change postulated to occur in cortical neurons in ATD.  

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References


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Primary cerebral lymphoma mimicking tuberculosis: case report

Sir: A 19 year old Chinese man presented to another hospital having suffered a generalised convulsion. He was previously well other than a one year history of weight loss, and had been fully immunised as a child, including BCG, at age 9 years. Examination at this time showed him to be unwell, but the only physical signs were pyrexia of 37.8°C, mild neck stiffness and photophobia. A full blood count showed a white cell count of 14.2 \( \times 10^9/l \) with a 61% lymphocytosis. A diagnosis of viral meningitis was made and a lumbar puncture performed which showed an opening pressure of 20 cm water, and CSF which contained 40 wbc/mm\(^3\) (98% lymphocytes), protein 0.4 g/l, glucose 2.6 mmol/l (blood glucose 5.0 mmol/l), cytology and Gram-stain negative. In view of the convulsion he was started on phenytoin and was transferred to the regional Neurological unit at the Royal Surrey County Hospital.

On admission to this hospital he was drowsy but orientated and gave a coherent history. There were no focal signs.

Investigations included: FBC, ESR, urea and electrolytes, liver function tests, calcium, protein electrophoresis, immunoglobulins, glucose, autoimmune profile, angiotensin converting enzyme, viral titres, syphilis serology, toxoplasma dye test, CSF Gram stain, CSF and serum cryptococcal antigens, CSF India-ink preparations, CSF oligoclonal study, CSF latex agglutination test for tuberculosis, tuberculosis test, ECG, chest and skull radiographs, upper gastrointestinal endoscopy, abdominal ultrasound, barium enema, Kveim test, stool, urine, CSF and blood cultures, bone marrow examination and 24 hour urinary calcium, all of which were either normal or negative.

A CT brain scan was performed which showed multiple enhancing lesions with contrast enhancement of the adjacent cortical folds suggesting meningeal involvement. The right frontal lesion showed oedematous characteristics but notably a densely enhancing nodule at the junction of the cortex and white matter said to be typical of a granulomatous process with tuberculosis being the most likely cause (fig. a). Quadraple therapy withisoniazid, rifampicin, ethambutol and streptomycin was therefore commenced. One week later the patient became acutely unwell with fever, generalised rash and severe oropharyngeal ulceration. A “septic screen” was negative and his condition was attributed to a drug reaction to either phenytoin or the antituberculous drugs. All medication was stopped and intravenous hydrocortisone given and his fever and rash settled. A repeat CT brain scan (fig. b) was performed 10 days after starting steroid therapy and showed virtual resolution of the multiple lesions seen previously. Quadruple therapy was then reintroduced and the steroid therapy reduced to a maintenance dose of cortisone acetate 25 mg tds. He suffered no further drug reaction.

His condition remained stable over the next 2 weeks but a further CT brain scan showed a new large, well circumscribed lesion in the right frontal area with surrounding oedema (fig. c). In view of the rapid occurrence of new cerebral lesions, while on anti-tuberculous therapy, it was felt that a histological diagnosis was required.

The patient was therefore transferred to Atkinson Morley's Hospital, London where he underwent a right frontal craniotomy and biopsy of the right frontal lesion. Histology was reported as showing a perivascular exude of lymphocytes and larger reticular endothelial cells which did not appear necrotic. The appearances were essentially non-specific but could be compatible with tuberculosis.

After operation he remained drowsy and clinically unchanged, but over the next few weeks progressively deteriorated developing a left-sided 6th, 7th, 9th and 10th cranial nerve palsies and tetraplegia. He died 3 months after presentation.

It was only possible to secure permission from the relatives for a limited necropsy to be confined to the brain, and this showed a diffuse cerebral lymphoma of the histiocytic/hodgkin type, with deposits in the brain-stem, cerebellum, and hemispheres (fig. d). Systemic lymphoma cannot, therefore, be completely excluded, but investigations in the early stages of the illness would suggest that the lymphoma was a primary cerebral lymphoma.

This case is presented because of the diagnostic problems it posed, because of the unusual clinical picture in which cerebral lymphoma mimicked cerebrospinal tuberculosis, and to emphasise how cerebral lymphomas may regress with steroid therapy. The patient presented with a progressive meningoencephalitis and the initial CSF findings of a lymphocytic pleocytosis with normal protein, glucose and normal Gram stain and culture were compatible with this diagnosis. However CT scanning at an early stage revealed the more diffuse nature of the condition with parenchymal involvement of at least four cerebral lobes.

Our case was complicated by a severe drug reaction, but in retrospect it was thought probable that it was the use of steroids to treat this reaction that led to regression of the lesions.

Tuberculosis was considered to be the most likely diagnosis and since early treatment is essential (the disease usually being fatal in 4 to 6 weeks in untreated cases) anti-tuberculous therapy was started. The normal CSF glucose and protein levels are usually unusual but not incompatible with the diagnosis.1 Acid-fast bacilli are seen in only 40% of cases on initial CSF examination,2 and the tuberculin test is negative in 50% cases in this situation.

