Nasopharyngeal angiofibroma

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NASOPHARYNGEAL angiofibromas are uncommon and unusual tumours. Unusual because, despite their being slowly progressive and histologically benign, they simulate malignancy by their seemingly relentless growth and destructiveness, though the latter is due to pressure erosion by the enlarging mass and not to infiltration of tissues. Moreover, their incidence and behaviour have prompted the theory that they are sex- and age-linked and hormonally influenced. Martin *et al.* (1948), Sternberg (1954) and Capps *et al.* (1961) are among many authors who believe that the tumours are restricted to juvenile, adolescent and young adult males, and that those lesions which do not prove fatal tend eventually to become inactive or even to regress by about the age of 20 to 25 years, when sexual maturity has been reached. It appears from other authenticated reports and observations, however, that these theories are not universally accepted or considered inflexible. Thus proven female cases, though definitely in the minority, have been reported by Figi and Davis (1950), Osborn and Sokolovski (1965) and Fitzpatrick (1970) among others, and while it has been shown that some lesions may continue to be active or even commence after the age of 25 years (Hubbard, 1958; Reddy and Farb, 1963; Conley *et al.*, 1968) there are also instances of cure or spontaneous arrest long before the age of maturity has been reached. No race is known to be immune and the variations in prevalence of the disease in different countries, as judged from reports in the literature, may be due partly to the degree of accuracy of diagnosis and partly to the fact that in some cases the tumour may undergo spontaneous arrest and therefore never reach hospital; while in others, particularly in developing countries, patients are disinclined to seek medical attention until a lesion becomes really uncomfortable or disfiguring. The three cases reported here are to the best of the authors' knowledge the first to be reported if not to be recognized in West Africa but, for reasons previously mentioned, are most unlikely to be the first to have occurred in this part of Africa.

Case reports

Case 1. A male patient, aged 16 years, was first seen in February 1972 when he complained of increasing nasal obstruction for two years, progressive protrusion of the left eye and intermittent epistaxis for one year, with some impairment of hearing and double vision for six months. On examination, he was found to have bilateral proptosis, worse on the left, and slight limitation of movement of the eyes but no chemosis. His nose was completely blocked and a little expanded by a tumour which presented in the right nostril as a smooth, very firm, pinkish-grey mass. There was very marked bulging of both the hard and soft palates into the oral cavity, and beyond this the tumour could be seen to be almost filling the oropharynx. Radiography showed some destruction of the sphenoid and opacity

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in the ethmoids and both antra. An intranasal biopsy was taken and, on postnasal palpation, the nasopharyngeal portion felt very firm, and filled the whole postnasal space. Bleeding from the nose was brisk but was eventually controlled by packing and diathermy. A clinical diagnosis of nasopharyngeal angiofibroma was made. A few days later, an elective tracheostomy was performed to provide a route for anaesthesia, and the very tough tumour was removed via a transpalatal approach. It was found that most of the ethmoids and the anterior wall of the sphenoidal sinus had been eroded. The mass was attached by a broad base to the right postero-lateral pharyngeal wall and had secondary attachments to the left lateral pharyngeal wall, most of the upper surface of the soft and hard palate and the left orbital periosteum. The bony part of the nasal septum had also been destroyed. Though it was obvious at the end of the operation that parts of the 'tumour' in the sphenoidal sinus and the left orbit had been left behind, it was considered hazardous to attempt further exploration or excision in a field partially obscured by fairly severe haemorrhage, since this might have risked damage to intracranial and intra-orbital structures.

The pathological report was as follows: 'Specimen received consisted of four separate pieces of irregular very firm tissue weighing 27 g. The largest piece measured 4 cm × 3 cm × 1·5 cm. The outer surfaces of all the pieces were brownish in colour and showed distinct nodularity. The cut surfaces had a firm fibrous feel and were uniformly whitish in colour.

