Do not forget tuberculous meningitis

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Tuberculous meningitis (TBM) is relatively uncommon compared with other types of meningitis and so it is easy to forget to consider it as an explanation for a patient's presenting problem. If untreated TBM is fatal in most cases.

Who is at risk?

- Children under aged 5 years,
- The elderly,
- HIV infected patients (in these patients TBM may be caused by an "atypical" mycobacterium especially *Mycobacterium avium-intracellulare*),
- Alcoholics,
- Diabetes mellitus,
- Patients with head trauma and
- Those on steroid therapy

The diagnosis

This is difficult – but it is made even more difficult by inadequate attention to a detailed history and physical examination. Always ask about previous tuberculosis (TB) and TB contacts.

Characteristically the onset begins and progresses slowly with malaise over 2 – 8 weeks and

- Low grade fever,
- Anorexia, nausea and vomiting,
- Abdominal pains,
- Headache,
- Irritability,
- Insomnia,
- Mental and behavioural disturbances.

The underlying pathology is often an exudative collection and inflammation at the base of the brain. In this area there are vital neurological and vascular structures and their involvement leads to the "second" stage of the disease:

- Cranial nerve abnormalities (especially affecting the oculomotor nerves III, IV and VI and also II, VII and VIII).
- Neck stiffness (meningismus),
- Papilloedema (40%) and sometimes
- Choroidal tubercles seen on retinal examination: these are virtually diagnostic.
- Optic atrophy.

The exudative inflammatory process may cause hydrocephalus the onset of which is indicated by

- Ocular palsies,
- Pyramidal signs in the legs,
- Urinary incontinence.

In infants there may be

- Opisthotonos,
- Tense fontanelle.

The endarteritis that may develop in association with the inflammatory process causes vascular occlusion and cerebral infarction and hence

- Hemiparesis / hemiplegia,
- Hemianaesthesia,
- Dysphasia,
- Hemianopia.

In children epileptic fits are more common than in adults and may indicate the formation of a tuberculoma.

During the physical examination of the patient especial attention should be paid to respiratory signs, lymphadenopathy and hepato-splenomegaly. Occasionally a lymph node biopsy or even a fine needle aspiration will give a positive answer on Ziehl-Neelsen staining.

If facilities permit a chest X-ray could be helpful: this will show features of TB (occasionally in a miliary pattern) in about a third of patients. A skull X-ray may show a calcified tuberculoma.

Differential diagnosis

Alternative diagnoses to TBM must be considered especially in the HIV infected patient. In all cases the HIV status should be checked (after appropriate counselling) if not already known. The main differential diagnoses are:

- Fungal meningitis (especially cryptococcal meningitis),
- Partially treated pyogenic meningitis,

- Carcinomatous or reticulosis involvement of the meninges.

The cerebrospinal fluid (CSF)

Papilloedema contraindicates a lumbar puncture. The CSF may be normal on first examination if the patient presents at an early phase of the disease. Therefore another lumbar puncture should be considered if TBM is still a possibility. However the most frequent findings are:

- Raised CSF pressure,
- Slightly cloudy (occasionally clear) CSF with
- Raised protein up to 5G/L.
- If there is a spinal blockage (obstruction of the spinal subarachnoid space) and the CSF protein is very high then the CSF may appear xanthchromic (Froin's syndrome).
- On standing a "spider's web" clot may appear and reflects the markedly raised protein.
- The CSF glucose is reduced sometimes to zero.
- CSF: blood glucose ratio is reduced (so always take blood at the time of the lumbar puncture for a blood glucose measurement).
- Pleocytosis with a total white cell count of 500 / mm3 – especially a lymphocytosis. However at an early stage polymorphs may predominate.
- Ziehl-Neelsen stains are positive (acid fast bacilli (AFB)) in less than 20% but are worth doing!!
- Examination of CSF for cryptococci (Indian ink or Gram stain) must be done.

If the patient is producing any sputum then at least three consecutive specimens should be examined for TB bacilli.

Management

Success in the treatment of TBM depends on an early diagnosis and start of anti TB treatment. This should continue for 12 – 18 months. Even if the diagnosis is not proven and TBM remains a possibility then a trial of treatment should be given. Monitoring of the CSF glucose weekly may indicate a gradual increase and hence an objective method of showing effectiveness of treatment. Except in the early stages steroid therapy may be beneficial although there remains some controversy [1]. The following schedule may be used:

- **Dexamethasone** intramuscularly 16mg/day in divided doses for adults and 0.5mg/kg/day in divided doses for children or
- **Prednisolone** orally 60mg/day for adults and 2mg/kg/day for children.

These doses should be gradually reduced over 3–6 weeks.

Prognosis and long term complications in survivors

Even in those centres with all facilities available mortality is up to 30%: in sub-Saharan Africa the mortality is probably about 50%. The mortality is highest in

- The very young and the very old,
- Pregnant women,
- The presence of malnutrition and
- Other co-morbid diseases (e.g. AIDS, diabetes mellitus).

Patients with TBM are at serious risk of fluid and electrolyte disturbances. This results from vomiting and lack of attention to fluid intake. In addition they are at risk of the syndrome of inappropriate antidiuretic hormone (SIADH) secretion [2] which causes impaired water excretion and thence hyponatraemia and hypoosmality. Therefore it is essential to keep careful fluid balance observations and act upon them.

A third of survivors from TBM may have long-term complications and these include:

- Mental impairment with learning difficulties,
- Blindness,
- Deafness,
- Squints,
- Recurrent fits,
- Residual weakness from e.g. hemipareses.

A common complication of TBM is hydrocephalus and occurs in up to 85% of children [3]: "The clinical features that suggest the presence of hydrocephalus are nonspecific. In any patient with TBM with altered sensorium, hydrocephalus should be suspected irrespective of the presence or absence of papilloedema. Hydrocephalus is also likely to be present in patients who are alert and who complain of increasing headache with or without vomiting and blurring of vision"

Grading of a clinical status can aid the indication of prognosis: the Medical Research Council staging for TBM is as follows:

- Stage 1: Fully conscious and no paresis

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