Brit. J. Ophthal. (1958) **42**, 212.

PSEUDO-TUMOUR OF THE ORBIT*

BY

HARVEY JACKSON

The National Hospital, Queen Square, and St. Thomas's Hospital, London

THE subject of orbital pseudo-tumour has been selected as one of interest to both the ophthalmologist and the neuro-surgeon: to the ophthalmologist because this is the most common of the expanding, space-consuming lesions to be found within the orbit; to the neuro-surgeon because proptosis is no uncommon manifestation of intracranial disease.

One may well ask what exactly is inferred in the term pseudo-tumour. First of all, let us consider the term as it has been applied elsewhere.

In so far as the neuro-surgeon is concerned, from time to time he encounters a case in which a state of increased intracranial tension presents with minimal or no physical signs as a basis for localization of the lesion. He may even be persuaded to undertake a subtemporal decompression for the relief of intractable headache or threatened visual failure. This sequence of events was more familiar in my early days in neuro-surgery, when I had the privilege and pleasure of working with Sir Percy Sargent, a time when the use of air-studies was not as frequent a measure as it is to-day. Some of Sargent's cases still appear at the National Hospital, continuing well after more than 25 years, perhaps with residual optic atrophy as the sole indication of their once parlous state. We are aware nowadays that such cases are probably explained on the basis of thrombophlebitis, otitic hydrocephalus, or even syphilis, but at one time they were referred to as cases of pseudo-tumour.

Yet other pathological conditions involve the orbit to give rise to clinical appearances mimicking those of neoplastic disease. In certain diseases deposits of different substances are to be found within the orbit: amongst these can be mentioned leukaemia, lipoidosis, sarcoidosis, and reticulosis. The orbital changes in these conditions are mere items in a generalized disorder.

Were the term pseudo-tumour to be applied in such fashion as to imply the existence of an increase in the intra-orbital contents through the formation of a mass of non-neoplastic nature, some conflict of understanding would be likely. Indeed, the inference would be that the term pseudo-tumour applied to any condition likely to be mistaken for neoplastic disease. This, however, is not the case, for the orbital pseudo-tumour is to be accepted as a rather precise form of pathology and not just a loose terminology. What then is it? It is a definite granulomatous mass, possibly of infective origin. Now it is not to be supposed that one type of granuloma, and one only, is to be found, for one may meet a number of different forms of granuloma affecting the

* Read at the combined meeting of the Society of British Neurological Surgeons and the 36th Annual Meeting of the Irish Ophthalmological Society in Dublin, May 16–18, 1957.

orbit. It is not unknown for one to encounter a tuberculous or syphilitic lesion, especially in foreign lands, although these pathologies are infrequently seen in England to-day. The writer has met only one case of each of these diseases in a large series of cases of orbital disease.

In spite of the above comments, it would certainly be unwise to omit regular blood examination in exclusion of syphilis in all cases of proptosis, but a positive Wassermann reaction does not necessarily indicate the underlying pathology. Recently the writer was referred a case in which penicillin had been administered, with immediate though temporary improvement, on the assumption that a gummatous infiltration existed, owing to the finding of a strongly positive Wassermann reaction. Rapid deterioration followed, with the result that a biopsy was undertaken; this confirmed the presence of a granuloma but it was not of a syphilitic nature.

Whilst the term orbital pseudo-tumour has been adopted by many clinicians, there are those who decry its use, others who suggest that it should be applied to supposedly neoplastic states where no tumour is found, and yet others who include a variety of granulomata involving the orbit, whether tuberculous, syphilitic, or of other causation.

The first description of the condition was made by Busse and Hochheim (1903), but it was Birch-Hirschfeld (1905) who labelled it "pseudo-tumour". Birch-Hirschfeld classified his cases into three groups:

(1) Exophthalmos, displacement and disturbed mobility, but exophthalmos cured by medicinal means—potassium iodide and quinine—of syphilitic, tubercular or haematogenous causation, although known tests failed to substantiate.

(2) Clinical diagnosis orbital tumour, but no tumour found at operation. Probably included some due to thyroid disease, varicose veins, diffuse lymphoblastoma.

(3) Abnormal mass of chronic inflammatory process of a non-specific nature, containing diffuse follicular areas. No evidence that poisoning or avitaminosis, climate, heredity, diet, allergy, glandular dysfunction, trauma, or occupation plays any part.