'Microscopic examination showed a tumour composed of a dense fibrous stroma surrounding thin-walled vascular spaces (Fig. 1). The stroma showed haphazardly arranged fibres of connective tissue with a few scattered fibrocytes. The nuclei of the fibrocytes were thin and spindle-shaped. The vascular spaces were few and widely separated by the fibrous stroma. The walls of the blood vessels were thin and their lumen narrowed as a result of compression by the surrounding stroma. Many of the vascular spaces appeared as slits lined by endothelium. The tumour showed in areas remnants of ulceration covering stratified squamous epithelium. Immediately below the areas of ulceration, there were focal collections of acute and chronic inflammatory cells.' A diagnosis of nasopharyngeal angiofibroma was made.

Post-operatively the proptosis improved, but to a less extent on the left. Later necrosis of the thinned central part of the palate left a defect of about 2 cm. in diameter. During the next six months, he had occasional bouts of slight epistaxis, but he has had none in the succeeding five years until 1977. The residual granuloma seemed to re-grow slightly into the postnasal space during the first few months but has apparently remained static for the past three years, and the proptosis has not increased.

Case 2. This female patient aged 13 years was referred to this hospital in June 1973 with a history of complete nasal obstruction and a painless swelling of the right cheek and side of the nose for about three months, occasional epistaxis and a protrusion of the right eye for about a month prior to being seen. A biopsy taken from part of the tumour found protruding from the right nostril was diagnosed as a fibrosarcoma. She was referred to this hospital after a course of Endoxana had proved ineffectual.

On arrival she was found to have, in addition to the above features, a discharging sinus close to and below the right inner canthus, a smooth rounded and very marked bulge of the palate into the oral cavity and a pinkish grey mass

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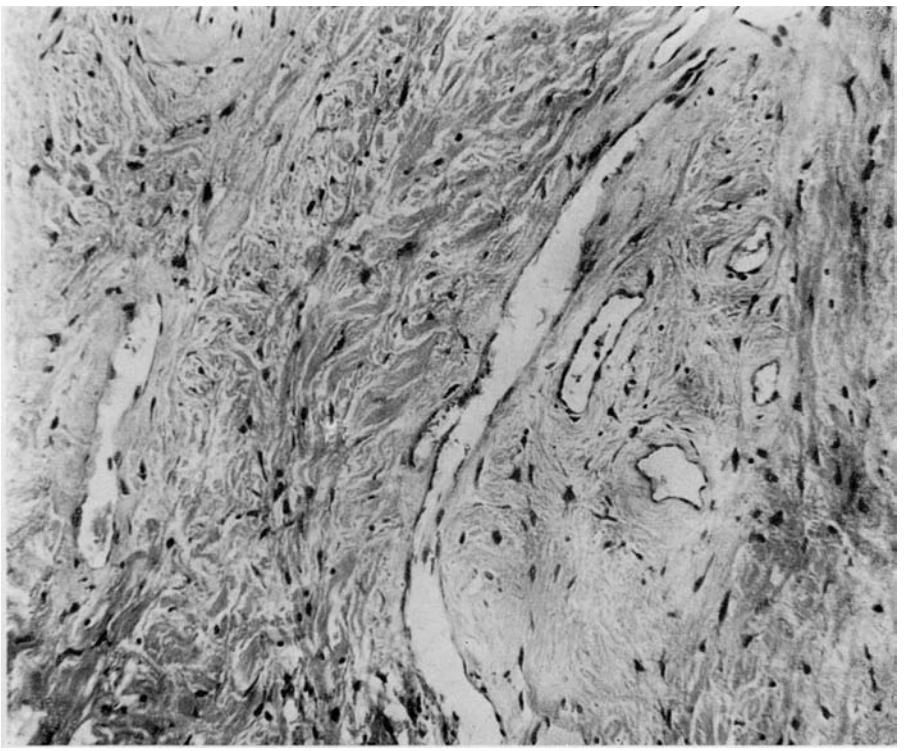


FIG. 1

Thin-walled vascular spaces compressed by surrounding scantily cellular fibrous tissue (H. & E. × 190).

