A RARE CASE OF NEUROSARCOIDOSIS: DIFFICULTIES IN DIAGNOSIS AND TREATMENT

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BACKGROUND

Sarcoidosis is a multi-organ immune-mediated disease, which manifests as neurosarcoidosis (NS) in approximately 10% of all affected patients. The diagnosis of NS requires a high degree of suspicion as well as histological confirmation. Neurological symptoms in patients with systemic sarcoidosis should not be assumed to be due to NS unless proven true. The etiopathogenesis of NS is not yet fully elucidated and a reliable biomarker assessing disease progression is missing. As a probable result, there is no definitive cure for NS. The goals of available treatments include: halting inflammation, prevention of disease worsening and restoring neurological functions whenever possible. With immunosuppression, clinical remission of NS occurs in the majority of patients. However, in some others, the disease may still progress, as no permanent cure is yet available. [1]

CASE REPORT

M.M. is a 59 years old female from Santo Domingo with history of high blood pressure, complaining, since many years, of short episodes of bilateral acuity loss, followed by migraine. In the last two years she developed postural instability, with several falls. She performed brain and cervical spinal cord MRI in 2013, showing subcortical white matter lesions, referred to chronic ischemic injury. At neurological examination in 2014 she had moderate psycho-organic syndrome, and ataxic syndrome with positive Romberg test and a slight numbness in hands and feet, lower limbs tendon reflexes were weak/absent.
Electroneurography study in 2014 (ENG) showed severe motor and axonal neuropathy.
CSF examination showed pleiocytosis (60 cells/mm^3 mostly lymphocites), very high protein level (3,2 g/L)31 mg%), hypoglicorrachia, intrathecal synthesis of IgG and oligoclonal bands both in serum and CSF. PRC for neurotropic viruses (HSV, VZV, JCV, CMV), tubercolosis test (both cultural and PCR) and research for fungal antigens in the CSF were all negative. Autoimmunity, infectivological tests, tumoral markers, immunofissation were all negative; anti MAG and anti sulfatides Antibodies (Ab) were negative, while Ab GM 1 and GM 2 IgM were detected (high title).
On brain MRI multiple subcortical white matter lesions with no Gadolinium enhance, T2 hyperintense, mainly localized at temporal poles, external capsule and inferior frontal gyrus bilaterally were detected, in association to a thickening of the pituitary peduncle (**FIGURE 1).** Also, ophtalmological evaluation showed bilateral uveitis. Total body CT Scan and PET revealed a widespread limphoadenomegaly and nodular hypodense lesions in liver **(FIGURE 2);** differential diagnosis was between lymphoproliferative and granulomatous disease. **Serum ACE test was also positive (177,8 U/L).**
The axillary and transbronchial biopsy discovered a granulomatous lymphadenitis without caseous necrosis or atypical cells, compatible with sarcoidosis. A diagnosis of probable neurosarcoidosis was made, in accordance to the most recent criteria. [2]

FOLLOW UP

On June 2014, she started oral steroid therapy (50 mg/day prednisone), on July azathioprine was added, with persistence of ataxic syndrome.
In accordance to Immunologist, the patient started Intravenous Immunoglobulin (two cycles), with a slight improvement of both deambulation and psycho-organic syndrome, and slight reduction of palpable lymph nodes. During the last year follow up, the patient performed again total body PET, brain MRI and ENG study, resulting unmodified (after about 6 months of therapy). Also Total body CT scan was unchanged. The patient is now treated with prednisone (10 mg/day) and azathioprine (50 mg/day because of leucopenia) with further neurological improvement .

DISCUSSION

We describe a rare case of CNS and PNS involvement during systemic sarcoidosis; the differential diagnosis and the treatment of this condition are very challenging.
Also the follow up of the patient is critical, because of the lack of a general consensus for the therapies of these conditions. [3]
The coexistence of CNS and PNS lesions associated to lympho adenomegaly suggest the diagnosis of neurosarcoidosis, alternative to lympho-proliferative disease.
The positivity of ACE test should be confirmed also by histological examination of lymph nodes.

References:
1- Bagnato F, Stern B. Neurosarcoidosis: diagnosis, therapy and biomarkers. May 2015, Vol 1, No 5, Pages 533-548.
3- Hebel et al. Overview of neurosarcoidosis: recent advances. J Neurol 2015 Feb; 262 (2); 258-267.
2- Baughman RP, Lower RR. Treatment of neurosarcoidosis. Clin Rev Allergy Immunology 2015.

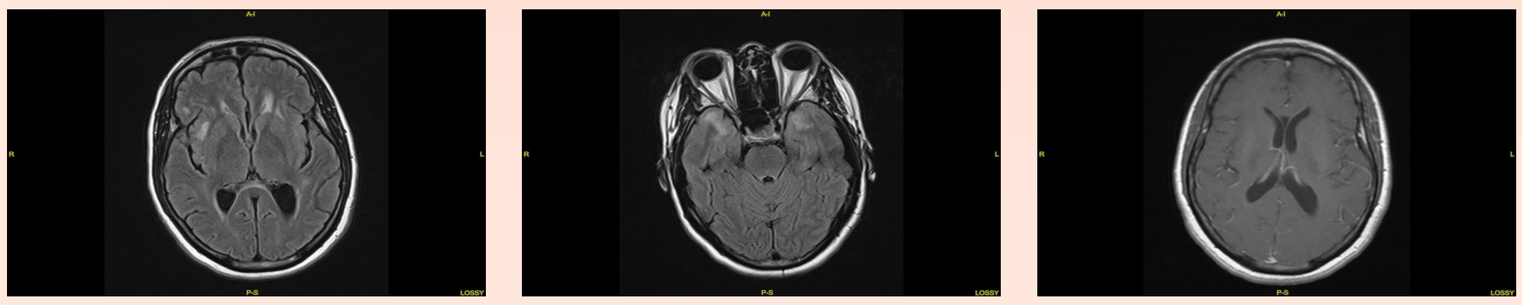

Figure 1: Encephalic MR, FLAIR, T2 and T1 post Gd sequences at admission.

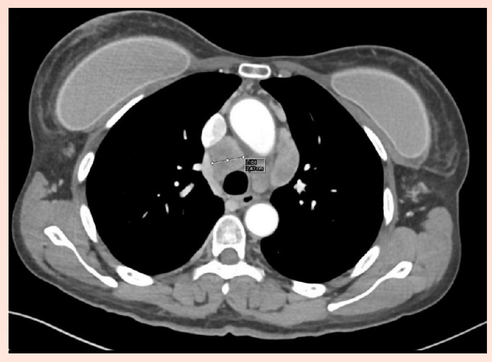

Figure 2: Thorax CT scan at admission