The subject appears to have lost attraction at this stage, for the literature is noticeably lacking until a monograph entitled "Les myosites orbitaires" was published by Offret (1939). Herein he describes 34 cases, of which six were tuberculous, five were syphilitic, and 23 of unknown nature. Offret held the opinion that the essential process was one of chronic endophlebitis related to a chronic sinus infection.

Dunnington and Berke (1943), who included endocrine cases, further complicated the subject by describing five groups:

(1) Syphilitic
(2) Tuberculous
(3) Myasthenia Gravis and Muscular Dystrophy
(4) Exophthalmic Goitre
(5) Idiopathic

Thus these authors confounded the changes of endocrine exophthalmos and pseudo-tumour.

My personal experience of the different types of granuloma to be found in 37 cases does not in any way differ from what can be surmised from the writings of the authors already mentioned. My impression, whether right or wrong, is that the term pseudo-tumour tends to be applied to any state simulating that induced by new growth. I should like to submit that the subject is by no means so negative, so far as identification on clinical grounds is concerned.

INCIDENCE

So far, a case of pseudo-tumour has not occurred in my series under the age of 24 years, but nearly all ages have been affected up to 75 years, the average age of my patients being 47·6 years. The relative incidence in my series of cases of proptosis is 12·3 per cent., for there have been 36 cases in 293 patients.

Of all the many causes of proptosis encountered by me, granulomatous diseases are the most frequent.

The two sexes appear to be involved differently, for the cases concerned included 25 women and only eleven men.

There would seem to be no special reason for a predilection for either side, yet the right side was involved in fourteen patients, and the left in eighteen. In some patients both orbits may be affected, usually at different times, the intervening period varying considerably in different cases. All four of my patients who developed bilateral disease were women.

The course of one of these was as follows (Figs 1 and 2, opposite):

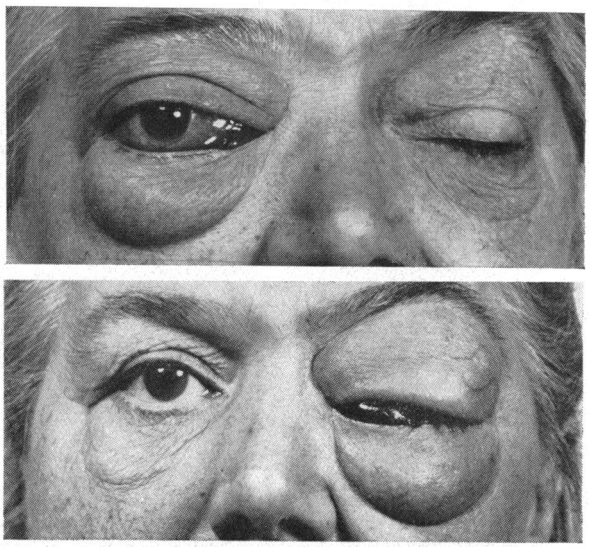
Case 1, a woman aged 52 years, presented with a history of 6 months' painless protrusion of the left eye.

Examination.—There was proptosis of 9 mm. (the eye being displaced downwards and outwards), chemosis, epiphora, and ptosis. The ocular movements were impaired, especially upwards and downwards. A firm mass was palpable in the upper and inner part of the orbit. The visual acuity was 6/9 in the right eye and 6/36 in the left; the fundi were normal and the visual fields full.

Operation (15.6.45).—Left orbital decompression was carried out; the localized mass was not excised but a portion was taken for biopsy. The histological report stated that the tumour consisted of lymphoid tissue, reticulum cells, and numerous eosinophils. The appearances might be those seen in lymphadenoma or other reticulosis.

Progress.—In September, 1948, the patient reported that she was well.

In September, 1952, she had an attack of acute nasal catarrh and both eyes became bloodshot. There was oedema of the right lower lid, chemosis, and proptosis, the eye catching on her glasses. The external ocular movements were much decreased on the right side, and in September, 1953, there was papilloedema of the right eye.



FIGS 1 and 2.—Right and left eyes involved but with a considerable period intervening.

In December, 1953, the papilloedema was less, the right eye much improved, and the left eye again more troublesome.

In September, 1954, a nodular mass was again palpable in the left upper lid. The proptosis was now right: 17 mm. and left: 20 mm. The visual acuity was 6/12 in either eye. A further biopsy done at this time gave lymphoid tissue with many mitotic figures.

