masses of neuroblasts traversed by poorly supported very thin walled vascular channels. It is the site of proliferation of neuronal and glial precursors. The association of the lesion with prematurity relates to four major factors[23]: first, the subependymal germinal matrix, which provides poor support for the small vessels coursing through it, does not dissipate until term; second, a disproportionate amount of cerebral blood flow appears to be diverted to the periventricular region because of the particularly exuberant vascular supply to the matrix; third, the integrity of the periventricular capillary bed appears to be tenuous and fourth, vascular autoregulation, the process by which cerebral arterioles constrict or dilate to maintain constant cerebral blood flow despite change in perfusion pressure, is impaired in the human newborn. Intraventricular haemorrhage can also occur in full term neonates [24] and it is usually from the choroid plexus [25].

The pathological distinction between uncomplicated SEH/ IVH and PVL is usually clear though the later may also be haemorrhagic[12]. PVL is generally considered to be a form of hypoxic ischaemic encephalopathy peculiar to the neonate, the anatomical distribution of the lesions coinciding with the functional zone between ventriculopetal and ventriculofugal components of the arterial circulation within the cerebral hemisphere[26]. Hypoxic ischaemia of the periventricular white matter leads to cellular swelling, oedema, necrosis and liquefaction. Secondary haemorrhage may occur into the necrotic tissue[27]. The precystic phase of PVL is a characteristic triangular echodense region in the parenchyma that precedes cystic degeneration. This is seen in those infants who die before the development of cysts[18]. The end stage of PVL is either focal gliosis with or without calcification when the initial lesions are small or periventricular cysts when they are more extensive, and cystic lesions are manifested more commonly after two weeks of life[18,19].

Risk factors associated with subependymal/ intraventricular haemorrhage:

Although the aetiology of SEH/ IVH in the neonates is unknown, multiple predisposing and precipitating factors have been suggested [28,29,30,31].

Gestational age : The incidence of IVH varies inversely with gestational age. The association with prematurity has already been described

Perinatal asphyxia : It is one of the important factors in the development of IVH. Asphyxia relates to four major factors[4]. Firstly, vascular autoregulation is severely impaired, thus exposing the periventricular capillary bed to a burst of pressure flow that might rupture. Secondly, cerebral blood flow is initially increased with asphyxia. Thirdly, venous pressure is increased with myocardial failure. Fourthly, direct injury to the metabolically active capillary endothelial cells may occur with hypoxic insults.

Blood gas disturbances (hypoxia, hypercapnia) : Hypoxia and hypercapnia especially due to hyaline membrane disease play the most important role in the occurence of severe IVH in the preterm infant[31]. Hypoxia and hypercapnia cause fluctuations in blood pressure and this pressure changes along with failure of autoregulation of the cerebral circulation in the immature brain leads to bleeding in the germinal matrix[22].

Acidosis : Levene et al [29] found that severe acidosis pH<7.1 was an important independent factor in the development of IVH and suggested that acidosis might reflect poor tissue perfusion, secondary to hypotension. After loss of control of blood flow to the germinal matrix by perinatal hypoxia, acidosis acts to produce change in the blood supply to the germinal matrix causing bleeding[26].

Infusion of base : The association of IVH with sodium bicarbonate, hypernatraemia and hyperosmolality has previously been described by Simmons et al[32]. Papile et al[33] suggested that rapid infusion of sodium bicarbonate was associated with periventricular haemorrhage (PVH). Sodium bicarbonate causes fluctuations in blood pressure in small preterm infants who have no autoregulation of cerebral circulation. As a result, cerebral blood flow changes directly with changes in blood pressure leading to bleeding in the germinal matrix.

Cardiorespiratory complications: Cardiorespiratory complication of neonatal care have long been considered to be the most important predisposing risk factors in the development of IVH. Respiratory distress syndrome (RDS) and its treatment by continuous positive airway pressure (CPAP)[34] or intermittent positive pressure ventilation (IPPV) [10,34] are such factors. Levene et al[29] found in their study that RDS, CPAP and IPPV all correlated very strongly with the development of IVH.

Rapid volume expansion : Expansion of intravascular volume with infusions of hyperosmolar solutions or blood products may increase cerebral blood flow, and secondarily, cerebral capillary pressure enough to rupture already dilated and possible damaged subependymal vessels[35].

