CLINICAL RECORDS

NASOPHARYNGEAL FIBROMA

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CASES of juvenile angiofibromata of the post-nasal space have been described recently in this Journal (Handousa, *et al.* (1954), Martin (1954), Fraser (1958), Osborn (1959), Weir and Doig (1960), Capps, *et al.* (1961) and Rao (1961)) and a further report might be considered superfluous but for the fact that of the seven cases of this unusual condition seen in Northern Ireland in the past 13 years, one ran an unexpected and tragic course.

Many views concerning the origin of these tumours have been put forward and recent theories suggest a hormonal basis because of the high incidence in young males, the belief that sexual maturity brings regression, and a response in some cases to androgens. Hypogonadism has been reported in the majority of patients from two series (Hayes Martin, *et al.* (1945), Carbonara and Salonna (1958)) but these findings have not been confirmed by other authors. In view of this disagreement we thought it would be useful to consider this aspect in our patients. In all cases a full physical examination was made and the 24 hour excretion of 17 ketosteroids (Norymberski (1953)) and Follicle Stimulating Hormone (Johnsen (1959)) was estimated.

Table I summarizes the histories of the seven patients who were all male and whose average age at the time of diagnosis was 14·7 years. In all cases the tumour was visible in the nasopharynx and in Case I, IV and VI it was also visible *viâ* the anterior naris.

Hearing: Audiograms of Cases III, IV, V, VI and VII were normal. In case I the drums were normal in appearance and in Case II both drums were retracted (in neither case were audiograms available). Because of its unusual course, Case VII is discussed more fully.

This patient was first seen at another hospital in *November, 1955*, when he complained of nasal obstruction and discharge. Bilateral antral washout was clear. His symptoms persisted and in *April, 1956*, examination of the post-nasal space was carried out under general anæsthesia. A firm tumour in the right side of the nasopharynx was found to extend forward into the right nasal cavity. Histological examination showed the features of angiofibroma. Low dosage irradiation was given and was followed by considerable regression. However, 6 months later the tumour was again very large and had caused marked broadening of the nose.

23.11.56

Preliminary tracheotomy. It was intended to remove the tumour by Wilson's transpalatal approach (Wilson, 1957), but digital investigation of the naso-

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Case No.	Age when last seen	Presenting Symptoms	Physical Examination	Biochemical Tests		Treatment	Present age and condition
				17 ketosteroids	Follicle Stimulating Hormone		
I	17 11/12	Nasal obstruction many years. Epistaxis 4 days (Profuse bleeding during S.M.R.)	Normal	Normal (15·3 mgm./24 hrs.)	Normal (1·75 mgm./24 hrs.)	Removal *viâ* Wilson's approach	23 Satisfactory Wife pregnant
II	17	Nasal obstruction for 9/12. Epistaxis Meningitis 2/12 ago—no organisms found in C.S.F.	Sexually normal. Rheumatic heart disease	Normal (8·5 mgm./24 hrs.)	Low (0·875 mgm./24 hrs.)	Profuse bleeding after biopsy. Removal after splitting soft palate. 4 pints blood.	29 Satisfactory Married: 2 children
III	14	Nasal obstruction for 6/12. Epistaxis for 3/52.	Wide span upper limbs otherwise normal	Normal (10·4 mgm./24 hrs.)	Low (below 0·8 mgm./24 hrs.)	Bled after E.U.A. laryngeal spasm, emergency tracheotomy. Removed *viâ* Wilson's approach (Hypotensive technique)	17 Satisfactory
IV	14	Nasal obstruction and epistaxis for 9/12	Normal apart from funnel deformity of thorax	Normal (13·3 mgm./24 hrs.)	Low (0·87 mgm./24 hrs.)	Removal *viâ* Wilson's approach. 1 pint blood	17 Satisfactory
V	19	Nasal obstruction 1 year. Epistaxis 4/12	Normal	Normal (5·8 mgm./24 hrs.)	Normal (1·75 mgm./24 hrs.)	Removal *viâ* Wilson's approach. 4 pints blood	22 Satisfactory
VI	13	Nasal obstruction and epistaxis for 6/12	Normal	Low (3·9 mgm./24 hrs.)	Normal (3·5 mgm./24 hrs.)	Removal *viâ* Wilson's approach 4 pints blood	13
VII	8	Nasal osbtruction for several months	Normal	Normal (5·1 mgm./24 hrs.)	Not done	Repeated removal and D.X.R. Died 21.2.60	