beyond this in the oropharynx. Radiography showed a large mass in the nasopharynx and an opacity in the right antrum. A biopsy was taken of the growth which, from its firm texture, site and size, was strongly suspected to be an angiofibroma in spite of the sex of the patient. This diagnosis was confirmed by histological examination. At subsequent operation via a sub-labial (Caldwell-Luc) approach the antral portion of the tumour was removed without difficulty and through a large erosion of the medial antral wall the remaining tumour was traced into the nasopharynx where it was found to be attached to the posterior wall by a stalk about 2 cm. thick. As it had not acquired any secondary attachments, separation of this stalk from the area of attachment allowed the whole mass, including the intranasal portion, to be delivered through the oropharynx without the need for a palatal incision. Bleeding during this operation was not as profuse as in the previous case and post-operatively the proptosis appeared to be satisfactorily corrected. The pathological report was as follows: 'Specimen received consisted of two separate masses of firm light brown tissue. The larger piece measured 4·5 cm × 3·0 cm × 2·5 cm and the smaller, 2·5 cm × 2·5 cm × 1·8 cm. Outer surfaces of both the masses were smooth, rounded and light brown in colour. Cut surfaces were firm, fibrous and uniformly whitish in colour.

Microscopic examination showed a tumour composed of a cellular fibrous stroma surrounding numerous scattered vascular spaces (Fig. 2). The stromal

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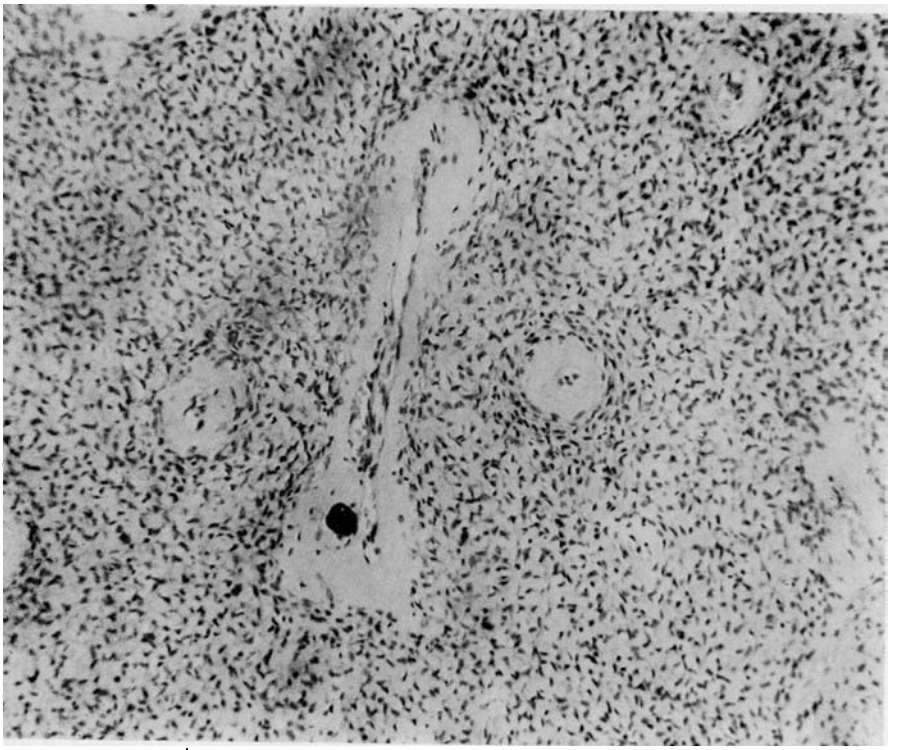


FIG. 2

Shows blood vessels with thick hyalinized walls surrounded by cellular fibrous tissue. An area of calcification is seen in the wall of one of the blood vessels (H. & E. × 190).

cells had plump, spindle, oval or stellate nuclei which appeared hyperchromatic but showed no mitotic activity or pleomorphism (Fig. 3). The blood vessels showed marked thickening and hyalinization of their walls and a few of them had focal areas of calcification. Their lumens were markedly narrowed as a result of the thickening of their walls, and in some cases were completely occluded by hyalinized thrombus.' A diagnosis of nasopharyngeal angiofibroma was made.

In view of the patient's sex, buccal smears and a skin biopsy were taken for chromosome studies and these showed a normal female sex chromatin pattern.