Coagulopathy : Coagulopathy defects have been considered a contributing factor in PVH. McDonald et al[36] demonstrated the association of hypocoagulability with IVH and with progression of haemorrhage in 50 prospectively studied premature infants.

Patent ductus arterious (PDA) : Several investigators have suggested that a hemodynamically significant PDA may be associated with alterations in cerebral blood flow velocity, predisposing the high risk infant to IVH [37,38].

Other factors implicated in IVH are hypothermia[29], prolonged labour[30] pneumothorax[10], oral and endotracheal suctioning[39], maternal infection, preeclamptic toxaemia, primiparity and male sex of the infant[29], multiple gestation[33], cocaine exposure[40], vaginal delivery [41] etc. Murton et al[22] observed in their study that delivery by caesarean section was associated with fewer IVH, whether or not it was undertaken electively or when the patient was already on labour. On the other hand, Tejani et al [42]stated in their study

that once labour ensued, the performance of caesarean section did not prevent SEH/IVH.

It is, thus, apparent that there is no single predisposing cause of IVH, but multiple factors may be operating to a lesser or greater degree depending on the maturity of the infant.

Clinical presentation and timing of subependymal/ Intraventricular haemorrhage:

Two clinical syndromes can herald the occurrence of haemorrhage[20]–one catastrophic in nature and the other of more gradual onset. These are discussed in more detail below.

Haemorrhage producing a catastrophic deterioration in the clinical condition of the neonate evolves in minutes to hours and consists of deep stupor or coma, respiratory abnormalities (irregular respiratory rhythm, hypoventilation, apnoea), decerebrate posturing, generalised tonic seizures, pupils fixed to light , eyes fixed to vestibular stimulation and flaccid quadriparesis. Other concomitants include signs of increased intracranial pressure (e.g bulging anterior fontanelle), hypotension, bradycardia, temperature derangements, abnormalities of glucose and water metabolism, metabolic acidosis and falling haematocrit. Infants with this syndrome usually does not survive.

A more saltatory deterioration in clinical condition occurs in the infants who usually do survive. The most common presenting signs are an alteration of consciousness and the quantity and quality of spontaneous and elicited mobility. These signs are followed in minutes to hours by subtle aberrations of eye position and movement, e.g. skew deviation and vertical drift of eyes, usually down; incomplete horizontal movement of eyes with doll's head maneuver; and hypotonia. The deterioration often ceases and the infant may stabilize or may even improve.

Intraventricular haemorrhage diagnosed by CT or ultrasound or found at autopsy may apparently be silent, producing no detectable abnormalities on general or routine neurological examination[2,43].

When does SEH/IVH occur ?

Initial attempts to time haemorrhage on the basis of pathological and clinical material suggested that IVH was an intrapartum or immediately postnatal event[29]. Although IVH has been reported in the stillborn infant, it is generally a condition that occurs after birth[29]. Almost all haemorrhages occur in the first week of life but the precise timing is disputed. Some centres claim that the onset of bleeding is distributed more or less equally between the first, second and third 24-hour periods[3,29]. Van de Bor et al[31] found 30% of SEH/IVH at first ultrasound examination after birth, while 55% were detected within 24 hours, 70% within 48 hours and 90% within 72 hours. After 108 hours no new haemorrhage was found. Rumach et al[44] suggested that in screening for SEH/IVH, it would be best to evaluate the brain at the end of first week of life.

Diagnosis by ultrasound:

A CT scan is a highly effective means of establishing the diagnosis of SEH/ IVH and of demonstrating the site and extent of the lesion. In addition, the size of the ventricles, pattern of ventricular dilatation and presence of major white matter lesions (e.g. PVL) may also be defined. Despite the value of CT scan, it must be recognized that the procedure is not without hazard to the small premature infant. The patient needs to be moved to the place where the machine is available.

Maintenance of ventilation, circulation and temperature are difficult during transport and during the procedure itself. Moreover, the radiation dose to the brain and eyes is comparable with that of conventional skull roentgenograms and the long-term effects of multiple scans over short time periods remain unknown.