PATHOLOGY

The actual nature of the orbital pseudo-tumour is that of a chronic granuloma, but structurally the components vary in their representations. The cellular content consists of lymphocytes and plasma cells with irregularly interspersed eosinophilic cells. The lymphocytes tend to be arranged in follicular formations. Fibrosis is present in a varying amount, some lesions being constituted largely of collagenous material, others being much more cellular.

Certain changes are to be seen in the extra-ocular muscles: striation disappears and the fibres stain poorly. The inferior rectus and the inferior oblique are more prone to be involved than the other muscles. These muscular changes have been taken as evidence that the disorder is a primary change in the muscles, hence the title of chronic orbital myositis applied by Dunnington and Berke (1943).

However, the infiltrations are not in any way restricted to the muscles but extend amongst the orbital tissues. The nerves may become invested but do not show evidence of implication. In fact, they appear to be very resistant to the process. The limitation of ocular movement common to the disorder is the result of infiltration of the muscles and not to paresis from nerve

involvement. Usually the mass is within the muscle cone, but it may be attached to the orbital periosteum (Figs 3, 4, 5, and 6).

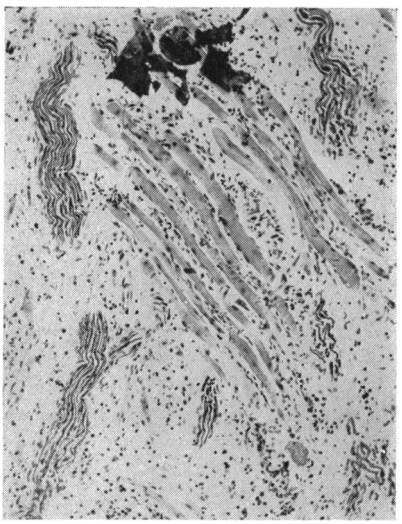


FIG. 3.—Follicular arrangement of lymphocyte cells. Oedema of extra-ocular muscles.

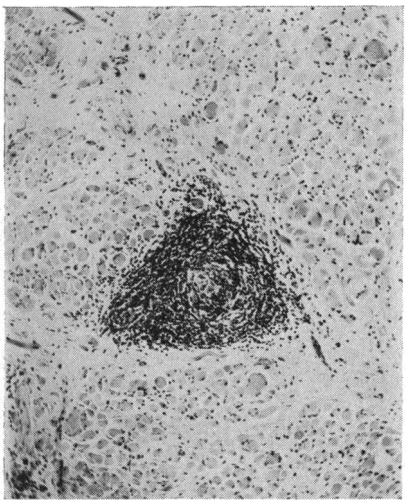


FIG. 4.—Rather diffused infiltration with inflammatory cells. Separation of muscle fibres by oedema. Preservation of nerve tissue.

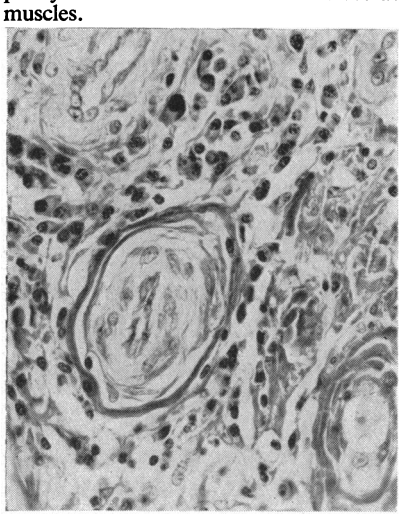


FIG. 5.—Infiltration by inflammatory cells of both lymphocytic and plasma cell types.

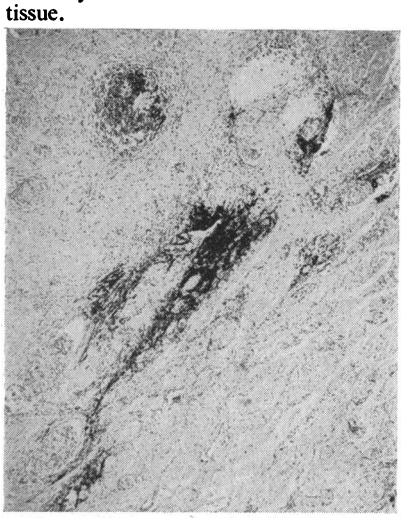


FIG. 6.—Follicular formations of lymphocytes. Degeneration of muscle fibres.