Case 3. A male, aged 15½ years, complained of progressive nasal obstruction and discharge for two years, during which period he had had intermittent attacks of headaches and epistaxis. He had also observed a protrusion of his left eye for about four months.

He was found on examination to have a very noticeable left proptosis with slight limitation of movement but no impairment of vision in that eye. A large smooth firm pinkish mass filled the nasal airway pushing the septum against the right lateral wall and protruding through the left nostril. A firm non-ulcerating tumour almost filling the oropharynx could be seen beyond a bulging of the hard and soft palates.

On radiography it was found that the sphenoidal sinuses were opaque and the floor of the pituitary fossa and part of the middle cranial fossa had been eroded.

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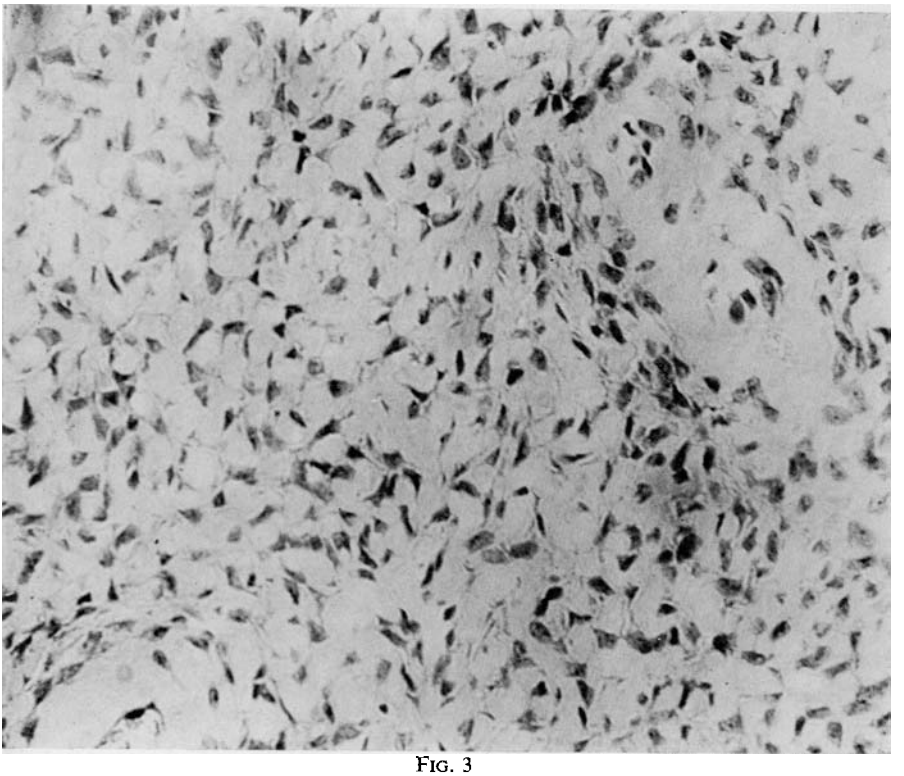


FIG. 3

Higher power view of the same field as Fig. 2 showing the stroma cells with plump nuclei. Mitotic activity is not seen (H. & E. × 280).

Carotid angiography demonstrated a vascular nasopharyngeal mass with the nutrient vessel arising from the left external carotid via the maxillary artery.

A pre-operative diagnosis of nasopharyngeal angiofibroma was made and the tumour was approached by the transpalatal route. The very vascular and tough nasopharyngeal mass was removed with some difficulty, but excision seemed complete. The portion which had eroded through the sphenoidal sinus had not acquired any secondary attachments and was extracted easily. Bleeding from the left maxillary and ethmoidal arteries was so brisk that the left external carotid had to be ligated and the left ethmoidal area cauterized. The residual cavity had also to be packed so firmly with BIPP gauze that postoperatively the proptosis appeared worse. The suture line partially broke down later and the resulting small defect was temporarily occluded with an obturator. The proptosis regressed completely after the packs were removed and at a later date the palatal defect was closed by a plastic surgeon.

Pathology report. 'Specimen consisted of a roughly oval, nodular, firm mass weighing 103 g. and measuring 7 cm × 6·5 cm × 4 cm. Its outer surface was smooth to feel and light brown in colour. The cut surfaces were white, fibrous to feel and showed faint trabeculations.

