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Case report

MERRF syndrome (Myoclonic Epilepsy with Ragged Red Fibres) presenting with cervicothoracic lipomatosis

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ABSTRACT

Introduction: Patients with MERRF syndrome (Myoclonic Epilepsy with Ragged Red Fibres) usually present with encephalomyopathy. However, progressive, recurrent cervicothoracic lipomatosis may be rarely observed.
Case report: The authors report 4 cases of MERRF syndrome associated with lipomatosis. In 3 patients, the diagnosis of MERRF syndrome was established on the basis of the clinical features of the lipomas and clinical interview revealing a personal or family history of lipomas and myopathy.
Discussion: In the presence of extensive spinal lipomatosis, the presence of other clinical signs of MERRF syndrome in the patient or the patient's family must be investigated. A diagnosis of MERRF syndrome can guide appropriate genetic counselling.

1. Introduction

MERRF syndrome (Myoclonic Epilepsy with Ragged Red Fibres) is a rare mitochondrial encephalomyopathy. Some cases present with cervicothoracic lipomatosis, which may be the first sign of the disease. We report a rare example of a family presenting giant lipomas, and one patient presenting lipomatosis, associated with MERRF syndrome. The purpose of this article is to highlight the association of cervicothoracic lipomatosis and MERRF syndrome, and the implications for screening and management.

2. Case reports

The first three cases concern three siblings harbouring the mutation most commonly observed in MERRF syndrome: 8344A > G in the MT-TK gene coding for lysine transfer RNA. Only one patient was diagnosed at the first visit. Clinical interview revealed the presence of multiple lipomas in the mother and several maternal uncles and aunts, with no other clinical signs of MERRF syndrome. The fourth case was a woman with a pathogenic variant (8363G > A) not diagnosed at the initial visit. Clinical interview revealed the presence of two cases of lipomatosis among the siblings, associated with myopathy in one case.

3. Case 1

This 50-year-old man presented with a giant lipoma of the thoracic spine associated with cervicothoracic lipomatosis present for 20 years. He had a history of MERRF mitochondrial disease with myopathy and cerebellar syndrome. Surgical resection started with resection of the very large thoracic spine lipoma (Fig. 1). The operative specimen weighed 3.5 kg. The postoperative course was complicated by serous effusion, requiring reoperation on the 15th postoperative day. Resection of the other lipomas was performed with no complications. Long-term follow-up revealed lipomatous recurrence at the surgical resection sites.

4. Case 2

This 60-year-old man consulted for resection of multiple cervical lipomas, the largest of which had a long axis of 15 cm. He did not present any other clinical signs of MERRF syndrome.

5. Case 3

This 40-year-old woman initially presented with a lipoma of the thoracic spine with a long axis of 12 cm. She subsequently developed other cervicothoracic lipomas, including several recurrences at sites that had been previously treated surgically. She also presented deafness, gait disorders and muscle pain.

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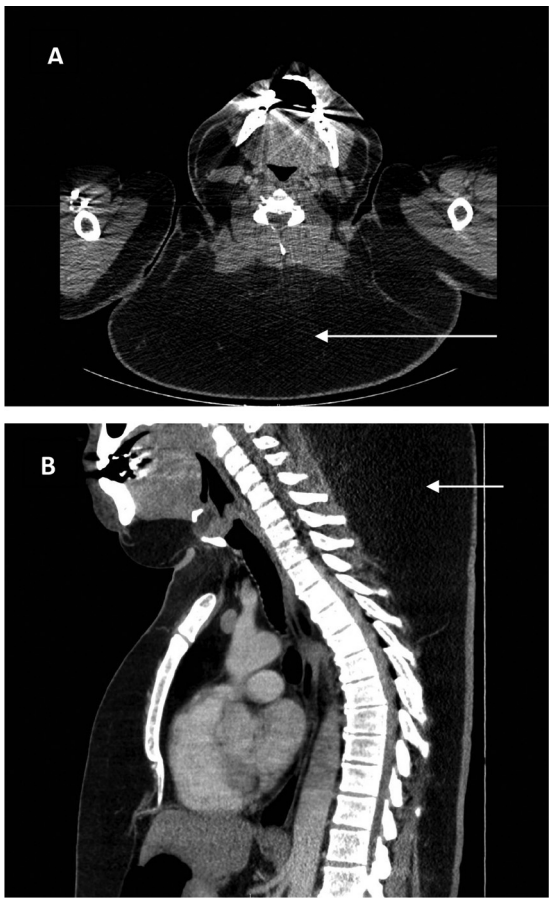

