Three patients with intracranial tuberculomas with unusual features

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SYNOPSIS  Three patients with verified intracranial tuberculomas are reported. One patient presented with attacks of hydrocephalus initially diagnosed erroneously as migraine, another had multiple tuberculomas and a fourth tuberculoma became apparent during treatment with antituberculous therapy. The third patient presented with a frontal lobe syndrome and the postoperative recovery was complicated by the development of hyperosmolar non-ketotic, non-acidotic diabetic pre-coma. Although there are no pathognomonic symptoms, signs, or radiological appearances of intracranial tuberculomas, a high index of suspicion should always be entertained during the investigation of non-European immigrants.

Before 1900 tuberculomas constituted a third of all intracranial tumours and more than 50% of intracranial tumours in children (Starr, 1889). In 1933 a survey of postmortem records (Garland and Armitage, 1933) revealed that 34% of all cerebral tumours were tuberculomas. By 1940 an analysis of 2,190 brain tumours collected from recent reviews (Wilson, 1940) showed that only 3.6% were tuberculomas and a more recent review (Maurice-Williams, 1972) demonstrated an incidence of 0.15% among 2,200 intracranial tumours seen at the Guy's-Maudsley neurosurgical unit from 1951–1972.

In 1970 Kocen and Parsons (1970) drew attention to some unusual neurological complications of tuberculosis, particularly in non-European immigrants, though none of their patients had intracranial tuberculomas. We wish to report three patients with verified intracranial tuberculomas who have presented to this unit in the past 12 months.

CASE 1

J.A., a 28 year old Indian engineer from Tanzania, had lived in England for five years. At the age of 26 years he had a dry cough which lasted for two weeks and a routine radiograph of the chest showed right hilar lymphadenopathy. He received no specific treatment and a chest radiograph five months later was normal. Thereafter he remained well until five months before admission when he developed intermittent severe occipital headaches which on occasions were associated with teichopia in the right homonymous visual field, nausea, and neck stiffness. Apart from a recent febrile illness, his general health was good. There was no relevant past medical or family history.

On admission to a local general hospital he was pyrexial (38.2°C), but otherwise examination was normal. Routine haematological and biochemical investigations were normal apart from a raised erythrocyte sedimentation rate of 40 mm in one hour. Examination of the cerebrospinal fluid and radiographs of the chest and skull were normal. The pyrexia and headaches continued and he was transferred to the Regional Neurological Centre, Newcastle upon Tyne. Apart from mild discomfort on extension of the neck, neurological examination was normal. He continued to show a regular evening pyrexia and seven days after admission he suddenly became unconscious and apnoeic and required artificial ventilation. The right pupil was pinpoint and the left normal in size but unreactive to light. After 15 minutes he regained consciousness, his pupillary reflexes returned but both fundi showed papilloedema and haemorrhages. An emergency pneumoventriculogram showed equal and marked dilatation of both lateral and the third ventricles and a space occupying lesion in the vermis of the cerebellum.

At operation (Professor Hankinson) a small firm irregular tumour was removed from the vermis. Histological examination revealed a necrotizing epi-
thelial and giant cell granuloma from which *Mycobacterium tuberculosis* was cultured. The patient was treated with dexamethasone, para-aminosalicylic acid, isoniazid, and streptomycin and made a satisfactory recovery.

**CASE 2**

B.S., aged 16 years, was born in Newcastle upon Tyne of Asian parents. Shortly after the patient's birth her father developed pulmonary tuberculosis and she was given BCG vaccination. The father's tuberculosis recurred in 1970, though during this time the patient received no chemotherapy. Her mother and one sister also had a history of previous tuberculous infection.

The patient was in good health until March 1971 when she developed anorexia, nausea, night sweats, and a non-productive cough. She was admitted to Newcastle General Hospital and a diagnosis of miliary tuberculosis was made and this was confirmed bacteriologically.

Treatment was commenced with streptomycin 0.75 g daily, isoniazid 300 mg daily, and ethambutol 1 g daily with progressive improvement in her symptoms and in the appearance of the chest radiograph. After three months the streptomycin was stopped. She received the remaining two drugs regularly for nine months but during two subsequent months the antituberculosis therapy was taken irregularly. At this time she developed generalized throbbing headaches and experienced an isolated episode of loss of consciousness. On recovery neurological examination was normal. An electroencephalogram showed no localizing features and examination of the cerebrospinal fluid revealed no abnormalities. During the following two months the headaches increased in severity and one week before admission to the Regional Neurological Centre she became aware of intermittent diplopia.

On examination the patient was apyrexial. She had bilateral papilloedema with haemorrhages and two choroidal tubercles in the right fundus but otherwise examination was normal.