Ultrasonic scanning is a safe and effective alternative to the CT scan. Use of real-time, mechanical sector scanner, placed over the anterior fontanelle and oriented in the coronal plane, provides excellent resolution of periventricular as well as intraventricular haemorrhage. The extent of intraventricular blood and severity of ventricular dilatation is demonstrated by the use of sector scanner oriented in the sagittal plane. Use of a linear-array transducer over the side of the cranium provides a horizontal projection (comparable to the usual CT scan), which is particularly useful to quantitate degree of ventricular dilatation. The ultrasonic technique is particularly attractive because portable instrument can be used, thus the infant need not be transported or otherwise disturbed. Several studies can be performed over relatively short time periods, without any harm from the pulsed ultrasound. For detailed technique of ultrasound, interested readers are advised to see the article by Bejar et al[9].

Prevention of haemorrhage:

At present, with the exception of post-haemorrhagic hydrocephalus, there is no prospect of treating neonatal cerebral insults once they have occured[45]. A variety of preventive measures have been suggested. Multiple trials in both preterm infants and experimental neonatal animals have examined the ability of pharmacological agents, including phenobarbitone[46], ethamsylate[47], vitamin E[48], pancuronium [49], superoxide dismutase [50], tranexamic acid[51], fresh frozen plasma[52], vitamin K_1[53] and indomethacin[54].

Phenobarbitone: Phenobarbitone decreases the cerebral blood flow, diminishes the cerebral metabolic rate, scavenges free radicals and blunts episodic rise in systemic blood pressure. Donn and his colleagues[46] reported a reduction of intraventricular haemorrhage in preterm infants treated with a one week course of phenobrabitone.

Ethamsylate: Ethamsylate is a known prostaglandin synthesis enzyme inhibitor. It also prevents capillary bleeding by its membrane-stabilizing effect. Ethamsylate probably decreases the risk of less severe grades of IVH.

Vitamin E : Chiswick et al [48] claimed that vitamin E, a free radical scavenger, significantly reduced the incidence of IVH in inborn patients of gestational age <32 weeks. They hypothesized that vitamin E exerted a protective influence on capillary endothelial membranes, thus preventing extension of subependymal haemorrhage into the ventricles.

Indomethacin : Indomethacin inhibits the cyclooxygenase pathway of prostaglandin synthesis. Some authors[54,55] reported that low doses of indomethacin (0.1 mg/kg every 24 hours for a total of three doses) also decreased the incidence of SEH/ IVH in very low birth weight infants without significant reduction in urinary output or other major side effects.

Because of the lack of universal acceptance, there is as yet no recommendation of routine administratioin of any drug to prevent SEH/ IVH.

Prognosis and sequelae of subependymal/ Intraventricular haemorrhage :

Over the past several years the mortality associated with SEH / IVH has been steadily declining. This relates both to increased detection of smaller lesions, provided by the use of real-time ultrasound, as well as to improved supportive measures, provided by current neonatal intensive care. The mortality varies from 55%[33] to 70%[2]. Survivors exhibit neurological sequelae and there is a close relationship between severity of the haemorrhage and subsequent neurodevelop-mental outcome[7,11]. SEH/IVH[11], ventricular dilatation[56] and PVL [15,19] have all been associated with handicap of varying severity. An attempt to relate ultrasound appearances to subsequent outcome is stated below.

Normal scans: There is remarkable

consensus that consistently normal ultrasound scans in premature infants who have received intensive care accurately predicts normal outcome. There is a risk of major disability in the order of 5% for premature infants who have been regularly scanned and who have showed no evidence of cerebral abnormality[12]. Parents can be strongly reassured that these babies are at very low risk for the subsequent development of cerebral palsy or severe developmental delay.

Germinal matrix haemorrhage– intraventricular haemorrhage:

Most authors[57,58] agree that echoes apparently confined to the region of the germinal matrix alone carry no increased risk of adverse outcome. The ultrasound appearance referred to as uncomplicated periventricular haemorrhage comprising echoes in or arround the lateral ventricle(s) but not associated with either parenchyma echodensities or subsequent ventricular dilatation, has been shown to have no increased risk of adverse outcome[12]. In summary, the outcome associated with grade 1 and grade–2 IVH is good, but there is a direct relatinship of grade–3 and grade-4 haemorrhages and major handicaps[59,60].

Non-cavitating echodensity:

The prognosis appears to be relatively good but they are not always benign[16]. It is possible that the ultrasound appearance of non-cavitating echodensity will be found to correlate with less severe forms of motor impairment than cerebral palsy[45].