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presentation, whilst a normal ESR is also recorded in only 50% cases. Our diagnosis was further supported by the CT brain scan findings which were said to be "typical of a granulomatous process" and the brain biopsy which although non-specific, "could be consistent with tuberculosis". In retrospect we were misled by these conclusions and the post-mortem diagnosis of cerebral lymphoma was therefore unexpected.

Other conditions in the differential diagnosis were thought to have been reasonably excluded. Metastases, multiple gliomata or meningiomas would be very rare at this age and their complete resolution on serial CT brain scans made them highly unlikely diagnoses.

Other granulomatous conditions were important possibilities. Although there was no evidence of systemic sarcoidosis, the disease can primarily affect the central nervous system with signs of meningeal involvement, cranial nerve abnormalities and hydrocephalus. Furthermore cerebral sarcoïd lesions may regress or even disappear with steroid therapy.

Primary cerebral lymphoma is rare, representing approximately 1% of cerebral tumours. There is a male preponderance and the peak incidence is in the fifth and sixth decades. The term "primary cerebral lymphoma" now supersedes older terminology such as "microglialoma" and "reticulum cell sarcoma" mainly because marker studies show that many of these tumours could not be derived from cells of the monocyte-phagocyte series such as the microglial or reticulum cells.

With hindsight the clue to the diagnosis in our patient lay in the serial CT brain scans which showed resolution of the parenchymal lesions after 10 days of steroid therapy and occurrence of new lesions when the steroid therapy was reduced. Remission of cerebral lesions due to primary cerebral lymphoma while on steroid therapy has been observed previously on several occasions, most recently by Vaquero et al who reported a case where lesions seen on CT scanning were not subsequently evident at surgery, referring to lymphoma as "the ghost tumour". This phenomenon is also recognised with cerebral infarcts, multiple sclerosis, and neurosarcoïdosis.

Recognition of this phenomenon may have led to the correct diagnosis in our patient and cerebral lymphoma should therefore be considered in any case where multifocal lesions regress on serial CT scans, with, or indeed without steroid therapy, since spontaneous regression is also reported.

The mean survival time in several series is 3 to 6 months untreated, rising to 18 months to 4 years if treated by a combination of surgery and radiotherapy. A correct diagnosis could have led to appropriate therapy with some prospect or benefit. It is impossible, however, to make such a diag-

Fig. (a) CT scan showing multiple enhancing lesions. (b) Repeat scan after ten days of steroid therapy showing clearance of the lesions. (c) Further scan showing a new lesion in the right frontal area after steroid therapy had been reduced. (d) Non-Hodgkin malignant lymphoma. Diffuse pattern showing large cell histiocytic type of high grade malignancy. (H & E X 400).
nosis with the negative biopsy in this case, so that although the importance of biopsy of such lesions cannot be over-emphasised, misleading results can make it impossible to proceed further. This is the great disappointment, and a lesson in this unfortunate case.

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References


A pituitary tuberculoma

Sir: Tuberculomas within the central nervous system are unusual manifestations of tuberculosis. They constitute only 0.15% of intracranial tumours. 1 Pituitary tuberculomas, mimicking adenomas and causing disruption of endocrine function are very unusual.

A 37 year old Philippino lady arrived in England in 1973. Four years later, in 1977, she had a cervical lymphadenectomy. Her Mantoux test at this time was positive, but no acid fast bacilli were seen in or cultured from the operative specimen. She was treated with three antituberculous agents for one month, followed by fluoxacillin and metronidazole. She remained well until January 1985 when, soon after a 1 month holiday in the Philippines, she presented with a 3 day history of severe bitemporal headache. This was associated with vomiting, and diplopia on lateral gaze to the right. Her periods had been regular for 12 months, and there had been no change in libido. Orbital examination, she had a right sixth nerve palsy, a right temporal hemianopia and depressed right corneal reflex.

Initial biochemical investigations revealed a low T4 of 60 nmol/l (normal 70-160 nmol/l) with an inappropriately low TSH of 0-9 mu/l. A 9 am cortisol level was low at 7 nmol/l (normal 9 am 250-650 nmol/l). CSF examination revealed 5 lymphocytes/mm³ protein 53 mg%. No acid fast bacilli were seen or cultured. A CT scan at this time showed a brightening lesion which was lobulated and occupied the sella turcica, expanding into the right suprasellar region (fig 1). Carotid and vertebral angiography showed the tumour to be avascular. Trans-sphenoidal exploration revealed a pale grey tumour of rubbery consistency, which was completely removed.

The centre of the tumour appeared necrotic. Histology (Dr Robin Barnard) showed an active chronic inflammatory infiltrate with the formation of focal granulomata within the pituitary tissue, compatible with the diagnosis of tuberculoma.

Ten days after operation she commenced treatment with rifampicin, isoniazid, ethambutol and pyrazinamide for 3 months, after which the ethambutol was stopped, and the other agents continuing for a further 15 months. The patient made a good recovery from the operation, with resolution of her neurological deficit. Her pituitary function

Pre-operative enhanced CT scan showing a mass in the pituitary fossa.