Fig. 1. CT scan of the cervicothoracic giant lipoma in case 1, with an anteroposterior diameter of 15 cm and a transverse diameter of 30 cm. Axial (A) and sagittal (B) sections.

6. Case 4

This 54-year-old woman had a history of gait disorders since childhood, sensory neuropathy and bilateral hypoacusis. She presented three submental, basicervical and nuchal lipomas at the age of 40 years. The subsequent course was marked by recurrences and new small lipomas in submental, supraclavicular, posterior thoracic and nuchal regions.

7. Discussion

Lipomas are soft, compressible, subcutaneous masses that are mobile in relation to the deep plane, not exceeding 5 cm in diameter in 80% of cases. They are mainly observed in adults between the ages of 40 and 60 years. Multiple lipomas are observed in 5 to 8% of cases and lipomas are associated with karyotypic abnormalities in 50 to 80% of cases. Lipomas only need to be resected for cosmetic reasons or in the presence of functional disability [1]. Lipomatosis can be observed in various diseases (familial multiple lipomatosis, multiple symmetric lipomatosis, MERRF syndrome, etc.).

MERRF syndrome or myoclonic epilepsy with ragged red fibres was first described by Fukuhara in 1980 [2]. The prevalence of MERRF syndrome is 0.9 cases per 100,000 in Europe. This progressively deteriorating disease usually begins in adolescence [3].

This encephalomyopathy is mainly characterized by myoclonic epilepsy and can be associated with short stature, cardiomyopathy, otorhinolaryngological signs (sensorineural hearing loss, swallowing disorders, spasmodic dysphonia), and ophthalmological signs (optic atrophy, ophthalmoplegia, pigmentary retinopathy) [4]. Three percent of patients present multiple lipomas [5].

MERRF syndrome is due to a mitochondrial DNA mutation transmitted according to non- Mendelian maternal inheritance [3]. Prenatal diagnosis is not recommended due to the possibility of heterogeneous tissue distribution of heteroplasmy. Genetic counselling is also complicated by the marked intrafamilial and interfamilial variability of expression.

The mutation most commonly observed, in more than 80% of patients, is the 8344A > G mutation in the MT-TK gene coding for lysine transfer RNA. A 8363G > A variant has also been described [3]. These mutations alter the synthesis of mitochondrial proteins and induce mitochondrial respiratory chain dysfunction. Progressive onset of symptoms can be explained by accumulation of mutant mitochondrial DNA in the tissues. Clinical expression of the mutation depends on several factors: heteroplasmy, tissue distribution and tissue susceptibility in relation to impaired oxidative metabolism.

The association between MERRF syndrome and axial lipomatosis has been studied in several families [6,7]. High levels of mutant mitochondrial DNA, abnormal mitochondrial ultrastructure and chromosomal anomalies have been detected in lipomas of patients harbouring the 8344A > G mutation [8,9]. In rare cases, lipomatosis is the only clinical feature of this mutation [8]. The proportion of clinically symptomatic patients increases with age [10]. Muscle biopsy shows the presence of ragged red fibres [3]. In the absence of any specific treatment for MERRF syndrome, multidisciplinary management adapted to the patient's symptoms is required [3].

8. Conclusion

In a patient with axial lipomatosis, recurrent or rapidly extensive lipomas, it is relevant to look for a personal or family history of epilepsy, myopathy, or neuropathy, raising a suspicion of MERRF syndrome. Muscle biopsy at the surgical incision should also be performed looking for ragged red fibres.

Disclosure of interest

The authors declare that they have no competing interest.

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