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Neurosarcoidosis: therapeutic success with methotrexate

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Summary: Sarcoidosis affects the nervous system in 5% of cases. Treatment with corticosteroids is usually effective. We describe the case of a patient with neurosarcoidosis in which therapy with prednisone failed whereas the result of methotrexate administration was satisfactory.

Introduction

Sarcoidosis is a multisystemic disease of unknown aetiology, characterized histologically by epithelioid-cell granulomas without caseation. The disease involves the nervous system in 5% of cases, either in isolated form or associated with other manifestations.[1-4]

Current treatment consists of the administration of corticosteroids.[1,4,5] Other immunosuppressants are recommended for the corticosteroid-resistant forms of the disease.[6-9]

We report the case of a patient with a diagnosis of sarcoidosis and a clinical observation of Heerfordt syndrome[10] (uveitis, parotid enlargement and facial palsy) first treated with prednisone, who nevertheless developed a cerebellar ataxia. As only high dose of prednisone produced response, but with undesirable side effects, methotrexate (MTX) was administered.

We are not aware of reports about the use of MTX in neurosarcoidosis; however, in this case, it proved an efficient alternative therapy.

Case report

A 44 year old Black woman was admitted to hospital complaining of a 20 kg weight-loss and of fever in the previous 4 months, associated with blurred vision and a generalized paraesthesia. Clinical examination showed a temperature of 37.8°C, enlargement of the left parotid, uveitis, visual acuity reduced by 50%, hepatomegaly and erythema nodosum. The neurological evaluation revealed left peripheral facial palsy, bilateral papilloedema and a weak left appendicular cerebellar syndrome.

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Laboratory findings disclosed an erythrocyte sedimentation rate of 24 mm/h (normal up to 12 mm/h), serum amylase 2030 U/l (50–300). Haemoglobin, haematocrit and white blood cells were normal. The spinal fluid had 8 white cells/mm^3 (lymphocytes 82%, reticulomonocytes 18%, proteins 59 mg/dl and normal glucose).

Chest roentgenogram showed enlargement of the mediastinum; gallium-67 scintigraphy showed increased uptake in retina, parotids, submandibular, supraclavicular and mediastinal lymph-nodes, liver and spleen. Computerized tomography (CT) of the head was normal. Conjunctiva and mediastinal lymph node biopsies were performed displaying non-caseating epithelioid cell granulomas.

The patient was given 40 mg of oral prednisone daily, with a good clinical response. Only papilloedema and facial palsy persisted. Three months later the patient returned, exhibiting dizziness, tremors of the extremities and fever. Neurological examination showed an overall cerebellar ataxia, bilateral papilloedema and left peripheral facial palsy. Laboratory findings were: normal spinal fluid; gallium-67 scintigraphy with no central nervous system accumulation, and CT of the head with peri-ventricular leuko-araiosis (rarefaction of the white matter) in fronto-parietal areas (Figure 1).

Only high doses of prednisone (120 mg daily) evinced a clinical improvement, but with undesirable side effects. We then decided to add MTX, and prednisone was discontinued. MTX was maintained at 25 mg/week intramuscularly.

The patient's condition remained stable, for almost 3 years, without side effects. Reductions of the MTX dosage always led to clinical deterioration.

Discussion

The patient exhibited clinical, laboratory, radiological and histopathological findings that

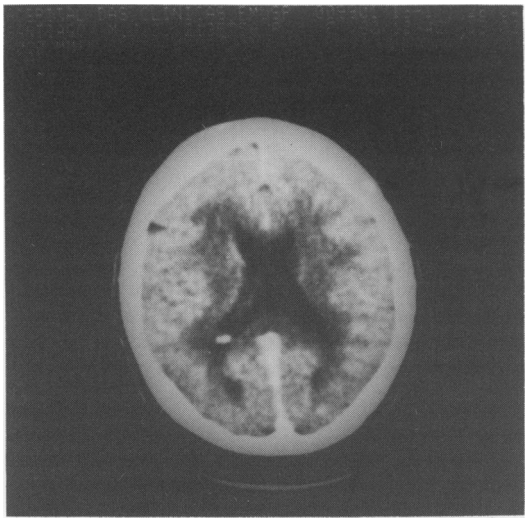

Figure 1 CT shows periventricular leuko-araiosis in fronto-parietal areas suggesting demyelination.

corroborate the multisystemic framework of the disease. Neurological involvement is infrequent and facial palsy is the most common manifestation.[2,3,4] Cerebellar ataxia is rare.[2,3] Facial palsy associated with uveitis and parotitis constitute the Heerfordt syndrome[10] found in this patient allied to papilloedema,[4,11-13] paraesthesias[6] and cerebellar[2,3] ataxia.

The neurological alterations due to sarcoidosis are secondary to granulomatous infiltration, haemorrhagic infarction or demyelination.[2,14] The CT scan is the best diagnostic procedure in neurosarcoidosis.[5,15] In our case it showed periventricular leuko-araiosis in fronto-parietal areas, suggesting demyelination.

The spinal fluid findings (lymphocytosis and high-protein level) indicate a meningeal inflammation, commonly described in neurosarcoidosis.[2,4] Although the gallium-67 scintigraphy was normal, it has low diagnostic sensitivity.[7,16]

There was excellent initial response to prednisone, a common finding in such cases. In spite of prednisone therapy, 3 months later the neurological symptoms worsened.

The daily dose was progressively increased to 120 mg, with undesirable side effects. The combination with MTX permitted the discontinuation of the corticosteroid.

Although there are records of other drugs,[6-9,17] used in sarcoidosis we are not aware of the current use of MTX in the neurological forms of the disease.[2,3,5,7,8,18]

An on-going follow-up proved that after almost 3 years the MTX produced no side effects and the disease remains under control. However, attempts to interrupt MTX therapy have not been successful. We concluded that in neurosarcoidosis cases unresponsive to corticosteroids, MTX may be a useful therapeutic arm.

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