Case II has been previously reported (Hunter and Biggart, (1950).)
(For adult males normal 17 ketosteroid excretion is 5-20 mgms. in 24 hours and normal Follicle Stimulating Hormone excretion is 1·4–2·8 mgms. in 24 hours.)

pharynx was followed by massive hæmorrhage. The soft palate was split longitudinally and the tumour removed as rapidly as possible, "piece-meal" and by electrocoagulation. Complete clearance appeared to have been obtained. Four pints of blood were transfused. At this operation the tumour was seen to have eroded part of the hard palate and to extend laterally into the area of the right foramen lacerum and pterygopalatine fossa. Following this, recurrences were removed on five occasions. In *June, 1958* the possibility of further radiotherapy was considered but was decided against because of the size of the tumour.

9.7.58

The patient was transferred to the E.N.T. Department of the Royal Victoria Hospital, Belfast.

The presence of right proptosis and swelling of the right cheek were noted and the tumour was seen to extend from the right anterior naris to the nasopharynx, causing displacement of the septum to the left. Both ear drums were opaque and lacked a light reflex but the audiogram was normal.

10.7.58

Right lateral rhinotomy incision. A large tumour mass was dissected off the right lateral walls of the nose and nasopharynx. Removal was thought to be incomplete in the nasopharynx. Erosion of the medial wall of the right antrum and the hard palate was noted. Profuse hæmorrhage necessitated intravenous infusion of five pints of blood. Following this, recurrences on the posterior and right lateral walls of the nasopharynx were treated with electrocoagulation on three occasions.

26.11.59

Diathermy coagulation of a further recurrence on the posterior wall of the nasopharynx was attempted but was attended by profuse bleeding and collapse of the patient which was treated by transfusion of blood under pressure. No further removal of the tumour was attempted. A cavity in the roof of the nasopharynx was noted.

3.12.59

Diathermy coagulation of the tumour area. One pint of blood was given and bleeding was controlled by diathermy and packing. During the next 3 weeks there was repeated bleeding and right acute otitis media which was treated successfully with Chloramphenicol.

21.1.60

Diathermy coagulation to an area of tumour in the roof of the nasopharynx $1\frac{1}{4}$ in. in diameter. Bleeding was moderate. Half a pint of blood given intravenously. Thereafter intermittent bleeding occurred. One month later a recurrence of the tumour was visible in the nasopharynx and destruction of the floor of the pituitary fossa was seen on X-ray examination.

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21.11.60

A further attempt to remove the tumour was made using hypothermia and hypotensive drugs. Shortly after the commencement of the removal, bleeding became very profuse and in spite of blood replacement, cardiac arrest occurred. Cardiac massage was unsuccessful.

Pathology

A complete autopsy was performed on Case VII. The relevant findings were confined to the nasal cavity and the base of the skull.



FIG. 1.

Case VII. Photograph showing the base of the skull. The tumour is seen in the region of the pituitary and in the right middle cranial fossa, close to the foramen ovale. (Actual size.)

On the posterior part of the palate there was a large cleft due to the previous operations. Only very small amounts of tumour were identified at this site.

On opening the skull and removing the brain the main features which were seen on the base of the skull are shown in Fig. 1. A protrusion of tumour about 1 cm. in diameter was seen in the region of the pituitary. It had been displaced posteriorly and a little to the left by the tumour, which had infiltrated up through the floor of the pituitary fossa. A further protrusion of tumour was seen in the right middle fossa close to the foramen ovale (Fig. 1). Further dissection showed that the tumour had infiltrated and destroyed the sphenoid bone between the two tumour outgrowths.

