**Leading Article**

**Neurobrucellosis**

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Brucellosis remains an important health problem in some parts of the world. The disease has virtually disappeared in Western countries but is still endemic in others. In Kuwait, with a population of 1.6 million, a total number of 1168 fresh cases of brucellosis were reported in 1985, an incidence of 68.9/100,000 population. The general presentation of brucellosis remains well recognized and is mainly that of generalized weakness associated with fever in addition to the various manifestations of the disease which may involve the joints as well as other organs. Excluding the common neuropsychiatric symptoms of malaise and generalized ill-health, which are commonly associated with systemic brucellosis, actual central nervous system (CNS) involvement is not very common. The incidence has been reported to be between 3 and 25% of cases of generalized brucellosis but the total number of reported cases with CNS involvement is small. Nine cases were reported in 1963 (Finchman *et al*.). Four further series have reported a total of 32 cases (Jogtekar & Nagalotimath, 1976; Abramsky, 1977; Larbrisseau *et al*., 1978; Bashir *et al*; 1985), the largest of which reported on eleven patients (Larbrisseau *et al*., 1978). A recent report of 19 patients, the largest number of cases from a single institution, indicates an incidence of neurobrucellosis somewhere between 3 and 5% of cases of generalized brucellosis (Shakir *et al*., in press). In endemic areas the mode of infection is usually through ingesting raw milk or cheese. The animals implicated are goats or cattle and, in our particular community, camels.

The presentation of neurobrucellosis is diverse. The commonest is that of an acute process with headache, vomiting, clouding of consciousness progressing to loss of consciousness with or without epileptic seizures. Papilloedema has been reported and the computed tomographic (CT) scan in those cases is usually normal but may show features of cerebral oedema. Examination of the cerebro-spinal fluid (CSF) reveals a lymphocytic type of reaction with a raised protein. The blood sugar may be low (below 2 mmol/l) in one-third of the cases. The organism can be cultured from the CSF in a minority of cases only. The pathology of the disease is assumed to be a direct effect of the organism or its toxin on the meninges and the brain. The diagnosis in endemic areas can be difficult in the acute stage, as a large number of the population have a positive agglutination titre. The blood and CSF enzyme linked immunosorbant assay (ELISA) has been reported to be specific (Sippel *et al*., 1982; Araj *et al*., 1986).

The presentation on the other hand can be completely different, with a much more chronic process involving the peripheral and/or the central part of the nervous system. The exact nature of the pathology here is not well understood. There are indeed very few reports on actual pathology, but epidural granulomata have been reported (Larbrisseau *et al*., 1978). In addition, spinal roots, both motor and sensory, showed demyelination. Ascending and descending tract degeneration of spinal cord has also been reported on autopsy (Finchman *et al*., 1963).

The peripheral form is that of a slowly progressive flaccid paraparesis associated with backache. The weakness is of a lower motor neurone type and usually involves the legs only. The process may take several months in evolution and the involvement clinically is that of a proximal polyradiculoneuropathy with areflexia and minimal superficial sensory involvement. Electromyography shows a predominantly proximal polyradiculoneuropathy with features of denervation, moderate slowing of nerve conduction velocity and delayed F wave latency and absent H reflex. The sural nerve potential is absent in some cases. Occasionally features of axonal involvement are noted in addition. The upper limbs are rarely affected. Examination of the CSF shows a raised protein, lymphocytic pleocytosis and reduced sugar content in some cases. High IgG content and oligoclonal bands have also been reported (Silva *et al*., 1980). The organism can rarely be grown from such cases although on occasions it has been cultured from the CSF (Sahs, 1978). Although myelography in such cases is usually normal, arachnoiditis has been reported (Shakir *et al*., in press). The diagnosis is confirmed in the suspected cases by positive serology (ELISA).

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case by the specific ELISA which is positive in blood and CSF.

The third major group of patients present with multiple CNS involvement, predominantly a myelitis with or without cerebellar ataxia. The condition is chronic and evolves over months or even years. The spasticity is usually confined to the lower limbs and gradually the patient may become totally paraplegic. Pyramidal signs are universal as well as retention of urine requiring catheterization. Hyper-reflexia, extensor plantar responses, absent abdominal reflexes and clonus are usually observed. Cerebellar ataxia may develop in conjunction with the myelitis or as a separate entity. The ataxia is severe associated with nystagmus and gross limb incoordination. Cranial nerve involvement is well recognized. Sensorineural deafness and papillitis are the two most common modes of involvement. Other cranial nerve palsies have also been reported (Sahs, 1978). Examination of the CSF again shows raised protein with lymphocytic pleocytosis and features which are similar to the group with predominantly peripheral involvement. The evoked responses are usually abnormal. Both visual and brainstem auditory evoked responses have been reported as abnormal, indicating optic nerve and a brainstem involvement (Shakir et al., in press).

Some cross-over is possible in the chronic variety. Patients with a predominantly polyradiculoneuropathy may have cranial nerve involvement as well as cerebellar ataxia. There may also be subtle signs of pyramidal involvement. On the other hand patients with myelitis and/or ataxia (central category) may have features of proximal polyradiculoneuropathy on electromyography. Chronic meningitis over months has also been reported (Singh et al., 1974; Strannegard et al., 1985).

The response to treatment is excellent in the meningocerebralitis group, even patients who are unconscious, requiring assisted ventilation, improve within a few days. Sequelae are rare. Tetracycline, streptomycin, cotrimoxazole and recently rifampicin have all been used in the treatment (Giunchi et al., 1971; Llorens-Terol & Busquets, 1980; Young, 1983). The most important point, perhaps, is the length of therapy. Shorter courses lasting 2 to 3 weeks may be followed by recurrences. The use of tetracycline 2 g/day and rifampicin 600—900 mg/day for 8 to 12 weeks with streptomycin 1 g/day for 6 weeks is recommended (Shakir et al., in press).

In spite of the above regimen, patients in the chronic category do not improve as well. Permanent neurological deficits can remain, especially when the spinal cord or cerebellum are affected. Deafness improves and abnormal brainstem evoked auditory responses may return to normal. The poor response is not helped by the use of prednisolone or repeated courses of therapy. In spite of the lack of a controlled study, steroids are still recommended for those patients with polyradiculoneuropathy or those with spinal or cerebellar involvement.

The clinical presentation of neurobrucellosis is therefore heterogeneous. The clinician should have a high index of suspicion, especially in parts of the world where the disease is endemic, and should perform the necessary tests on blood and CSF. This is important to differentiate this condition from other chronic infections especially tuberculosis.

The presentation of this illness, especially the chronic central form, mimics that of multiple sclerosis with multiple sites of CNS involvement associated with the abnormal CSF, raised IgG and the presence of oligoclonal bands in addition to the abnormal evoked responses. It is therefore advised that the possibility of neurobrucellosis should be excluded in endemic areas and in patients who have lived in such areas before diagnosing multiple sclerosis. The ELISA in these cases is vital as the standard agglutination test may be positive in a large percentage of the population without clinical significance.

References


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