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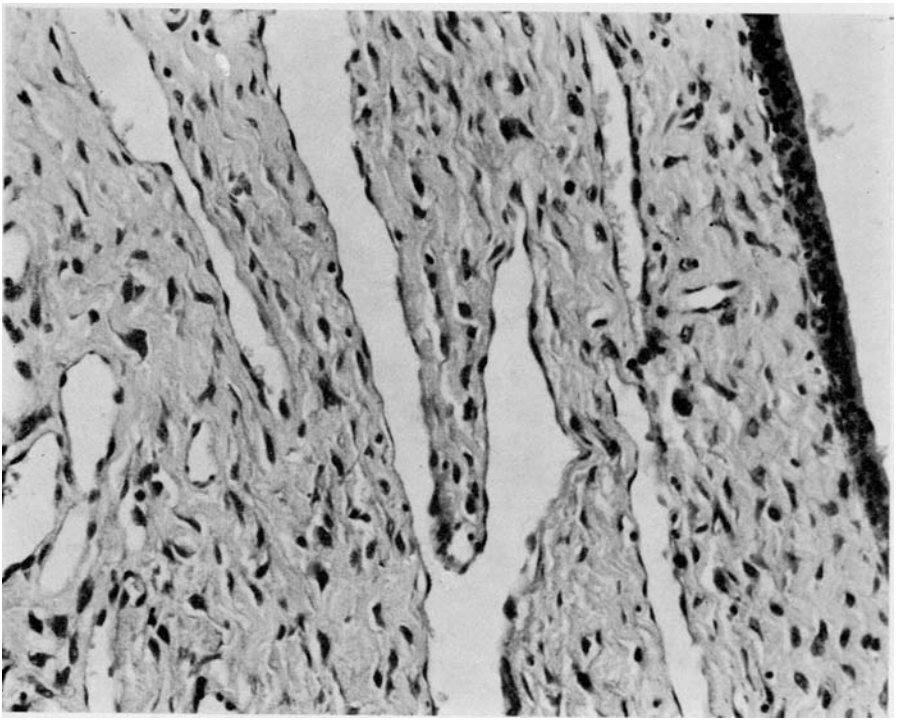


FIG. 4

Shows tumour covered by pseudostratified columnar epithelium. The tumour is composed of a number of thin-walled vascular spaces surrounded by moderately cellular fibrous tissue (H. & E. × 200).

Microscopic examination showed a tumour covered externally in areas by columnar ciliated to pseudostratified columnar epithelium. The tumour was composed of numerous thin-walled vascular spaces of varying shapes and sizes, surrounded by abundant, moderately cellular fibrous stroma. The stromal cells were spindle elongated and were arranged in bundles. The nuclei were by and large thin and spindly. Some of them however were plump but showed no mitotic activity.

Diagnosis: Nasopharyngeal angiofibroma.'

Comment

This curious and controversial tumour has been and will remain intriguing until its true aetiology is known. It almost always originates in the nasopharynx as its name suggests, but isolated lesions have been reported in the posterior end of the inferior turbinate (Weir and Doig, 1960), the sphenoidal sinus (Reddy and Farb, 1963) and the maxillary antrum (Maniglia *et al.*, 1969) in each case without any apparent lesion or origin in the nasopharyngeal walls.

As regards its nature Sternberg (1954) thought it might be a development from an embryonic rest. Harma (1958) and Osborn (1959) suggested that it was not a neoplasm but a proliferation of erectile tissue commencing about the age of

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puberty. Girgis and Fahmy (1973) from their histological studies, considered it to originate in paraganglionic tissue identified in relation to the terminal portion of the internal maxillary artery, and suggested the name 'Glomus Nasopharyngis'. The traditionally postulated theory of age and sex linkages have also stimulated speculation of a hormonal association (Martin *et al.*, 1948; Schiff, 1959; Weir and Doig, 1960; Fitzpatrick, 1970), some of these authors remarking on sexual underdevelopment of some of the patients affected. All three patients described in this paper appeared, clinically, to be of normal sexual development for their ages.