Cavitating periventricular leucomalacia:

In general terms, this ultrasound appearance carries a poor prognosis[59], but the accuracy of the prediction can be refined by attention to the size, number and position of the echolucent cavities. Lesions confined to the frontal or parietal areas of the periventricular white matter may be associated with less severe forms of cerebral palsy [12]. In contrast, lesions of the occipital periventricular white matter[12] and infants with bilateral cavitating lesions[61] have a very high risk of severe motor impairment.

Various complications reported in different studies are as follows[12,56,62]:

The mild abnormalities :

These included subtle disturbances in the quality of posture or movement and do not interfere with ambulation, such as clumsiness, awkwardness, balance disturbance, dystonic limb movements evident in some postures but not in others.

The major handicaps :

These cause moderate to severe disturbances in the quality or posture and movement that interfere with the child's ability to achieve age appropriate motor milestones. Included in the major handicaps are cerebral palsy in the form of hemiplegia, quadriplegia, diplegia, double hemiplegia, etc. and developmental delay (DQ<80). Also included are sensory-neural hearing loss, visual impairment which includes strabismus, myopia, nystagmus, amblyopia, anisometropia and blindness, language deficits, seizure disorder and pronounced fine motor incoordination. Language deficits includes expressive and receptive delay.

As stated, there is no prospect of treating neonatal cerebral insults once they have occured except the post-haemorrhagic hydrocephalus. Cerebral perfusion must be maintained, and this will require maintenace of adequate blood pressure and if necessary, lowering of increased intracranial pressure. Cerebral overperfusion must be prevented, especially because of the impaired vascular autoregulation. Thus, arterial hypertension, hypercapnia, hypoxaemia, acidaemia and rapid infusion of hyperosmolar solution or colloid should be avoided. Diligent support of temperature, ventilation and metabolic support is critical. Moreover, serial assessment of ventricular size by sonar is necessary to detect ventricular dilatation.

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CASE REPORTS

Giant Cutaneous Horn—A Case Report

P L SAHA, FCPS

Summary :

A 65 years old man presented with giant cutaneous horn from the upper left corner of the forehead. The horn assumed a gigantic appearance within a short period of one year. Excision of the horn was done under local anaesthesia and base pathology showed squamous cell carcinoma. During one year of follow-up, there was no recurrence. Unusually big 13 cm size cutaneous horn of short duration with base pathology of squamous cell carcinoma is presented.

(J Bangladesh Coll Phys Surg 1995; 13: 123–125)

Introduction:

Cutaneous horns are not a rarity, but certainly they are of curiosity. It is a clinical term for protruding skin lesion largely composed of keratin and resembling the shape of animal horn and this clinical appearance can result from a variety of conditions. Therefore, cutaneous horn should not be used as a pathological term[1]. Cutaneous horn reflects a disordered growth pattern of underlying epidermal keratinocytes. The changes may vary from benign lesions such as a viral or seborrhoeic wart to a skin malignancy in the form of squamous cell carcinoma, but the most common cause is solar keratosis[2]. A giant cutaneous horn arising from scalp with base pathology of squamous cell carcinoma is a rare entity.

Case report:

Mr. A H, a 65 years old man presented with a painless, progressive horn like growth projected from the upper left corner of his forehead for one year (Fig-1). He was socially embarrassed because of the horn but otherwise asymptomatic until last four weeks when it was giving him moderate pain following an accidental trauma. The patient was maintaining a good general health. On examination, a non-tender hard horn of 13 cm length, broad at base and pointed at apex was found arising from left fronto-temporal junction. The horn was curved downwards and broken partially at its base with ulceration at the broken area. The horn was mobile. No

