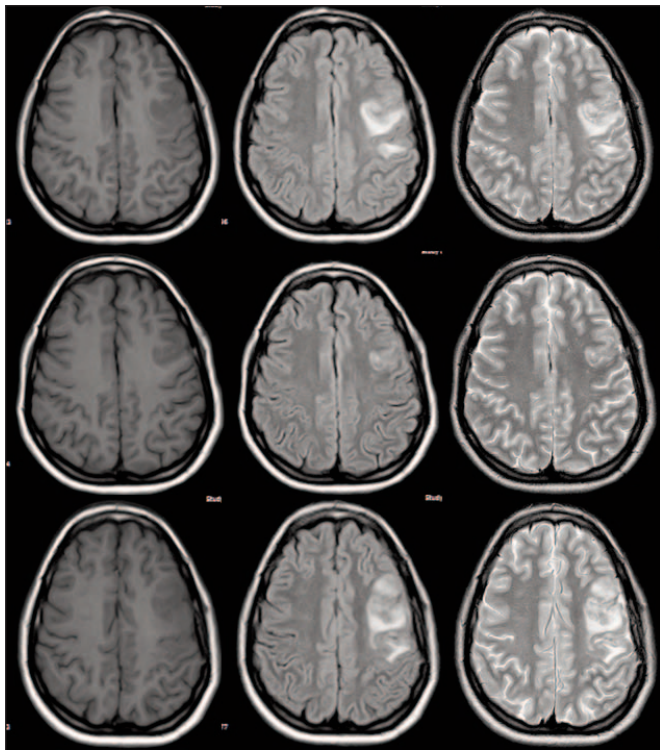


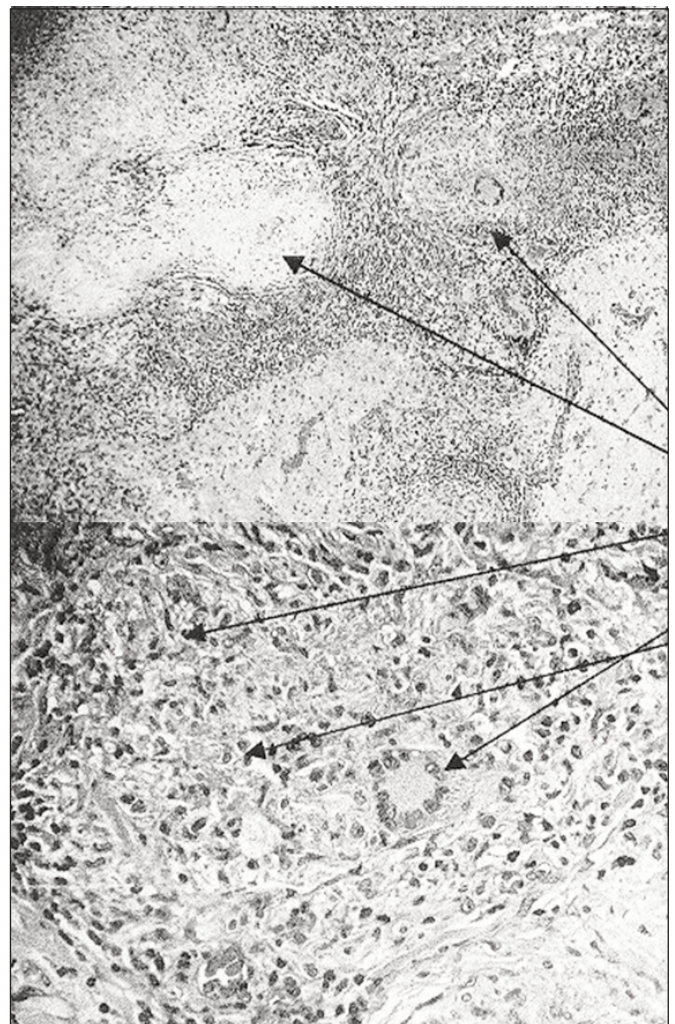
**LETTERS TO THE EDITOR****TO THE EDITOR****Steroid-Dependant Idiopathic Caseating Intracranial Granuloma**

A 22-year-old woman was seen because of the sudden onset of inability to speak associated with weakness of the right side of the body. She had been evaluated two years earlier at another hospital because of a single generalized tonic-clonic seizure followed by weakness on the right side of the body. At that time, an magnetic resonance imaging (MRI) of the head showed a focal area of edema in the left parietal lobe. The attending physician prescribed intravenous dexamethasone for a few days, with rapid clinical improvement, and did not perform further diagnostic tests. The patient was discharged asymptomatic on levetiracetam therapy, and remained well until the episode that motivated the present evaluation. On current admission, general physical examination was unremarkable, and the neurological examination only revealed mixed aphasia and a right sensorymotor deficit. Magnetic resonance imaging of the head showed an ill-defined lesion in the left parietal lobe, surrounded by edema (Figure 1, top row). The lesion showed an irregular pattern of enhancement after gadolinium administration. A



**Figure 1:** T1-weighted, FLAIR, and T2-weighted MRI on admission (top row) showing an ill-defined lesion in the left parietal lobe. Two months after the start of corticosteroid therapy, the lesion disappeared (central row), and one month after corticosteroids were tapered-off, the lesion reappeared with similar characteristics when compared to before therapy (bottom row).

