Chemical Meningitis with Intracranial Tumours

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SUMMARY

Two patients with intracranial epidermoid tumours who had a chemical meningitis as part of their clinical course, are described.

The importance of recognising this as a presenting complaint is stressed. The pathogenesis and treatment are discussed.


The epidermoid-dermoid intracranial tumours contain material rich in keratin, cholesterol, and lipoid. When these chemicals enter the subarachnoid space, an aseptic meningitis results, usually due to spillage during removal of these tumours, and as such, presents as a postoperative complication. When spontaneous leakage from these tumours occurs, a chemical meningitis results which could be the first indication of the presence of a tumour. The postoperative meningitis is common, but the pre-operative type is rare. We present 2 cases to illustrate both these clinical pictures.

CASE REPORTS

Case 1

The patient, a 46-year-old White man, described his illness as beginning in November 1972, when he developed symptoms in his right leg, suggestive of meralgia paraesthetica. He was operated on for this, and apart from mild wound sepsis postoperatively, made an uneventful recovery.

After discharge from hospital, he developed headaches, blurring of vision, and weakness of his legs. The headaches were so severe that he took between 16 and 20 tablets daily of an aspirin, phenacetin and codeine preparation, to relieve them.

On 5 January 1973, he had a small haematemesis and melaena, for which he was again admitted, this time to a private nursing home. The cause of the bleeding was thought to be an acute salicylate gastritis, and as such, presented as a postoperative complication. When spontaneous leakage from these tumours occurs, a chemical meningitis results which could be the first indication of the presence of a tumour. The postoperative meningitis is common, but the pre-operative type is rare. We present 2 cases to illustrate both these clinical pictures.

Examination: All systems were completely normal except for the central nervous system which showed signs of gross meningeal irritation. No focal neurological signs were present.

Investigations and course: Lumbar puncture (Table I). There was no growth on culture of the cerebrospinal fluid (CSF). No organisms were seen by Gram-stain, and no acid-fast bacilli, cryptococci or malignant cells were seen in the CSF. The Wassermann reaction was negative. A tentative diagnosis of a partially-treated meningitis was made, and the patient was treated with intravenous penicillin and gentamicin.

The X-ray films of the chest and skull were normal, and the blood Wassermann reaction was negative on 2 occasions. An electro-encephalogram showed a left-sided diffuse abnormality, and the brain scan showed increased uptake in the right temporal area. A right carotid angio-gram was therefore performed and was completely normal. Full blood counts, urea, electrolytes and blood culture, were repeatedly normal.

When the patient had not responded adequately to 48 hours of therapy with intravenous penicillin and gentamicin, intravenous sodium cephalothin was added. On 15 January 1973, 10 days after admission, a lumbar puncture was repeated (Table I).

The patient improved clinically, but since he had developed a severe superficial thrombophlebitis, the intravenous medication was changed to oral penicillin, sodium cephalothin, and intramuscular gentamicin. The brain scan and electro-encephalogram were repeated, and both were within normal limits.

On 21 January, the patient complained of increasing thirst and polyuria and he was thought to have developed diabetes insipidus. This was confirmed by biochemical investigation, and treatment with intramuscular pitressin tannate in oil, gave him marked symptomatic relief.

Lumbar puncture was repeated on 22 January (Table I), and improvement continued until 29 January, when he developed exacerbations of his clinical signs of headache, neck rigidity, and pyrexia. At the same time he developed a right homonymous hemianopia. Another lumbar puncture confirmed a flare-up of his meningitis. Intravenous penicillin and gentamicin were recommenced and intravenous hydrocortisone added. After 48 hours, the patient improved remarkably in that his temperature subsided and his symptoms were relieved.