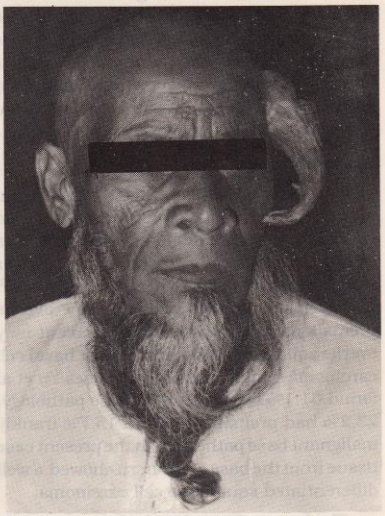

Fig-1: *Giant cutaneous horn from upper left corner of the forehead.*

Dr. Panna Lal Saha, Assistant Professor, Paediatric Surgery, Chittagong Medical College.
Correspondence to : Dr. Panna Lal Saha, Asstt. Professor, Paediatric Surgery, Chittagong Medical College, Chittagong
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enlarged regional lymphnode could be detected. Under local anaesthesia the cutaneous horn was excised with 3mm healthy skin from the margin. No difficulty was experienced during the operation except some gap in the skin after closure of the wounds. The patient went home after the operation. Post-operative recovery was uneventful. The wound healed within a month, and looked perfectly healthy even after one year of operation.

On examination, excised specimen showed a curved horn. It meassured 13 cm in length and had a dimension of 4.5 x 3.5 cm at the base. The surface of the horn was shrivelled and greyish in colour. The horn had hard consistency and appeared to be made of keratin. The skin around the base of the horn had rolled out margins. The cut surface of the skin at the base and the margin revealed granular, white, tumerous tissue. Sections were taken from the margin and the horn itself. The former revealed a well differentiated squamous cell carcinoma and sections made from the horn revealed laminated layers of keratin forming numerous keratin pearls. From these features it was concluded that this keratin was of epidermal type.

Discussion:

Cutaneous horns are most often benign with hyperkeratosis superimposed on an underlying seborrhoic keratosis, verruca vulgaris, angiomas, trichilemmoma or epidermoid cyst in 50 to 60 percent of cases [3]. However, 20 to 30 percent may overlie premalignant keratosis and 20 percent may overlie squamous cell carcinoma or basal cell carcinoma [3]. In a study of 643 cases Yu et al found 61.1% to have benign base pathology, 23.2% had premalignant and 15.7% frankly malignant base pathology. In the present case, tissue from the base of the horn showed a well differentiated squamous cell carcinoma.

The keratin formed in the horn is usually of epidermal type, but occasionally it has trichilemmal features. When this is the case, the lesion is referred to as trichilemmal keratosis, verrucous trichilemmal tumour and trichilemmal horn[1]. In present case, sections made from the horn revealed laminated layers of keratin forming numerous keratin pearls but there was no trichilemmal keratin lamination in any site. Hence this horn was of epidermal type. Cutaneous horns have been regarded by some as obligatory precancerous or malignant lesions[4]. In a series of 230 cutaneous horns[5] premalignant or malignant changes were seen at their bases. Others[6,7,8] have reportd a much higher incidence of benign histological features. Studies on parameters that are commonly associated with premalignant base pathology have prduced conflicting evidence with regard to age and sex of the patients and shape of the lesion[4,6,9]. Large cutaneous horns, particularly giant horns, are said to be commonly derived from malignant base [4,9]. The present case showed a base pathology of squamous cell carcinoma. A case was reported with a Kaposi's sarcoma as base pathology of a cutaneous horn[10].

Best [6] and Mehergan [10] found cutaneous horns more common in males. In contrast Yu[4] in his 643 case series found cutaneous horns more common in females. However, horns with premalignant base pathology were more commonly found in males. Cutaneous horns with a wide base or low height to base ratio were more likely to show either premalignant or malignant base pathology[4]. The coexistence of other premalignant skin lesions increased the likelihood of finding a horn with premalignant base pathology [4], but in present case no other premalignant skin lesion was present.

In treating cutaneous horn one must be aware of association of malignancy with cutaneous horn. Wide excision of base of skin must be done and in each case histopathology from the base of the horn is mandatory.

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COLLEGE NEWS

(J Bangladesh Coll Phys Surg 1995; 13: 126–128)

Continuing Medical Education :

24-5-95 : Maj. Genl (Retd). A R Khan
Chief Consultant, BIRDEM, Dhaka
delivered lecture on "Recet advances in the field of diabetes mellitus".

16-6-95 : Prof. A K M Kafiluddin
Professor Emeritus, NIPSOM, Dhaka
delivered lecture on "The crisis of public health–a new approach to solve it."

