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 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. 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. So, it seems that we are facing with either an extremely rare, or a previously unrecognized condition, that may have been neglected in the past. The main difference between our patient and those reported by Ghavanini and Munoz, 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, is clinically characterized by non-encapsulated lipomas in a thoraco-cervico-cranial distribution along the trunk. Multiple symmetric lipomatosis is regarded as a mitochondrial disorder and frequently associated with other neurological abnormalities. 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 quadriparesis 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
lactate but an increase during cycling, up to 3.1 mmol/l. Nerve conduction studies were normal. Muscle biopsy showed neither ragged-red-fibers (RRFs) or COX-negative fibers nor accumulations of lipids but electron microscopy revealed marked increase of glycogen subsarcolemmally but also within the sarcoplasm, and subsarcolemmal accumulations of mitochondria, which appeared to be enlarged. Subsarcolemmally, there were also fibrillary bodies. Screening for the tRNA(Lys) m.8344A>G and m.8363G>A and mtDNA deletions is under way.

**Discussion**

Multiple symmetric lipomatosis, first described by Brodie in 1846, is clinically characterized by non-encapsulated lipomas in a thoraco-cervico-cranial distribution but also of the arms. In single cases lipomas may be even found in the mediastinum. Men are much more frequently affected than females (30:1). Age at onset ranges between 20 and 50 years. Multiple symmetric lipomatosis is frequently associated with mitochondrial disorders, most frequently MERRF syndrome. The underlying genetic defect is the transition m.8344A>G in the tRNA(Lys) gene, the transition m.8363G>A in the tRNA(Lys) gene, single mtDNA deletions, or multiple mtDNA deletions. Lipomatosis may be associated with stroke-like episodes, Parkinson syndrome, spasticity, Wernicke's encephalopathy, cerebellar atrophy, ataxia, optic atrophy, hearing loss, external ophthalmoplegia, myopathy, axonal neuropathy, encephalopathy, cerebellar atrophy, ataxia, optic atrophy, hearing loss, external ophthalmoplegia, myopathy, axonal neuropathy. Some authors described a close relationship to alcoholism, metabolic disturbances, or malignances. Multiple symmetric lipomatosis is more frequent in adults as compared to infants. Children with MSL may additionally present with obesity, developmental delay, mental retardation, diabetes, lactacidosis, or hypothyroidism. Sural nerve biopsy may demonstrate mixed axonal and demyelinating polyneuropathy with extensive loss of myelinated fibers and conspicuous onion bulb formations, as well as structural mitochondrial abnormalities on electron microscopy. Muscle biopsy may show subsarcolemmal accumulations of mitochondria, ragged-red fibers, lipid storage, or deficiency of complex I (NADH), II (SDH) or IV (COX). Biochemical investigations of the muscle homogenate may accordingly reveal a complex-II or complex-IV defect. Therapy of lipomas is essentially surgical, but this approach is critical since lipomas are not encapsulated, extremely vascularized, and surgical excision is not always successful as they frequently recur shortly after surgery. Surgical reduction of fat bulges may be more successful in cases with severe augmentation of fat. Lipomatosis in mitochondrial disease has to be delineated from lipomatosis: an unusual cause of childhood obesity and mental retardation. Eur J Paediatr Neurol. 2000;4:63-7.

**References**