On 5 February an air encephalogram was performed, and this showed a large filling defect in the region of the anterior part of the third ventricle (Fig. 1), which suggested the presence of a craniopharyngioma or epidermoid cyst. A specimen of CSF collected at the encephalogram was examined for the presence of keratin or cholesterol crys-
TABLE I. RESULTS OF REPEATED CEREBROSPINAL FLUID EXAMINATIONS OF CASE 1

<table>
<thead>
<tr>
<th></th>
<th>11 January</th>
<th>15 January</th>
<th>22 January</th>
<th>29 January</th>
<th>6 February</th>
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<tbody>
<tr>
<td>Protein</td>
<td>7500</td>
<td>150</td>
<td>200</td>
<td>400</td>
<td>70</td>
</tr>
<tr>
<td>Globulin</td>
<td>++ ++</td>
<td>++</td>
<td>++ ++</td>
<td>++ ++</td>
<td>--</td>
</tr>
<tr>
<td>Sugar</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Normal</td>
<td>48</td>
<td>Normal</td>
</tr>
<tr>
<td>Chloride</td>
<td>107 mEq/L</td>
<td>112 mEq/L</td>
<td>120 mEq/L</td>
<td>--</td>
<td>110 mEq/L</td>
</tr>
<tr>
<td>Polymorphs</td>
<td>1520</td>
<td>55</td>
<td>13</td>
<td>835</td>
<td>0</td>
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<tr>
<td>Lymphocytes</td>
<td>240</td>
<td>200</td>
<td>55</td>
<td></td>
<td>120</td>
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</table>

Fig. 1. Case 1. Air encephalogram. Note defect of anterior part of the third ventricle.

tals. None were found. In view of these findings, the patient was submitted to operation.

Operation: On 9 February, the suprasellar region was explored from a right, pterional approach under the operating microscope set at 10-fold magnification. No abnormalities were found in the region around and above the pituitary fossa. The exploration was continued more posteriorly, by opening the deepest part of the Sylvian fissure. A growth, cystic in substance, was found extending towards the midline and into the interpeduncular fossa. The right posterior communicating artery and the proximal part of the posterior cerebral artery, were partly involved in the tumour, which extended forwards above and behind the optic chiasma.

A small incision was made into the capsule, and a piece of capsule was removed for histological examination. As some of the putty-like material was removed, the patient developed fluctuations in his blood pressure and an irregularity of the pulse. Since the tumour was obviously not removable, the operation was abandoned.

Course: Postoperatively the patient initially responded sluggishly to command. He developed a sharp rise in systolic blood pressure, which was controlled with intramuscular dihydralazine. As his blood pressure returned to normal, his level of consciousness also deteriorated and he became deeply comatose. During the 9 postoperative days until his death, he developed severe diabetes insipidus, serum sodium-potassium disturbances and renal failure. At postmortem there was evidence of widespread disease in his cardiovascular and renal systems. An epidermoid tumour was found in the brain, as described (Fig. 2).

Case 2

A 29-year-old Coloured woman came to the hospital, complaining that she had experienced a generalised convolution, her first ever, 9 months previously, and had had 4 other fits in the ensuing period. She had noticed weakness in the left side of her face, and her left arm and leg. She had intermittently noticed a slight weakness of the left arm and leg over a 4-year period.

On examination, all systems were completely normal except for her central nervous system. Her mental state and speech were normal. Her cranial nerves were intact except for a left central facial paresis and a left homonymous hemianopia. There was weakness of all muscle groups in the left arm, more marked proximally and in
The extensor group of muscles. There were increased tone, increased tendon jerks, and Hoffmann's sign was present. Co-ordination was poor and sensation normal.

The abdominal reflexes were absent on the left. In the lower limbs there was mild weakness on the left, with increased tone and tendon jerks. Her right plantar response was flexor and the left extensor. Sensation and co-ordination were normal. Her gait showed a left hemiparesis and Romberg's sign was absent. The patient's peripheral blood showed no haematological nor biochemical abnormalities, and she had a sedimentation rate of 15 mm in the first hour. The CSF was normal, and the Wassermann reaction was negative.

An electro-encephalogram showed mild, irregular slowing over the right temporal area, accentuated by hyperventilation. Brain scanning showed slight filling at the right base, but was otherwise normal. X-ray films of chest and skull were normal. A right carotid angiogram was performed. There was no shift from the midline, but the main middle cerebral trunk was elevated by a mid- and posterior temporal tumour (Fig. 3). The anterior choroidal artery was displaced upwards, suggesting the presence of a temporal tumour. Air encephalography was performed. The contents of the posterior fossa appeared normal. The anterior end of the third ventricle was displaced 5 mm to the left by a right temporal lobe tumour, which had displaced the right temporal horn about 10 mm laterally, and had deformed it. In addition, the spoon of the anterior horn had been truncated anteriorly by a growth in the region of the hippocampus. The distribution of the cortical gas was normal and equal on both sides.