28-6-95 : Prof. M A Mannan
President, Neurology Foundation, Dhaka
delivered lecture on "Cerebro -vascular disease and its management"

9-8-95 : Dr. Sirajul Haque
Consultant, BIRDEM, Dhaka
delivered lecture on "Diabetic micro-angiopathy"

23-8-95 : Dr. Chowdhury Ali Kawser
Associate Prof. of Paediatrics, Institute of Child and Mother Health, Dhaka
delivered lecture on "Cirrhosis of liver- is it reversible ?"

Examination News:

Results of FCPS Part I, FCPS Part II and MCPS Examination held in July 1995 are given below:

577 candidates appeared in FCPS part I Examination held in July 1995 of which 66 candidates came out successful. Subjectwise results are as follows:

Subject	Number appeared in theory examination	Number qualified for viva-voce	Number passed
Medicine	161	64	22
Surgery	145	33	11
Paediatrics	68	5	3
Obst & Gynae	87	34	11
Ophthalmology	42	16	8
ENT Diseases	17	2	1
Psychiatry	5	0	0
Anaesthesiology	20	4	1
Radiology	10	2	0
Radiotherapy	2	2	1
Physical Medicine	6	5	4
Haematology	12	4	3
Microbiology	1	0	0
Histopathology	1	1	1
Total	577	172	66

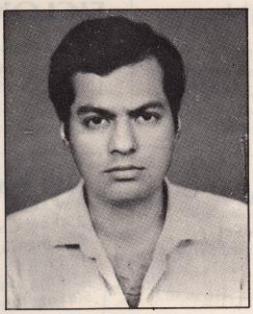
104 candidates appeared in FCPS part II Examination in different subjects. List of candidates who satisfied the board of examiners is as follows:

Roll No.	Name	Graduated from	Speciality
5	Dr. Md. Abdul Alim	Mymensingh Medical College	Medicine
6	Dr. Shyamal Sarker	Dhaka Medical College	Medicine
9	Dr. Anup Kumar Saha	Dhaka Medical College	Medicine
15	Dr. A R M Saifuddin Ekram	Dhaka Medical College	Medicine
18	Dr. Md. Fazlul Hoque	Mymensingh Medical College	Medicine
23	Dr. Abdul Wadud Chowdhury	Dhaka Medical College	Medicine
25	Dr. A M M Yahia	Dhaka Medical College	Surgery
26	Dr. A K M Nazrul Islam	Chittagong Medical College	Surgery
28	Dr. Rafiques Salehin	Sher-e-Bangla Medical College	Surgery
29	Dr. Mohammad Shoaib	Dhaka Medical College	Surgery
32	Dr. D A Hassan Chowdhury	Sylhet Medical College	Surgery
35	Dr. G M Zakir Hossain	Rajshahi Medical College	Surgery
36	Dr. Anwarul Haque	Chittagong Medical College	Surgery
37	Dr. Ranajit Kumar Mallick	Dhaka Medical College	Surgery
40	Dr. M Abdul Mannan Khan	Sir Salimullah Medical College	Surgery
48	Dr. A K M Khurshidul Alam	Sir Salimullah Medical College	Surgery
50	Dr. Probodh Kumar Biswas	Mymensingh Medical College	Surgery
53	Dr. Tapan Kumar Saha	Dhaka Medical College	Surgery
55	Dr. Md. Kamrul Islam	Dhaka Medical College	Surgery
59	Dr. M E H Shahryar Sabet	Chittagong Medical College	Surgery
60	Dr. S M Ashraf Ali	Chittagong Medical College	Surgery
61	Dr. A B M Moniruddin	Sher-e-Bangla Medical College	Surgery
62	Dr. Mahbub Mutanabbi	Dhaka Medical College	Paediatrics
63	Dr. Bakul Kanti Deb	Chittagong Medical College	Paediatrics
65	Dr. Md. Asgar Hossain	Rajshahi Medical College	Paediatrics
67	Dr. Md. Jahangir Chowdhury	Chittagong Medical College	Paediatrics
69	Dr. Md. Shafiqul Alam	Rajshahi Medical College	Paediatrics
71	Dr. Nurun Nahar Fatema Begum	Sylhet Medical College	Paediatrics
72	Dr. Md. Zafrul Bari Rashed	Rajshahi Medical College	Paediatrics
74	Dr. M. Anwar Hossain Khan	Chittagong Medical College	Paediatrics
75	Dr. Md. Abdur Rouf	Sir Salimullah Medical College	Paediatrics
76	Dr. Bikash Kumar Majumder	Dhaka Medical College	Paediatrics
78	Dr. Arup Dutta	Chittagong Medical College	Paediatrics
79	Dr. Serajun Noor	Chittagong Medical College	Obst & Gynae
80	Dr S M Mahtab-e-Alam	Rangpur Medical College	Obst & Gynae
81	Dr. Sharmin Rahman	Sir Salimullah Medical College	Obst & Gynae
83	Dr. Saria Tasnim	Dhaka Medical College	Obst & Gynae
84	Dr. Shahidul Islam	Sylhet Medical College	Ophthalmology
86	Dr. Md. Golam Haider	Sylhet Medical College	Ophthalmology
92	Dr. S S Afsar Al Mahmood	Chittagong Medical College	ENT Diseases
96	Dr. Nezam Uddin Ahmed	Mymensingh Medical College	Anaesthesiology
99	Dr. Aneesul Islam Shakir	Chittagong Medical College	Anaesthesiology
101	Dr. Md. Abul Hashem	Chittagong Medical College	Radiotherapy
103	Dr. Md. Taslim Uddin	Sylhet Medical College	Physical Medicine