A full blood count and routine biochemical tests were normal apart from an erythrocyte sedimentation rate of 30 mm in the first hour. A radiograph of the chest revealed no abnormality but that of the skull showed demineralization of the dorsum sellae and clindom processes. A 99technetium brain scan demonstrated three areas of increased uptake in the left temporal, parietal, and parieto-occipital regions. An electroencephalogram was diffusely abnormal and dominated by persistent underlying delta activity and a left carotid angiogram showed displacement of the anterior cerebral artery and internal cerebral veins to the right by 8 and 7 mm respectively.

A diagnosis of intracranial tuberculomas was made and she was treated with dexamethasone, streptomycin, isoniazid, and rifampicin with progressive improvement of her headaches and the fundal appearances.

Three months later the patient was readmitted with a six day history of severe right hemicranial headaches. On examination she was apyrexial. There was tenderness to percussion over the right parietal region, mild neck stiffness, and bilateral papilloedema. The choroidal tubercles were still evident in the right fundus, but otherwise examination was normal. A 99technetium brain scan now showed a fourth area of abnormal activity in the right parieto-occipital region. The antituberculous therapy was changed to pyrazinamide 1 g twice daily, prothionomide 500 mg twice daily, isoniazid 600 mg daily, ethambutol 1,200 mg daily, and rifampicin 600 mg daily and, in view of the progressive nature of the disease, it was decided that surgical intervention was necessary to obtain tuberculous material for culture and sensitivity studies. At operation (Mr. Kalbag) three tuberculomas were found in the left cerebral hemisphere, on one of which a biopsy was carried out. Acid-fast bacilli were seen on direct microscopy and histological examination showed a necrotizing granuloma. Unfortunately, no organisms could be cultured and guinea-pig inoculation was negative.

The above antituberculous regime was continued for three months when it was reduced to rifampicin and isoniazid. During this period she complained of listlessness, difficulty in concentration, impairment of recent memory, and depression. Although these symptoms have slowly improved it has been impossible to wean her from the dexamethasone as a reduction below a dosage of 1 mg daily resulted in headaches and papilloedema.

**CASE 3**

C.K., a 42 year old Indian lady who has lived in Great Britain for six years, was referred to a general hospital for investigation of a persistent vaginal discharge. Histological examination of a cervical biopsy revealed chronic granulomatous tissue and *Mycobacterium tuberculosis* was cultured from the biopsy material. Treatment was commenced with streptomycin, isoniazid, and rifampicin. During this time it was noted that her behaviour was odd, a radiograph of the skull revealed erosion of the pituitary fossa and she was transferred to the Regional Neurological Centre.

The patient spoke no English but from her relatives
we learnt that there had been progressive deterioration
in her personality and memory during the previous
two years: she had been acting strangely and on
occasions had been found wandering in the streets by
the police. She had complained of intermittent
frontal headaches which in recent months had be-
come more severe and during the previous four weeks
had become confused and disoriented. There was a
vague history of visual deterioration and unstead-
iness on walking, but no symptoms suggestive of
pituitary failure. There was no relevant past medical
history or family history.

On examination she was drowsy but rousable
though cooperation was poor. There was no papil-
oedema or optic atrophy, the uncorrected visual
acuity was 6/24 bilaterally but because of the
language barrier and personality change the visual
fields could not be charted. The other cranial nerves
were normal. Tone, power, and coordination of the
limbs was normal but there was slight reflex domi-
nance in the left lower limb associated with an equi-
 vocal plantar response. There was no apparent
sensory deficit.

Normal investigations included a full blood count
and erythrocyte sedimentation rate, serum urea and
electrolytes, calcium, phosphate, serum trans-
aminases, and thyroid function tests. A glucose
tolerance test showed a latent diabetic curve. Exami-
nation of the cerebrospinal fluid revealed one white
cell per cu mm and 50 mg/100 ml. of protein. The
chest radiograph showed diffuse pulmonary shadow-
ing in a peribronchial distribution above the right
hilum and that of the skull enlargement of the pitui-
tary fossa with complete destruction of the
dorsum sellae and posterior clinoid processes. A
99technetium brain scan revealed an area of in-
creased uptake to the right of the midline in the
suprasellar region and bilateral carotid angiography
confirmed the presence of a large suprasellar space
occupying lesion which had totally obstructed the
right anterior cerebral artery and partially obstructed
the left. A pneumoventriculogram demonstrated a
tumour lying in the region of the genu of the corpus
callosum, anterior margin of the foramen of Monro,
and lamina terminalis, which was causing partial
obstruction of the foramen.

At operation (Professor Hankinson) the pole of
the right frontal lobe was removed to expose a
yellow, firm, lobulated tumour, 5 cm in diameter,
which originated from a small area on the right side
of the falk. The macroscopic appearance was sug-
uggestive of a meningioma but histological examina-
tion showed that the bulk of the tumour was acellular
and necrotic and surrounded by tuberculous granula-
tion tissue. In Zeil-Neilson stained sections a small
number of acid-fast bacilli were found.