Histologically, nasopharyngeal angiofibroma presents a characteristic picture which is diagnostic, but certain variations as illustrated by the three cases presented here may occur in the histological features. This tumour has two distinct components, one being a vascular network and the other a connective tissue stroma. The vascular component in the first case is rather inconspicuous and is made up of thin-walled slit-like endothelial lined spaces whereas in the second case, the vessels are thick-walled and are prominently seen. The hyalinization and focal calcification of the walls of the blood vessels in this case may indicate a stage of regression of the tumour. The fibrous stroma also shows marked variation in the degree of cellularity. In the first case, the stroma is densely fibrotic and cells are scanty. In the second case, the stroma is markedly cellular and the cells have plump, hyperchromatic nuclei. On casual examination, one tends to be impressed by the cellularity of the tumour and may speculate on the possibility of sarcomatous change. However, closer examination fails to reveal mitotic activity or other cellular features of malignancy. The histology of the tumour in case number three is intermediate to that seen in the other two cases from the points of view of both the prominence of the vascular spaces and the cellularity of the stroma. Variations such as these may be seen not only in different tumours, but also in different areas of the same tumour.

Angiography is a useful line of investigation since it may provide evidence of silent intracranial extension if any, though it may not necessarily demonstrate its full extent. As has been shown in Case 3, angiography may demonstrate the probable nutrient vessel, usually a dilated internal maxillary artery (English *et al.*, 1972; Samy and Girgis, 1967) and thus indicate on which side carotid ligation should be performed if it becomes necessary.

Investigations of sex hormones and chromosomes have so far been only of academic interest with regard to the sex and hormone linkages of the disease, and they have no bearing on treatment or prognosis. The rationale for giving hormones in the form of androgens and oestrogens (Conley *et al.*, 1968; Walike and Mackay, 1970) is now based on the idea that they reduce the vascularity of the tumour and not, as was perhaps previously intended (Martin *et al.*, 1948), accelerate the onset of sexual maturity. Irradiation therapy has been given partly for the same reason but in addition Briant *et al.* (1970) and Fitzpatrick (1970) have claimed improvement or cure in many cases within about two years of starting treatment. However, critics of this form of therapy, among whom are Batsakis *et al.* (1955) and Conley *et al.* (1968), suggest that it might produce malignant change or cause damage to important adjoining structures such as the pituitary gland and the eye.

Surgical excision has always been the most reliable form of treatment but not infrequently has had to be mainly palliative or incomplete when there has been

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risk of damage to important structures. It has been estimated that about 50 per cent of all cases fall into this category and may require as many as five surgical interventions (Hubbard, 1958; English *et al.*, 1972; Conley *et al.*, 1968). Cryosurgery has been used to minimise haemorrhage (Smith *et al.*, 1964; Conley *et al.*, 1968) though it has not always proved successful. Carotid occlusion is considered more effective (Biller *et al.*, 1974). Access to the tumour has been by the sublabial, the transpalatal, or the lateral rhinotomy approach or combinations of these depending on its site, size and direction of spread.

Prognosis depends on a number of factors such as the rate and direction of spread, the unpredictability of serious complications, the unreliability of cessation of activity, let alone of regression, and on the operability of the tumour when first seen. Few deaths have been recorded and malignant changes have rarely been observed (Fitzpatrick, 1970; Hormia and Koskinen, 1969; Figi and Davis, 1950). Although the progress of each of the three cases described has been good, perhaps the long-term prognosis should remain guarded until cessation of activity for at least two, three or perhaps more years is proven; but not necessarily till the reputed age of 'sexual maturity'.

Summary

Three cases of nasopharyngeal angiofibroma have been described along with the histopathological findings, treatment and a brief review of the literature on the subject. It is of interest that one of these cases, histologically proven, was a female and this in spite of some rigidly held views about the strict sex linkage of the lesion. The tumour is uncommon but it is possible that unfamiliarity with the histopathology, as well as the likelihood of cessation of activity at any stage, may in part be responsible for its low recorded prevalence. The progress of each patient after four, two and one year respectively gives cause for some optimism, but the long-term prognosis must remain guarded.

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