Mollaret's meningitis associated with cerebrospinal fluid leak
A case report

M. L. PLIT, G. B. MILLER, F. E. BERKOWITZ, J. H. GEAR

Summary

Mollaret's meningitis or the benign recurrent meningitis syndrome is a rare disorder not previously described in Africa. The syndrome has a characteristic clinical presentation with spinal fluid pleocytosis, often with unusual 'epithelial' cells. With contemporary techniques no causative organism has been incriminated. The aetiology remains speculative, but we report on a patient found to have a cerebrospinal fluid leak, which may represent a factor in the pathogenesis of this disorder.

The syndrome of benign recurrent aseptic meningitis is a rare disorder first described in 1943 by Calvo Melendo. Mollaret published similar cases in 1944, but the clear identity of the syndrome remained controversial until Frederiks and Bruyn1 published diagnostic criteria which characterized the syndrome. These are: (i) recurrent attacks of fever, associated with signs and symptoms of meningeal irritation; (ii) the attacks, lasting some days, may be accompanied by generalized myalgia and are separated by symptom-free intervals lasting for weeks or months; (iii) during the attacks there is spinal fluid pleocytosis of a mixed type including endothelial cells, leucocytes and lymphocytes (the endothelial cells are not pathognomonic); and (iv) the disease is followed by resolution without residual signs. With contemporary techniques no causative organism has been incriminated. Only about 30 cases have been described, mostly occurring in Europe,1 and in this paper we report the first case described in Africa. Furthermore, our patient had a cerebrospinal fluid (CSF) leak which in association with benign recurrent attacks of meningitis represents a previously undescribed entity.

Case report

A 54-year-old woman worked as a typist at the National Institute for Virology for 8 years until September 1980. Although she did not handle laboratory specimens she did come into contact with the specimen labels. She was first admitted to the Fever Hospital, Johannesburg, in October 1978 complaining of a severe frontal headache of sudden onset, neck stiffness, photophobia, nausea and vomiting and generalized myalgia. She gave a history of having suffered a similar attack in 1973.

On examination her temperature was 30°C, her pulse rate 84/min, and her blood pressure 110/70 mmHg. She had moderate neck stiffness and a positive Kernig sign, but the rest of the examination revealed nothing abnormal. The results of CSF examination are shown in Table 1. Stool culture for enterovirus and blood cultures were negative. The total white cell count was 6.7 x 10^9/l and the haemoglobin value 15.4 g/dl; the differential cell count and ESR were normal.

A diagnosis of viral meningo-encephalitis was made and the patient recovered after 3 days on symptomatic treatment only. She was readmitted in January 1981. While driving her car she suddenly developed symptoms similar to those on her first admission; in addition she complained of chest pain and a peculiar sensation as if her 'car was moving backwards', which resolved spontaneously after a few seconds. She also gave a history of three milder attacks during 1979.

<table>
<thead>
<tr>
<th>TABLE I. CEREBROSPINAL FLUID FINDINGS</th>
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<td>First admission</td>
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<tr>
<td>Pressure (mmHg)</td>
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<td>Lymphocytes (lml)</td>
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<td>Neutrophils (lml)</td>
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<td>Erythrocytes (lml)</td>
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<td>Glucose (mmol/l)</td>
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<td>Chloride (mmol/l)</td>
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<td>Microbiological examination</td>
</tr>
</tbody>
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Date received: 5 January 1982.
She was again mildly pyrexial with neck stiffness and a positive Kernig sign. The rest of the examination was negative.

The results of CSF examination are shown in Table 1. Stool culture for enterovirus and blood cultures were again negative. The blood count, ESR and serum urea and electrolyte values were normal and liver function tests were negative. C-reactive protein was absent. Serum total protein, albumin and immunoglobulin levels were normal, although the electrophoretic pattern demonstrated beta-gamma fusion. Complement fixation tests for mumps, herpes simplex virus I and II, varicella-zoster virus, Leptospira and Brucella, haemagglutination inhibition tests for arbovirus and agglutination tests for Cryptooccus, typhoid, and Brucella infections were negative. Antinuclear factor and tuberculin skin tests were also negative. The ECG and chest and spinal radiographs were normal. Radiographs of the sinuses demonstrated a small sessile polyp on the inferior recess of the right maxillary antrum.