Whatsoever the agent of causation, the fact that the part of the orbit most often involved is the inner wall and the floor is suggestive that relationship with accessory sinuses bears import. In addition, the muscles most often involved are the inferior ones. The inference is that the granuloma results from chronic infection, most likely of sinus origin. That the condition is inflammatory in nature seems likely from the variability in the intensity of the

reaction, the intervention of pain, congestion of the sclera, and chemosis. But the nature of the agent responsible for the reaction is difficult to ascertain. No specific organisms have been isolated; indeed, no causative organism has been found in the cultures taken from some of my own cases, nor has anything been cultured on animal inoculation.

It is not to be surmised that one and only one form of granuloma does occur. Excluding known pathologies such as tubercle, because these are well recognizable, there are other definitely infective granulomata.

In one case in the writer's experience, a mass developed in the orbit of a patient in whom a suspicious solitary shadow was revealed on radiography of the chest. The natural assumption was that the orbital lesion was of metastatic nature originating in a primary malignancy of the lung, but both masses proved in due course to be granulomata.

It is to be noted that infective lesions within the orbit in the way of abscess, cellulitis, and infection associated with foreign bodies have been encountered, but none of these disorders is included in my collection of pseudo-tumours.

As a result of my experiences I am becoming persuaded into considering the possibility that the lesion we have under review is one of a rather specialized form in some way related to the air passages. My attention has also been drawn to comparable disorders occurring in the lung.

DIAGNOSIS

PROPTOSIS

Wherever an expanding, space-consuming intra-orbital mass develops, proptosis is to be expected. Are there any points relative to the proptosis suggestive of the underlying pathology? Undoubtedly the duration of the patient's disorder excludes certain possibilities, particularly when the history is of long standing. One of the main lesions to be differentiated from pseudo-tumour is malignant disease, for both can be of short duration. But a pseudo-tumour may prove to have been in existence for several years, in which case the history usually affords evidence of variability, perhaps in the degree of prominence of the eye, perhaps in the intensity of other symptoms.

PAIN

Though not an essential accompaniment of a granulomatous disorder, pain is quite a frequent feature. The distribution of the pain is not indicative, for it may affect the eye or be referred to the frontal or temporal region. The intensity varies considerably in relationship with any tendency to activation in the lesion. The onset of pain late in the history of any orbital disease may have more serious implications, perhaps indicating some superimposed change.

Pain is not by any means a common feature of disease within the orbit. Its very presence calls for special attention, for innocent new growths are not usually associated with pain. The presence of pain as a complaint from the early days of a recognized disorder should call for alertness in excluding malignant disease. In the writer's experience, pain as a manifestation of a

benign tumour has appeared only in the presence of a neurofibroma, except in the very late stages.

Modes and Modifications

The variability in the symptomatology which seems to characterize the pseudo-tumour is by no means restricted to this one pathology, for one meets a variable degree of proptosis in haemangioma. With the tumour of vascular genesis, however, pain is not a feature. Several factors contribute to the explanation of the variations. First is the general state of the patient, for any intercurrent illness tends to give rise to an exacerbation of activity in the orbital lesion. The writer has observed such a reaction in different patients with an influenzal attack, an outcrop of boils, acute appendicitis, chest infections, dental abscess, and even episodes of acute acne.

In female patients a not uncommon factor in this rather fluctuating course is the influence of menstruation. What part this plays is explained by more than one effect. No doubt the physical and emotional responses of a woman are apt to be influenced thereby; but the congestive response is probably influenced by hormonal changes in addition to the rather oppressive weariness and reduced tolerance attendant on menstruation.

Restricted Ocular Movements

Ocular movements are usually affected, but the extent of the restriction differs between the limitation of upward movement, upward and outward movement, and complete immobility. The basis of this diminished action is the infiltration of the extra-ocular muscles in the granulomatous formation. Once affected, it is exceptional for full and complete restoration of movement to take place; diminution of upward movement is a common residual finding. As stated previously, the inferior rectus and inferior oblique muscles are those most often involved. There is generally no suggestion of actual paresis, indeed, the oculo-motor nerves, although surrounded by cellular masses, are particularly insusceptible, and no evidence of degeneration has been found.

Changes in the Fundus Oculi

No specific changes take place, in fact the optic disc may remain normal; alternatively, gross papilloedema is seen from time to time. Any prolonged disorder is apt to be accompanied by optic atrophy. Occasionally one may see oedema of the retina as well as of the disc. More often than not, no change is to be seen. Once again, it is worthy of mention that the existence of papilloedema together with pain in a case of short history should arouse concern lest a malignant growth be present.