**Operation:** A right temporal osteoplastic craniotomy was performed. The subtemporal and tentorial hiatus regions were explored under the operating microscope set at 10-fold magnification. A tumour extending through the tentorial hiatus into the temporal lobe was found. The tentorium was split. The tumour partly enveloped the posterior cerebral artery and superior cerebellar artery. It extended into the interpeduncular fossa and the cerebellopontine angle. The tumour contained a putty-like material. After removal of most of the contents the capsule was removed, except for the small part adherent to the cerebral peduncle on the right. The histology was that of an epidermoid tumour (Figs 4 and 5).

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**Fig. 3. Case 2.** Right carotid arteriogram showing elevation of middle cerebral artery.

**Fig. 4. Case 2.** Histology of the solid part of the tumour.

**Fig. 5. Case 2.** Histology of the tumour showing the cyst lining.

Because of severe cerebral swelling, a partial temporal lobectomy was performed 2 hours after the primary procedure. The postoperative course was marked by considerable meningo-meningism, most probably due to the spillage of tumour contents, which lasted for 3 weeks postoperatively (Table II). Six months after the operation the patient still had a mild right-sided hemiparesis, but was otherwise well and had returned to work.
TABLE II. RESULTS OF REPEATED CEREBROSPINAL FLUID EXAMINATIONS POSTOPERATIVELY IN CASE 2

<table>
<thead>
<tr>
<th>Days postoperative</th>
<th>24 July</th>
<th>26 July</th>
<th>31 July</th>
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<tbody>
<tr>
<td>Protein</td>
<td>100</td>
<td>100</td>
<td>40</td>
</tr>
<tr>
<td>Globulin</td>
<td>++</td>
<td>Trace</td>
<td>Trace</td>
</tr>
<tr>
<td>Sugar</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Chloride</td>
<td>—</td>
<td>113</td>
<td>—</td>
</tr>
<tr>
<td>Polymorphs</td>
<td>35</td>
<td>23</td>
<td>68</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>2</td>
<td>2</td>
<td>18</td>
</tr>
<tr>
<td>Culture</td>
<td>— ve</td>
<td>— ve</td>
<td>— ve</td>
</tr>
</tbody>
</table>

DISCUSSION

If, between the 3rd and 5th foetal week, disordered embryogenesis leads to the inclusion of cutaneous or ectodermal epithelium, heterotopia of such elements results. With further growth of these tissues, tumour formation follows. The resulting specific tumour then depends upon the degree of differentiation of the trapped epithelium. In this way dermoids or epidermoid cysts may be formed.

A typical dermoid cyst consists of squamous epithelium with dermal appendages. The epidermoid cysts are grossly similar to the dermoids. Histologically, the epidermoids have no dermal appendages and consist of 4 layers, as originally described by Bailey. The most characteristic feature is the white, glistening capsule, which led to the term ‘pearly tumours’ or ‘tumeurs perlées’ as they were named by Cruveilhier. The central portion of the tumours consists of laminated keratin, epithelial debris from the desquamating lining, fatty material, and cholesterol. The consistency depends upon the proportions of these substances, which vary from thick buttery or putty-like material to an almost fluid consistency. Variations in the colour of the capsule and content have been described.

Dermoids and epidermoids are characteristically found in certain areas of the nervous system, depending on the stage of embryogenesis at which the ectodermal elements are sequestrated. Dermoids are also more commonly found in the spinal canal than are epidermoids, usually in the lumbosacral region. Dermoids are often accompanied by persistent defects in the closure of the overlying bone and skin, resulting in a dermal sinus in continuity with the cyst. Epidermoids result from ectodermal inclusions during a later stage of development, and are found more often in lateral positions, such as the cerebellopontine angles, diploic regions, orbits, petrous bones, the parapituitary area and the rhomboid fossae.

It has become customary to call the solid or cystic varieties of tumour with ectodermal elements, found in an intimate relationship to the pituitary gland or stalk, craniopharyngiomas. The logic of separating epidermoids from craniopharyngiomas is doubtful, as they are structurally very similar. The origin from Rathke’s pouch is not yet generally accepted.