Histological examination of the tumour, and the six previous biopsy specimens, showed that all possessed similar features. There were large vascular

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spaces which were lined by a single layer of endothelium (Fig. 2) and were surrounded by varying amounts of fibrous tissue. All of the later biopsies revealed in addition some vascular spaces which had thick cellular walls which, however, failed to show the normal staining characteristic of muscle (van Gieson and Picro Mallory methods) (Fig. 3). In no area was there any evidence of malignant change, though in some areas the nuclei of the fibrous stroma had a more stellate appearance than usual (Sternberg, 1954). There were no definite histological changes in the hypothalamic nuclei.

Histological sections from the other six patients were available. All of them showed the same thin-walled vascular spaces, with fibrous stroma, and in four cases there were in addition irregular and thick walled vascular spaces. Case V was the only one which showed fragments of elastic tissue in a few of the vessel walls (Osborn, 1959).

Discussion

The most significant feature in this series of patients was that in one, who died at operation, a post-mortem examination revealed that the tumour had spread intracranially.

As many reports as possible of this condition have been consulted by us, and although most authors refer to the possibility of intracranial spread with serious consequences, only two specific reports of this occurrence could be discovered. Denker in 1921, described a male aged 17 (Case XII) who died at operation. At post-mortem, the tumour was found to have extended through the foramen ovale and indented the undersurface of the temporal lobe of the brain. In 1958, Härmä reported on a boy who died post-operatively—at post-mortem the tumour was seen to be extending through the cribriform plate between the crista galli and the sella turcica.

There are several reports of patients where erosion of the base of the skull or intracranial spread seem likely to have occurred but cannot be proved because of insufficient evidence. For example, Goldsmith (1923) reports a patient who died of circulatory failure during operation in whom an erosion of the base of the skull was noted during the attempted removal of the tumour. Hill (1942) reported the occurrence of a pneumocephalus in a boy of 13 who had received radiotherapy. On X-ray examination ". . . a stalk could be seen running upward and forward from the tumour to the pneumotocele". The pneumocephalus shortly subsided and at the time of the report the tumour had diminished and the patient was well. In Brunner's case I (1942), who survived, there was a "suspicion of erosion of the base of the skull" on X-ray. Figi (1940) refers to a patient in whom the tumour was seen to involve the sphenoid and sella turcica on X-ray, but no further details are given. Another patient is described by Figi and Davis (1950) who died of meningitis 3 months after electrocoagulation and irradiation. Lambert (personal communication) had a patient in whom central destruction of the basisphenoid was clearly visible on X-ray 10 years ago, who was treated by radiotherapy, and who is at present alive and well. Finally, Acuña (1956) briefly refers to a patient—still alive at the time of the report—in whom "the tumour had destroyed the sella turcica and caused permanent blindness".

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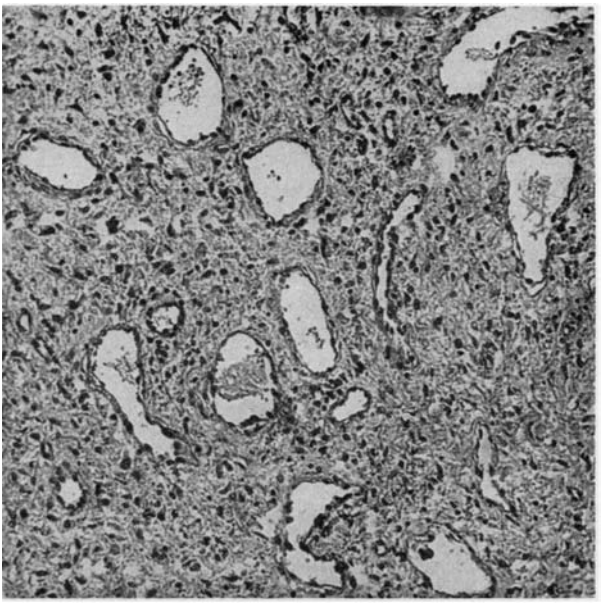


FIG. 2.
Case VII. Section to show thin walled vascular spaces with fibrous stroma (H. & E. × 125).