Disturbance of Vision

Interference with vision applies mainly to visual acuity and duplication. One would have thought that, as defective mobility of the eye is a common feature, double vision would occur with regularity, yet this appears in only about half the cases. Visual acuity comparable with that of the good eye is quite common, and field defects are exceptional on ordinary testing.

PALPABLE MASS

From time to time a mass is palpable at the orbital outlet, being usually situated medial to the eye. No known physical characteristics enable the nature of the mass to be recognized, although other manifestations may enable a diagnosis to be reached.

CONFIRMATORY INVESTIGATION

In the writer's opinion, the various data herein described should be so informative as to permit the true pathological diagnosis to be reached in a high proportion of cases. What confirmatory evidence then should be sought? Certain investigations are routine; these include blood counts, sedimentation rates, serological reactions for syphilis, and radiography.

In so far as the pseudo-tumour is concerned, little confirmation is required, but differentiation from, or the exclusion of, other pathologies may be advisable.

Other tests will be indicated by the clinical state of the patient. Should the clinical condition be considered indicative of intracranial extension, for instance, analysis of the cerebro-spinal fluid may be helpful.

Naturally, when malignant disease is to be surmised, one must consider whether it is likely to be primary or secondary, and if the latter, where the source is situated.

Radiology.—The aid forthcoming from radiographic examination is rather of a negative quality. Plain *x* ray is generally negative, although soft tissue penetrations can reveal the presence of associated oedema through the blurring of details.

Should the mass extend through the sphenoidal fissure, this channel may be shown to be dilated in comparison with the normal side. This occurred only once or twice in my own series (Fig. 7).

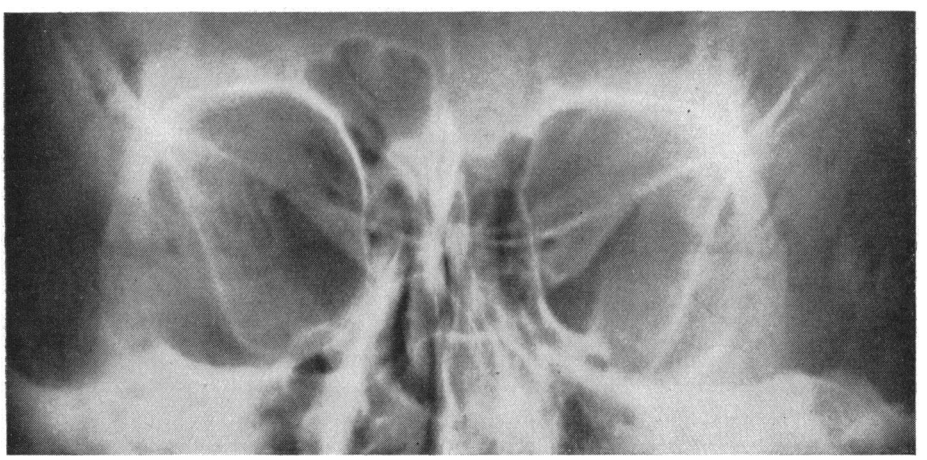


FIG. 7.—Distension of sphenoidal fissure. Mass extending from the orbit into the middle fossa.

Several of the cases in my series had been investigated by the neurologist before reaching the neuro-surgeon, largely with a view to the diagnosis of intracranial tumour. Some of these patients had been subjected to pneumo-encephalography, and also arteriography, with negative findings. Rarely, in fact, are these procedures worthwhile unless there is other evidence to suggest that a lesion is of orbito-cranial distribution (Figs 8, 9, 10, and 11).