220 candidaes appeared in MCPS Examinaions in different subjects. List of candidates who satisfied the board of examiners is as follows :-

Roll No.	Name	Speciality
19	Dr. Md. Shah Nawaz	Medicine
25	Dr. Md. Bazlur Rahman	Surgery
26	Md. Mohammad Ali	Surgery
28	Dr. S M Amir Hossain	Surgery
45	Dr. Sabina Sultana	Paediatrics
46	Dr. A B M Shahidul Alam	Paediatrics
60	Dr. Md. Mabhub-Ul-Karim Khan	Paediatrics
65	Dr. Akhter Jahan Umme Nasima Begum	Obst & Gynae
67	Dr. Ayesha Rahim	Obst & Gynae
76	Dr. Anwara Begum	Obst & Gynae
79	Dr. Tauhida Begum	Obst & Gynae
103	Dr. Karuna Thapa	Obst & Gynae
110	Dr. Banani Chowdhury	Obst & Gynae
117	Dr. Sahana Razzaque Ali	Obst & Gynae
134	Dr. Zahidatun Nessa	Obst & Gynae
154	Dr. Golam Kibria Md. Afzalul Bashar Khan	Ophthalmology
155	Dr. Prakash Kumar Chowdhury	Ophthalmology
186	Dr. Selina Khatun	Dental Surgery
188	Dr. Quazi Rakibus Sultan	Dermatology & Venereology
190	Dr. Mir Hamde Samey	Forensic Medicine
191	Dr. Md. Mohebhullah	Forensic Medicine
196	Dr. Sakib Md. Ahsan Habib	Family Medicine
199	Dr. Md. Nazrul Islam	Family Medicine
200	Dr. Abul Fattah Md. Ahsan Ali	Family Medicine
201	Dr. Mohammad Fazlul Hoque	Family Medicine
205	Dr. Ruhini Kumar Das	Clinical Pathology
207	Dr. Golam Mohammad Quraishi	Clinical Pathology
212	Dr. Md. Faruk Mia	Clinical Pathology
213	Dr. Md. Rahimgir	Clinical Pathology
217	Dr. A S M Ataur Rahman	Clinical Pathology
218	Dr. Md. Shahjahan Ali	Clinical Pathology
220	Dr. Akhtar Jahan Sayara Begum	Clinical Pathology

OBITUARY



Dr. Kazi Zaheed Ashraf, FCPS (Surgery)

Dr. Kazi Zaheed Ashraf died on 28th April, 1994 by motor launch accident while he was going to join his new assignment as Resident Surgeon in Sher-e-Bangla Medical College, Barisal. He was born on 2nd July, 1961 in Dhaka. He graduated in January, 1986 from Dhaka Medical College. He passed Fellowship Examination in Surgery and was admitted a Fellow of the Bangladesh College of Physicians and Surgeons in January, 1994. He served in various capacities in Bangladesh Health Services.

He left behind his wife and one son to mourn his death.

May Allah rest him in peace.