routine metabolic work-up was normal. A set of serum immune diagnostic tests for the detection of antibodies against HIV, HTLV-I and HTLV-II, *Taenia solium* cysticercosis, tuberculosis, HSV, and Cytomegalovirus were negative. X-ray films of the chest as well as high-resolution computed tomography (CT) scan of the chest and abdomen were normal. In addition, ANCA antibodies were negative and serum ACE levels were normal. A lumbar puncture yielded a clear cerebrospinal fluid (CSF) under normal opening pressure; cytochemical analysis was unremarkable. The CSF had negative Gram stain, Indian-ink preparation, Ziehl-Neelsen staining, and VDRL. Polymerase chain reaction (PCR)-based assay for mycobacteria detection as well as bacterial and fungal cultures were also negative. Biopsy of leptomeninges and cerebral cortex was performed. Histopathological examination revealed granuloma formation



**Figure 2:** Microscopic examination of the lesion revealed foci of caseating necrosis surrounded by a dense mononuclear cell infiltrate and multinucleated giant cells (arrows) (HE).

with central caseating necrosis and an intense mononuclear infiltrate with multinucleated giant cells (Figure 2). The patient was started on intravenous dexamethasone therapy which was switched in a few days to oral prednisone. She experienced marked improvement on the aphasia and sensory motor deficit, and was discharged two weeks later, with a normal neurologic examination and asymptomatic. Two months after discharge, a new MRI showed almost complete resolution of the lesion (Figure 1, central row). Then, prednisone was gradually tapered over two weeks. One month later, she was re-admitted because of progressive headache and vomiting. Repeated MRI showed growth of the lesion, which had a similar size and aspect than in the MRI taken on the first admission (Figure 1, bottom row). Intravenous dexamethasone was re-started, with rapid clinical improvement.

Intracranial caseating granulomas with no infectious organism detected is a rare occurrence. Ghavanini and Munoz<sup>1</sup> recently described eight such cases, evaluated at a University Hospital in Toronto during an eight year period. Those cases were clearly idiopathic, since the authors performed histopathological study of the lesions as well as a number of diagnostic tests to exclude the possibility of non tuberculous causes of intracranial granulomas, such as sarcoidosis, ANCA-associated vasculitides, plasma-cell granulomas, and other conditions<sup>2,3</sup>. The same occurred in our patient, where histological findings of a caseating granuloma and the normality or negative results of all performed exams make those diagnoses highly unlikely. Also, the long-term evolution (more than two years), the absence of fever, the normality of CSF examination, the negative results of PCR-based assay, and the rapid response to corticosteroid therapy excluded the possibility of tuberculous infection. After a thorough MEDLINE search, we failed to find

more reports on this topic, since all published cases of idiopathic or “pathogen-free” intracranial granulomas have been non-caseating<sup>4,5</sup>. So, it seems that we are facing with either an extremely rare, or a previously unrecognized condition, that may had been neglected in the pass. The main difference between our patient and those reported by Ghavanini and Munoz<sup>1</sup>, is the recurrence of the lesion when corticosteroids were tapered off, suggesting that immunomodulatory therapy only provides transient relief and not a complete cure. Further follow-up of these patients would be helpful to settle the long-term prognosis of this condition.

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#### TO THE EDITOR

##### Atypical Multiple Lipomatosis as Sole Manifestation of a Mitochondrial Disorder

Multiple symmetric lipomatosis (MSL), also known as Mandelung's disease or Launois-Bensaude syndrome<sup>1</sup>, is clinically characterized by non-encapsulated lipomas in a thoraco-cervico-cranial distribution along the trunk<sup>1</sup>. Multiple symmetric lipomatosis is regarded as a mitochondrial disorder and frequently associated with other neurological abnormalities<sup>1</sup>. Symmetric lipomatosis only in a limb distribution and without almost any other clinical manifestations of a mitochondrial disorder, as in the following case, is rare.

#### CASE REPORT

The patient is a 50 year (y) old Caucasian male, height 179cm, weight 90kg, who had developed multiple non-encapsulated lipomas of the lower arm and the thighs since the age of 20 y. From the age of 33 y he experienced exercise-induced muscle cramps and myalgias and easy fatigability. Since

the first occurrence he had counted 40 to 60 of them, of which four were resected because they caused local pain (one of them from the right axilla). The patient is an active sportsman who even became European champion in clay-pigeon shooting. He had a history of previous alcohol abuse. The family history was positive for mitochondrial disorder in his mother and the sister of his mother, who both manifested without lipomatosis but predominantly as myopathy including the respiratory muscles. A cousin of the index patient, the daughter of his mother's sister, also presented with multiple lipomas and diffuse muscle wasting on the upper arms. The grandmother on the mother's side had presented with obesity, diabetes, stroke, and short stature (156cm). The index patient's mother developed spastic quadraparesis and muscular respiratory insufficiency requiring mechanical ventilation from the age of 43. Clinical neurological investigation revealed anacusis on the left side, reduced or absent muscle tendon reflexes, and multiple small subcutaneous, non-encapsulated lipomas on the lower arms, slightly above the right arm, and on the thighs. Blood chemical investigations revealed hyperuricemia and hyperlipidemia. Lactate stress testing at 30W on a cycle ergometer revealed normal resting