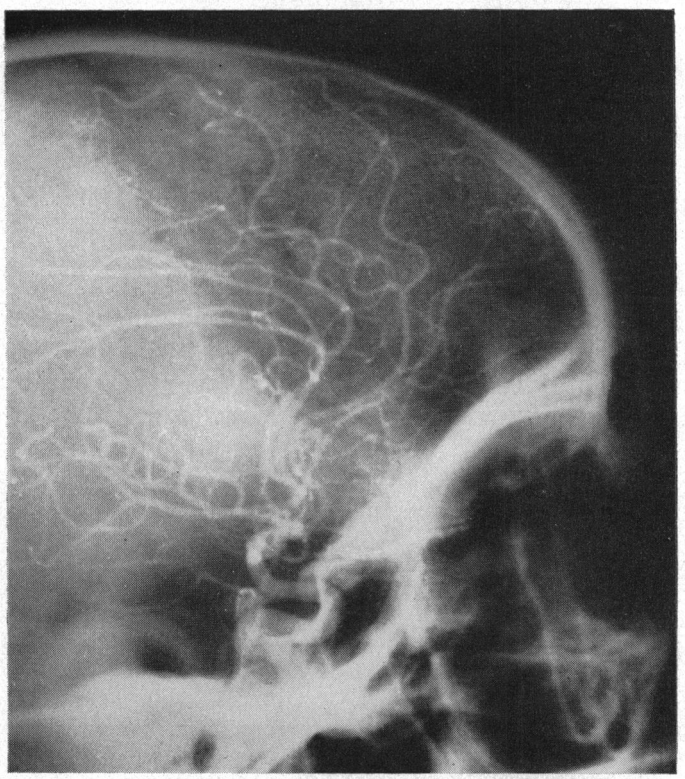


FIG. 8.—Opening up of carotid siphon by tumour extension, lateral view.

We are encountering some very strange types of granulomatous masses in patients from the Mediterranean area and the Middle East, and some of these lesions have involved the brain also. Whether they are all of one cause from the infective aspect one cannot as yet determine.

Case 2, a Greek woman, 25 years of age, presented with pain over and around the right eye for a period of 5 months. In addition, there was right temporal headache. Shortly after the onset she noticed that vision in the right eye was defective, and in the course of 3 or 4 days she became unable to see with it. Proptosis was noted from the beginning.

Examination.—Irreducible proptosis in the right eye, with right ptosis. Visual acuity 6/60 in the right eye and 6/12 in the left. The right pupil was larger than left, and reacting sluggishly.

Laboratory Investigations.—Blood count (white blood cells) 10,000: polymorphs 63 per cent., leucocytes 32 per cent., monocytes 4 per cent., eosinophils 1 per cent.

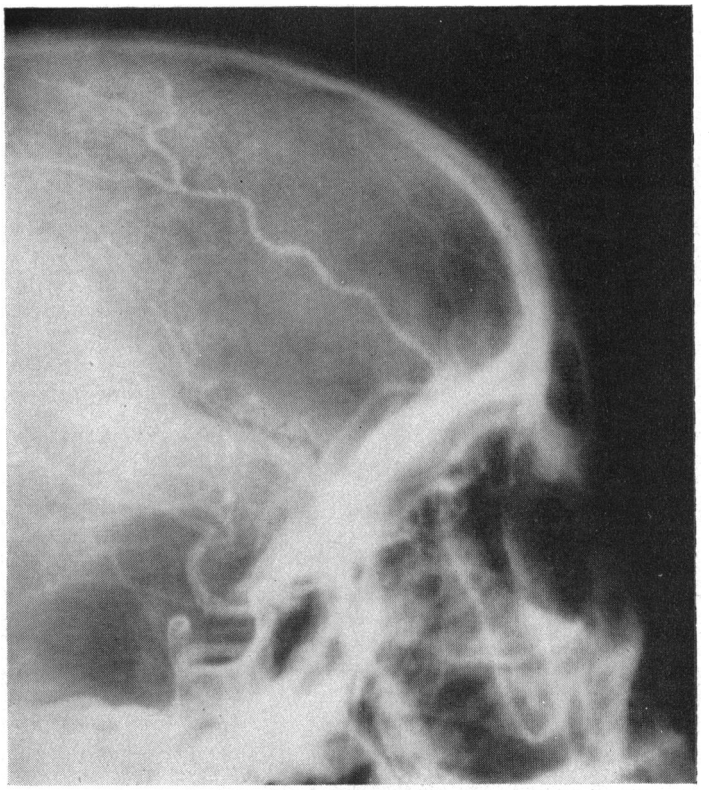


FIG. 9.—Opening up of carotid siphon by tumour extension, lateral view.

Erythrocyte sedimentation rate 26:39. 28:41.
Wassermann reaction negative in blood and cerebrospinal fluid.
Cerebrospinal fluid total protein: 45 mg. per cent., 2 cells; Lange: 3322211000.
Skull *x* ray showed a dilated sphenoidal fissure.

Owing to the cerebrospinal fluid protein and Lange count, it was felt that some intracranial extension of the disease existed. Consequently it was decided to submit the patient to arteriography. The arteriogram shows an informative displacement of the right middle cerebral artery.

