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S. El Mahou, B. Jamard, A. Constantin, A. Cantagrel, B. Mazieres, M. Larocque
CHU RANGUEIL, Service de Rhumatologie Professeur Mazieres,
1 avenue Jean Poulhes, Toulouse 31059, France.
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Correspondence to: S. El Mahou.
E-mail: elmahousoumaya2003@yahoo.fr

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Two cases of meningeal involvement in Wegener’s granulomatosis

Sir, Meningeal involvement in Wegener’s granulomatosis (WG) has rarely been described [1]. In a systematic English literature review using electronic bibliographic databases (EMBASE, MEDLINE, CINAHL) we found only 43 cases previously reported.

Magnetic resonance imaging (MRI) with gadolinium contrast is the most useful technique for detecting meningeal disease. Two distinct patterns of thickening distribution in WG were recognized by Murphy et al. in 1999 [2]: diffusely abnormal meninges unrelated to sinus or orbital disease and focal dural enhancing thickening adjacent to sinus or orbital disease. We have observed two cases of this rare condition:

Case 1 (GP, male): at the age of 49 this patient experienced his first occurrence of chronic crusty-bloody rhinitis and sinusitis, unresponsive to conventional topical therapies. One year later, in 2000, he visited an ophthalmologist for the abrupt onset of double vision and partial visual loss in the right eye. Ophthalmic evaluation revealed a swollen disc and horizontal diplopia. MRI of the brain was normal. Diagnosis of primary retrobulbar optic neuropathy was made and treatment with topical injection of corticosteroids (CS) led to resolution. In the following months the patient experienced worsening of sinonasal symptoms and multiple recurrences of optic neuropathy during tapering of CS therapy. In 2001 the patient came to our attention for severe exacerbation of ocular abnormalities during low-dose therapy. Right eye pain, blurred vision and diffuse headache were present. Fundus examination revealed severe optic disc oedema and high-dose CS treatment had to be restored. A paranasal sinus computed tomography (CT) scan disclosed thickening of maxillary sinus and nasal mucosa and otolaryngologist evaluation described septal perforation and diffuse crusty rhinitis. MRI of the brain showed a diffuse enhancing leptomeningeal thickening over the convexity of the right hemisphere and bilaterally over the interhemispheric fissure and the intracranial surface of sphenoidal greater wings (Fig. 1A). The right mass extended to the superior orbital fissure. Examination of cerebrospinal fluid revealed only a moderate pleocytosis and a chest X-ray was normal. The erythrocyte sedimentation rate (ESR) was 87 mm/h, C-reactive protein (CRP) 27 mg/dl and antinuclear antibodies were 1:320. Antineutrophil cytoplasmic antibodies (ANCA) were absent. A paranasal mucosal biopsy showed necrotizing granulomas and areas of leukocytoclastic small vessel vasculitis. Also a meningeal biopsy was performed and a T-lymphocytic inflammatory picture was found. Diagnosis of WG was made according to 1990 ACR criteria [3] and treatment with oral cyclophosphamide 150 mg, prednisone 1 mg/kg body weight and cotrimoxazole was started. In few weeks the patient’s symptoms completely resolved and inflammatory indices returned to normal. After 15 months immunosuppressive therapy was shifted to oral methotrexate, 20 mg/week. Following imaging revealed no residual meningeal disease.

FIG. 1. T1-weighted, contrast-enhanced MRI scan of the head. (A) Case 1: diffuse leptomeningeal thickening over the convexity of the right hemisphere and bilaterally over the interhemispheric fissure. (B) Case 2: thickening of left-sided leptomeninges and dura of the skull base.
Case 2 (CE, female): at the age of 61 the patient began suffering from chronic sinusitis, otitis media with bilateral hypoacusia and bloody rhinitis. She was first admitted to a neurology division for the onset of bilateral VII cranial nerve palsy. Paranasal sinus CT scan showed a marked bilateral mucosal thickening of maxillary, sphenoidal and ethmoidal sinuses with mastoiditis. Brain MRI and chest X-ray were normal. ESR was 117 mm/h and CRP 30.2 mg/dl. The patient started treatment with oral CS (prednisone 25 mg) and penicillin for 10 days without improvement. Prednisone was then increased to 1 mg/kg body weight, and azathioprine 100 mg and cotrimoxazole were started. After 6 months the patient developed severe temporal headache and was referred to our division. Brain MRI was repeated and disclosed enhancing thickening of left-sided temporal leptomeninges and dura of the skull base (Fig. 1B). Other similar meningeal abnormalities were present over the ethmoidal area. Meningeal biopsy disclosed diffuse perivascular T-lymphocyte and multinucleated giant cell infiltrations with areas of necrosis. Perinuclear ANCA (pANCA) were found and WG was diagnosed according to 1990 ACR criteria [3]. Treatment with azathioprine was stopped and oral cyclophosphamide 75 mg was started. After 6 months' treatment complete clinical remission was achieved and laboratory findings were normal. Cyclophosphamide was tapered and then changed with azathioprine. Follow-up revealed complete disappearance of meningeal abnormalities at MRI.

Diffusion of granulomas to the meninges in WG is a rare event. It has been supposed that granulomas derive from remote or contiguous regions of the upper airways [4].

Our two patients had a form of WG limited to the upper airways and diagnosis was achieved thanks to biopsy, as the typical ANCA cytoplasmic pattern and systemic involvement were absent. When meningeal disease developed, the patients were being treated with CS alone and with CS plus azathioprine respectively. This may have favoured extension to the CNS. MRI revealed a diffuse thickening pattern in patient 1 and focal enhancing adjacent to sinus in patient 2.

We found that most patients previously described in the literature were diagnosed as having meningeal involvement while disease was limited to the respiratory tract. This implies that they were usually being treated with CS therapy alone or in association with weak immunosuppressive therapy. Recognizing meningeal disease is necessary to promptly institute treatment with cyclophosphamide.

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G. Di Comite, E. Bozollo, S. Bianchi, M. G. Sabbadini
Divisione di Medicina Interna a Indirizzo Reumatologico; Oftalmologia e Scienze della Visione, Hospital San Raffaele, Milan, Italy
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Correspondence to: G. Di Comite, Divisione di Medicina Interna, 1° piano settore A, via Olgettina 60–20132, IRCCS H. San Raffaele–Milano, Italy. E-mail: dicomite.gabriele@hsr.it