Just how common is the association of these tumours with meningitis? The incidence of craniopharyngiomas ranges from 0.8% to 3.0% of all intracranial tumours, and that of other stratified epithelial tumours, from 0.2% to 1.2%. In this relatively small group of tumours, associated meningitis occurs in only a small number.

The intraspinal and cerebellar groups often have an associated dermal sinus which is a potential portal of entry for bacteria. Bacterial meningitis, often recurrent, is a well-documented condition for the intraspinal tumours. Aseptic meningitis due to spillage of tumour contents, is much less common. This is usually reported during the postoperative period, especially in subtotal removal of intracranial tumours. The postoperative variety has an incidence of about 1.6%. Examples of aseptic meningitis resulting from spontaneous leakage from these tumours (case 1) are only rarely reported and are always well worth mentioning.

Aseptic leptomeningitis presents as recurring bouts of fever, meningism, pleocytosis with a total cell count up to 1000/cm³ and a failure to culture organisms from the cerebrospinal fluid. The reaction is sudden and striking but of short duration, and is often preceded and followed by intervals comparatively free from symptoms.

Originally, cholesterol was incriminated as the precipitating cause of the aseptic meningitis, but it is now almost certain that keratinous material is mainly responsible for the reaction. Keratinous debris is often identified under the light microscope. Under the polarising microscope it shows birefringence. Cholesterol is also birefringent, but crystalline rather than amorphous in nature. Abundant keratinous material is obvious during histological examination of these tumours. The central portions consist of laminated keratin, and keratohyaline granules are present. Cholesterol clefts, however, are often found only in the connective tissue adjacent to the brain, and not in the central keratin-containing areas. Thus it has been postulated that the cholesterol is not formed by keratin degeneration, but from cerebral tissue and therefore should not be so irritant. In one of the very few publications on the ultrastructure of craniopharyngiomas, the presence of keratin and parakeratotic masses is stressed, but cholesterol is of minor importance.

The pathological reaction to the irritants ranges from mild leptomeningitis to more severe changes, such as widespread granulomatous meningitis, ependymitis, cerebellar degeneration, posterior radiculitis, and dorsal column demyelination. In all cases reported, the beneficial effect of glucosteroid therapy is stressed. Since chemical and bacterial meningitis may coexist, it is safest to start antibiotic therapy initially, after obtaining specimens for laboratory investigation. Once the diagnosis is established and the patient responds to steroid therapy, a protracted course of antibiotics is not necessary. The condition is best prevented by guarding against spilling at operation and by leaving as little as possible of the capsule behind.

We wish to thank Dr H. A. Brown of the Department of Medicine, Groote Schuur Hospital, under whose care case 1 was admitted.

REFERENCES
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S. A. Mediese Tydskrif


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Familial Type II Hyperlipoproteinaemia

CLINICAL FEATURES AND RESULTS OF TREATMENT

IN CHILDREN AND YOUNG ADULTS

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SUMMARY

Thirty-four patients with familial type II hyperlipoproteinaemia were seen over an 8-month period at a lipid disorders clinic for children and young adults. Of the 34 patients, 5 were classified as homozygous, 27 as heterozygous type IIa, and 2 as heterozygous type IIb. Clinical manifestations of the disease were present in all 5 homozygous patients and in 12 of the 29 heterozygotes. The most common physical finding was Achilles tendon xanthoma. The high incidence of physical signs in our patients stresses the importance of such features in the young. For the purpose of treatment the heterozygotes were divided into 2 groups:

(a) children under the age of 15 years;
(b) young adults from 16 to 25 years of age.

Patients in both groups received a minimum of 6 weeks' dietary treatment followed by combined dietary and cholestyramine therapy (Questran; Mead Johnson). The decrease in serum cholesterol on diet alone was similar in both groups. On combined therapy, the children showed a decrease in serum cholesterol of 27% compared with 15% in the young adults. A general fall in the serum cholesterol of 36% was achieved in the children, compared with 19% in the young adults. In 3 homozygotes diet alone produced a fall in serum cholesterol similar to that found in the heterozygotes. In 2 patients who had cholestyramine added to the diet, a further decrease of 20% in serum cholesterol was achieved.