Operation.—Exploration was decided upon, the operation to expose the middle fossa as well as the orbit. The day before operation she was seized by a generalized convulsion, an event that verified the invasion of the cranial cavity. At operation a granulomatous mass was found to involve the posterior extension of the orbit, track through the sphenoidal fissure, and involve the meninges within the middle fossa. A portion of the dura mater was excised over the temporal pole, thereby exposing a whitish thickening of the arachnoid extending along the superficial cerebral blood vessels.

Histological Report.—The leptomeninges are thickened through infiltration by round cells, plasma cells, polymorphs, and some endothelial cells.

It is not suggested that this is a typical pseudo-tumour, but it is one of the forms of granuloma one may meet. No micro-organism could be seen in sections, and nothing was grown on culture.

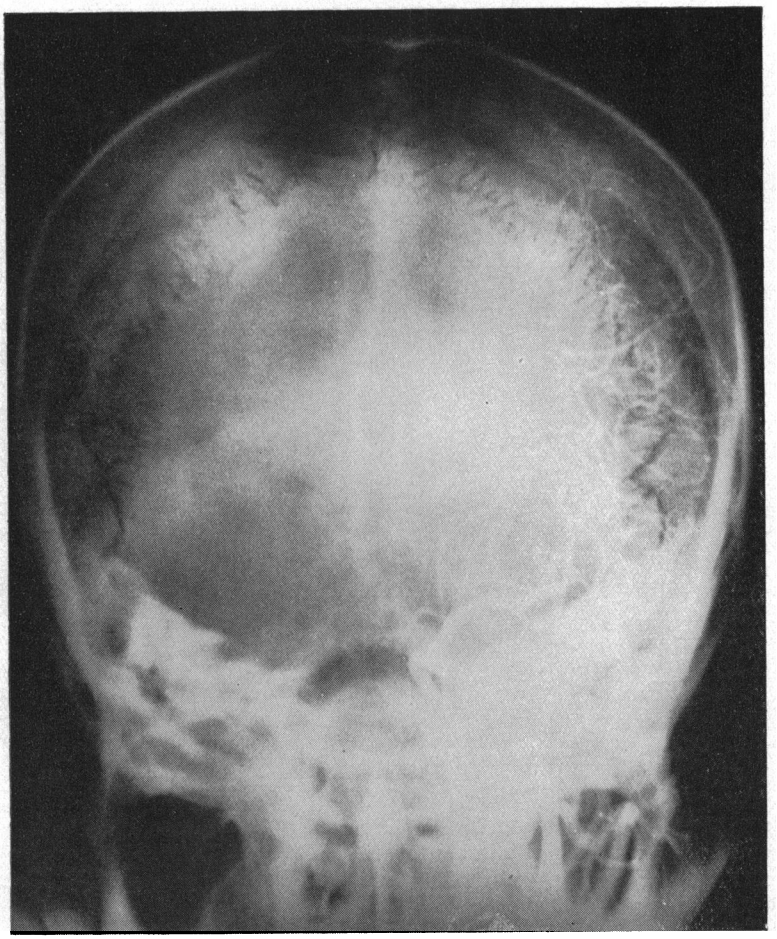


FIG. 10.—Deviation of middle cerebral artery displaced by posterior extension.

TREATMENT

Where the history is of such duration, or so definitely remittent that one feels confident that malignant disease can be excluded, one can feel justified in observing the effects of conservative treatment, but should any doubt exist it is desirable that a biopsy be carried out before any treatment is undertaken. With a positive pathological proof or adequate clinical assessment, it is worthwhile to try the effect of iodide and mercury, and perhaps also arsenic even though syphilis is not suspected. These several elements can be exhibited in the form of Donovan's solution (Mist. hydrarg. et arsen. iod.). Many cases under my care have made such satisfactory response to this treatment that resolution of the process has followed, with almost if not complete recovery. I saw almost complete recovery in some cases, though upward movement of the eye does not invariably return to the full.