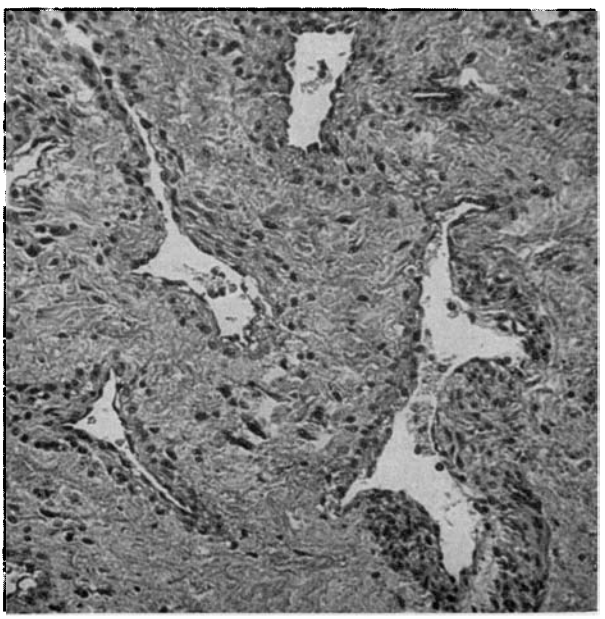


FIG. 3.
Case VII. Section to show thick walled vascular spaces (H. & E. × 150).

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Since only these nine instances could be found in a literature comprising between 350 and 400 proven tumours another case of intracranial spread seems worth reporting.

Previous writers, seeking to explain the origin of these tumours, suggested that they might arise from the embryonic occipital plate, the pharyngeal aponeurosis or the pharyngobasilar fascia. These theories did not explain the predominantly male incidence—most of the reported occurrences in females were probably not true angiofibromata—nor did they explain the vascular nature of these tumours which has been comprehensively described by Harma (1958) and Osborn (1959). Hayes Martin *et al.* (1948) and later Osborn (1959) sought an explanation on a hormonal basis and an interpretation of this nature is supported by the findings both of Hayes Martin *et al.* (1948) of underdeveloped secondary sexual characteristics in over half of their patients, and of Carbonara and Salonna (1958) of hypogonadism in the four patients whom they investigated. On the other hand, Handousa *et al.* (1954) and J. S. Martin (1954) referring to this aspect, state that they were unable to find any physical sexual abnormality in series of 70 and 5 patients respectively. No mention is made by them of any endocrinological investigation.

Of the seven cases described in this paper, in only one (Case III) was there any suggestion of significant physical abnormality. This patient has a span of $73\frac{1}{2}$ in. which is excessive compared to his height, which is $70\frac{1}{4}$ in. Such a finding is normally regarded as a eunuchoid feature.

The daily excretion of 17 ketosteroids of all but one of the patients was normal. (In Case VI a finding of 17 ketosteroid excretion of 3·9 mgm. in 24 hours is not altogether abnormal in this age group.) The daily excretion of Follicle Stimulating Hormone of three patients was less than that usually accepted as normal for adolescent males (Case II, III and IV). However, if it be remembered that the endocrine system is in a state of flux at puberty, it would seen unwise to make any firm assessment of pituitary function on the basis of this evidence alone. (It is significant that one of these patients has since fathered two normal children.) Only by recourse to testicular biopsy and sperm counts, which would not have been justified in these patients, could the possibility of hypogonadism be completely ruled out. It is therefore concluded that sexual abnormality was not a significant contributing factor in these seven cases of angiofibroma of the postnasal space.

Summary

Seven cases of angiofibroma of the post-nasal space are described. All were young males. One of these terminated fatally and at post-mortem intracranial extension of the tumour was found to be present. Only two references to this complication, proven by post-mortem, could be found in the literature, although it is likely that this had occurred in seven other cases.

The suggestion that sexual abnormality was an ætiological factor in this disease prompted an endocrinological examination of our patients. This consisted of full physical examination and the estimation of 24 hour excretion of 17 ketosteroids and Follicle Stimulating Hormone. No evidence of endocrine abnormality was found.

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