The patient again recovered within 3 days on symptomatic treatment only.

She was readmitted for the third time in May 1981 with similar symptoms to those on the previous admissions, but she also complained of blurring of vision and admitted to a watery discharge from her nose which had become more profuse just before the onset of the attack. There was no history of significant head or other trauma. On examination she was well orientated but drowsy with mild pyrexia, neck stiffness and a positive Kernig sign. The rest of the findings were negative.

The CSF findings are shown in Table 1. Stool culture for enterovirus and blood cultures were again negative. Most of the previous serological tests were repeated and the results were again negative. In addition, Coxsackie B1-B5 neutralization tests showed titres of less than 1:10 and the Toxoplasma indirect fluorescent antibody test was negative. The patient once more recovered within 3 days without specific treatment.

A computed tomography scan of the brain was normal, but a subsequent scan performed after intrathecal injection of metrizamide revealed a CSF leak into the nose. Unfortunately the leak persisted and tube drainage was required. She was readmitted for the third time in May 1981 with an exacerbation of her symptoms. She was again mildly pyrexial with neck stiffness and a positive Kernig sign. The rest of the examination was negative.

The ready access of bacteria to the central nervous system in the absence of other organ system involvement; specifically, absence of eye, mucous membrane and skin lesions differentiate Mollaret's meningitis from the uveomeningitis syndromes such as Behçet's disease, sarcoidosis, and the Harada and Vogt-Kayanagi syndromes. The CSF is clear and the pressure may be slightly increased. The cell count ranges from less than a few hundred to several thousand per millilitre. Mononuclear cells predominate, mostly being lymphocytes, although an initial polymorphonuclear leukocytosis may occur. The frequent presence of large atypical cells with irregular nuclear and cytoplasmic membranes remains an enigma, and they have been variously labelled as 'endothelial', 'epithelial', 'histiocytes' and 'monocytes'. Since these cells undergo rapid autolysis, forming 'ghost cells', the CSF should be examined as soon as possible. The CSF protein level is usually increased, glucose levels may be low and chloride levels are normal.

Blood changes have been inconsistent and nonspecific. The most frequent feature is probably eosinophilia, which has been described in at least 4 cases. However, this finding alone provides insufficient evidence to support an 'allergic' aetiology.

There are no residual abnormalities and the patient is asymptomatic between attacks, although a mild pleocytosis may persist. The intervals between attacks are variable and may last years, as was demonstrated in our patient after her first episode. The number of attacks per patient is also variable, the average being 5, although a woman who had 37 attacks has been described.

The aetiology of Mollaret's meningitis remains speculative. Suggestions have included auto-immune disease, allergy and occult parameningeal foci related to previous trauma that may periodically disseminate small numbers of organisms into the CSF. The demonstration of a CSF leak in our patient may be incidental but could represent a factor in the pathogenesis of the disorder. It is possible that the use of the metrizamide scan technique might have revealed this abnormality in other cases. The ready access of bacteria to the central nervous system in the presence of such an anatomical defect is clear. However, our patient's recovery without antimicrobial treatment and the absence of direct or serological evidence of infection virtually excludes this. A further possibility is the presence of an associated anatomical derangement, such as a cyst that may accumulate irritative material (e.g. lipoid) and periodically spill its contents into the subarachnoid space. This is supported by a description of a child with a cystic teratoma causing recurrent chemical meningitis. The significance of our patient's maxillary antral polyp is unclear.

We recognize that although recurrent meningitis with other causes bears a superficial resemblance to Mollaret's meningitis, the latter remains only a diagnosis by exclusion. In view of the possible association between Mollaret's meningitis and CSF leaks we recommend that metrizamide scanning or a similar technique be employed when a case is suspected.

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REFERENCES