The patient made an uneventful immediate post-
operative recovery, but remained confused, dis-
oriented and incontinent. Blood glucose estima-
tions were initially normal but three weeks after the
operation she became drowsy and the biochemical
tests showed marked abnormalities, glucose 520 mg/
100 ml., sodium 174 mg/l., potassium 3:5 mEq/l.,
chloride 127 mEq/l., bicarbonate 27 mEq/l., and
urea 85 mEq/l. A diagnosis of hyperosmolar, non-
ketotic, non-acidotic diabetic pre-coma was made
and the patient was treated with large quantities of
intravenous fluids and insulin with progressive im-
provement. Three months later, although she was
fully mobile, there had been no change in her mental
state or incontinence. She required no hypoglycaemic
agents and a glucose tolerance test showed a normal
response.

DISCUSSION

Although now rare in Great Britain, tubercu-
losmas still represent a significant proportion of
intracranial tumours in the world, varying from
2-4% in Japan (Katsura et al., 1959) and 15% in
Chile (Assenjo et al., 1951) to 30-5% in Bombay
(Dastur and Desai, 1965).

They may present with equal frequency in the
supratentorial and infratentorial compartments
and occur most frequently in the first three
decades of life. Symptoms of raised intracranial
pressure are the usual presenting features but
there are no specific symptoms or signs which
distinguish them from other intracranial tumours
(Sibley and O'Brien, 1956; Dastur and Desai,
1965). Tuberculosis elsewhere in the patient is a
common finding (Dastur and Desai, 1965)
though as many as 50% may have a negative
chest radiograph. A family history of tuberculosis
is variable but may be a useful diagnostic clue if
present.

It is uncommon to see calcification of tubercu-
losmas on plain skull radiographs, the incidence
varying from 0-6% (Sibley and O'Brien, 1956;
Ramamurthi and Variadarajan, 1961) and con-
trast radiology shows no diagnostic features. A
sudden reduction in calibre of blood vessels
traversing the tumour, such as occurred in case 3,
should arouse one's suspicions but is not patho-
gnomonic (Dastur and Desai, 1965). Although
angiography usually reveals an avascular space
occupying lesion, subcortical tuberculomas may
show a mild increased vascularity resembling that
of low grade meningiomas (Ramamurthi
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and Varadarajan, 1961). Brain scanning is a comparatively recent diagnostic technique used in the investigation of cerebral pathology and for this reason has not been available in those countries where tuberculomas are most common. Cases 2 and 3 showed a markedly abnormal uptake of the isotope, presumably due to surrounding oedema and local disturbance of the blood-brain barrier, and scanning may prove to be a useful screening procedure. It is important to realize that the presence of multiple areas of increased uptake should not always lead to the conclusion that the patient has multiple tuberculomas (see case 2).

At operation a tuberculoma may resemble a low grade astrocytoma, a metastatic lesion or, as 50% may have dural adhesions (Dastur and Desai, 1965), a meningioma. This is of some importance at operation, for if this fact is not appreciated the specimen may be fixed in formalin and the opportunity of obtaining material for culture and sensitivity studies is lost. The incidence of multiple tuberculomas is variable; they are not mentioned by Dastur and Desai in their series of 114 verified tuberculomas but Castro and Lepe (1963) quote an incidence of 16% and Asenjo et al. (1951) found 32% of multiple tuberculomas in their material.

All three patients were Asians. Case 1 presented with intermittent attacks of hydrocephalus diagnosed erroneously as migraine. Case 2 presented with a classical history of raised intracranial pressure and her past medical history and family history suggested the probable diagnosis. An unusual feature was the development of a fourth tuberculoma while on adequate antituberculous therapy, though recurrences elsewhere in the body in patients on long-term therapy have been reported previously (Dastur and Desai, 1965). As the patient was in hospital when this fourth lesion developed, she was known to have received regular antituberculous medication and drug resistance was therefore thought to be the probable explanation. However, a change in the antituberculous therapy produced little improvement. Although the patient has symptomatically improved, the brain scan 12 months later still demonstrated four areas of abnormal uptake and on each occasion that the dexamethasone has been withdrawn the headaches returned and papilloedema became evident. The explanation of this is not clear but benign intracranial hypertension secondary to long-term steroids appears unlikely. The confusion, personality change, and progressive dementia in the third patient were undoubtedly related to interference with the blood supply to the frontal lobes. The hyperosmolar, non-ketotic, non-acidotic diabetic pre-coma which complicated postoperative recovery was presumably precipitated by surgery though we have not encountered this before.

A leader writer in the Lancet (1970) wrote 'Tuberculosis of the nervous system has become so uncommon in the United Kingdom that it is rarely the first diagnosis that comes to mind'. While we agree with this, we feel that a high index of suspicion should always be entertained, particularly when investigating non-European immigrant patients and those with a past medical history of family history of tuberculosis.

We should like to thank Dr. J. B. Foster for allowing us to report on case 1.

REFERENCES