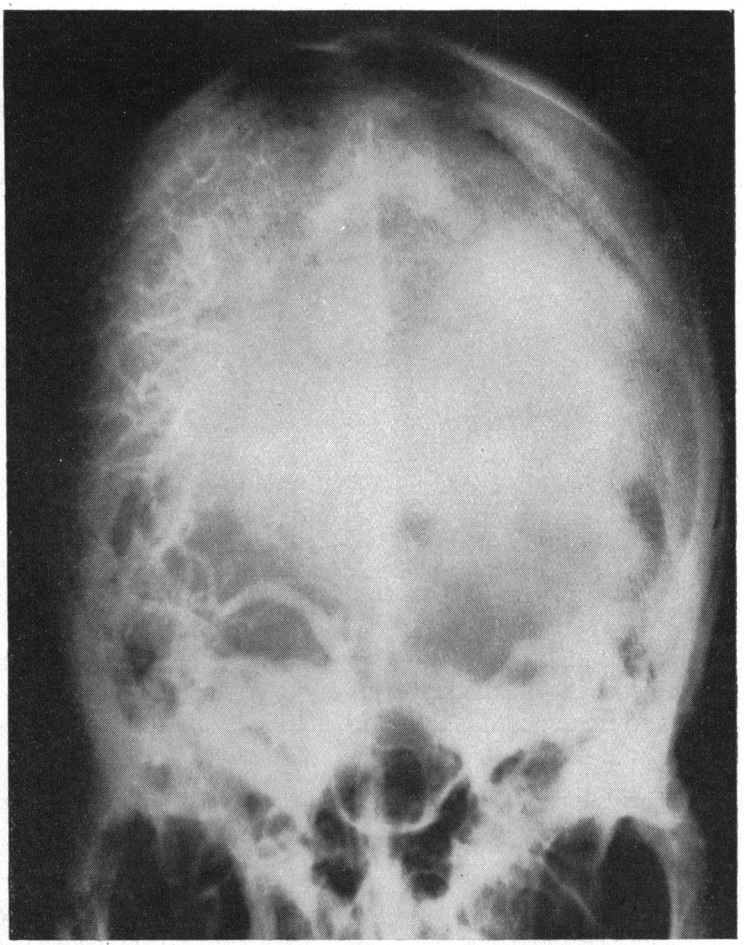


FIG. 11.—Deviation of middle cerebral artery displaced by posterior extension.

Case 3, a woman aged 67, attended because of shooting pain in the right temple, extending to the vertex, of about 12 months' duration. Visual acuity became defective after a few weeks so that by the time she was seen she could only recognize hand movements with the affected eye, whilst the visual acuity in the left eye was 6/9. She had a moderate proptosis with ptosis. Her blood pressure was 260/120. The optic disc showed slight pallor. *X* rays were negative. Altogether a rather difficult decision was called for, but the serious possibility of a malignant condition seemed to require exclusion. However, the patient refused admission to hospital and remained adamant despite due warning. She was put on Donovan's solution against one's wishes, but after 10 months the ophthalmic condition had resolved and there remained only slight limitation of upward movement.

In the absence of a satisfactory response one has to consider other forms of medicinal treatment. It is then that cortisone may be given trial.

The question of further surgical treatment applies only where a satisfactory response is not forthcoming, and then only if associated signs are such that some relief is essential. Tarsorrhaphy may be required in control of

excessive chemosis. Gross displacement of the eyeball may need orbital decompression. Finally, it may well be advisable to resort to the local removal of a mass, if only for cosmetic purposes (Fig. 12).

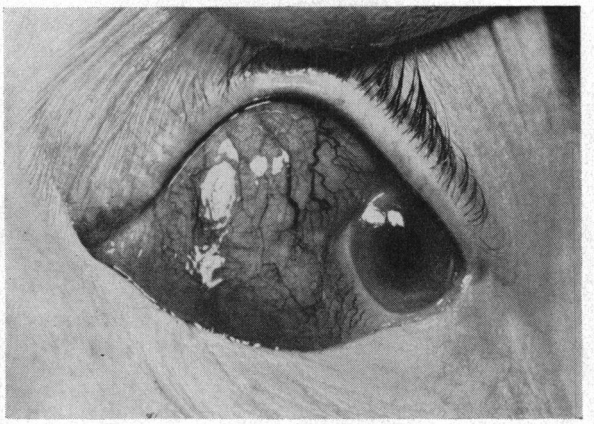


FIG. 12.—Large protuberant mass under conjunctiva for which local excision was carried out.

Finally, if other methods fail to give relief, deep *x*-ray therapy may help. In so far as this last form of treatment is concerned, the writer has had no personal cases so treated and is therefore unable to offer any advice or record of its application.

My grateful acknowledgements are due to the Departments of Pathology, Photography, and Radiology, at The National Hospital, Queen Square, London.

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