CASE REPORT

Madelung lipomatosis presenting as a manifestation of myoclonic epilepsy with ragged red fibers (MERRF) syndrome

Robert Christopher Gilson, BS, and Sandra Osswald, MD
San Antonio, Texas

Key words: lipoma; Madelung; myoclonic epilepsy with ragged red fibers.

INTRODUCTION
This is a unique case of a patient with a history of myoclonic epilepsy with ragged red fibers (MERRF) syndrome presenting with Madelung or multiple symmetric lipomatosis. We discuss the etiology of MERRF syndrome and its link with Madelung lipomatosis via a common mitochondrial mutation that can be present in both diseases. The appearance of Madelung lipomatosis should prompt physicians to search for other neural, muscular, and pulmonary findings that may lead to a diagnosis of MERRF syndrome.

CASE REPORT
A 57-year-old woman presented with a history of multiple painful subcutaneous masses especially around her neck but also bilaterally on her upper arms, back, abdomen, and upper legs. The patient was referred from the neurology department for management of these painful masses, which were obstructing her ability to breath and sleep, forcing her to require home oxygen and a wheelchair for ambulation. She could not lie on her back because of the prominence of the lipomatosis behind her neck and upper back. Our patient reported a history of myoclonus epilepsy with ragged red fibers (MERRF) syndrome with symptoms including cardiomyopathy, peripheral neuropathy, ataxia, muscle weakness, and myoclonus. She reported multiple family members having MERRF syndrome including her mother, maternal grandmother, maternal great grandmother, sisters, brothers, her sons, and nephews with variable presentations and lipomas.

Physical examination found the patient seated in a wheelchair on supplemental oxygen. Multiple symmetric large, variably sized tender masses were easily apparent and palpable around her neck, upper back, upper lateral arms, mid and lower back, lower abdomen, and upper thighs (Figs 1-3).

DISCUSSION
MERRF syndrome is a rare syndrome inherited by maternal transmission caused by mutations in mitochondrial DNA and affects roughly 1 in 5000 people. MERRF syndrome begins in childhood and affects the nervous system, skeletal muscle, and other body systems. Clinical findings can include myoclonus, seizures, muscle weakness, ataxia, dementia, optic atrophy, peripheral neuropathy with altered sensation, pulmonary and cardiac abnormalities, and lipomas. Most are derived from mutations of a tRNA generating mtDNA MT-TK gene 8344.1

Madelung disease or multiple symmetric lipomatosis is also a rare condition characterized by diffuse and symmetric accumulation of fat in the cranial-cervical-thoracic-upper limb region.2 The massive accumulation of lipomatosis around the neck has been termed buffalo hump or borse collar. The face and distal extremities are typically spared. It predominantly affects men between the ages of 30 and 60 with an incidence of about 1 in 25,000. The Mediterranean region and alcohol consumption are also notable factors. Of interest, in certain cases,

From the University of Texas Health, San Antonio.
Funding sources: None.
Conflicts of interest: None disclosed.
Correspondence to: Robert C. Gilson, BS, 13 Grants Lake Dr, San Antonio, TX 78248. E-mail: Gilsonrc@livemail.uthscsa.edu.
JAAD Case Reports 2018;4:822-3.

2352-5126
Published by Elsevier on behalf of the American Academy of Dermatology, Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
https://doi.org/10.1016/j.jdcr.2018.05.004
neurologic features were noted such as peripheral neuropathy, myopathy, sensorineural deafness, myoclonus, and optic nerve atrophy. In their literature review, Chong et al\textsuperscript{2} reported that excessive alcohol intake was reported in 49.3\% of cases, peripheral neuropathy in 59\%, myopathy in 11\%, and central nervous system features in 10\%.

Results of family studies suggest autosomal dominant or mitochondrial inheritance in multiple symmetric lipomatosis, and it is the possible mitochondrial inheritance that is of interest here. Chong et al\textsuperscript{2} reported 2 cases of multiple symmetric lipomatosis with the MERRF A8344G mutation. Olsen et al\textsuperscript{3} reported that the same MERRF mutation was reported in 16\% of multiple symmetric lipomatosis cases with postulated hypertrophy of brown adipose tissue. Holme et al\textsuperscript{4} reported a case of multiple symmetric lipomas with the MERRF A8344G mutation as the only manifestation of disease in a carrier of MERRF syndrome. This mutation was found in the lipomas of the mother who did not manifest neuromuscular disease. She had 4 sons; the eldest had MERRF syndrome, and the second son had exercise-induced muscle pain but no neurologic signs. The youngest sons were healthy. Through these findings, it is suggested that patients with multiple symmetric lipomatosis be screened for mitochondrial dysfunction, as it could have implications for future management and genetic counseling.\textsuperscript{1} The clinical diagnosis of MERRF is based on the following 4 features: myoclonus, generalized epilepsy, ataxia, and ragged red fibers in the muscle biopsy.

Our patient had findings of Madelung lipomatosis and MERRF syndrome, with subsequent genetic confirmation. These lipomas, particularly cervical lipomas, can be progressive, infiltrative, and massive. Fortunately, they only rarely have demonstrated malignant transformation to liposarcoma. These lipomas can be very difficult to remove and can frequently recur after surgery. Our patient was referred to a plastic surgeon for evaluation to see if she would be a candidate for at least partial removal to improve her ability to breath and sleep.

This case demonstrates the potential relationship between Madelung lipomatosis and MERRF syndrome. We believe one should be aware that patients presenting with a classic Madelung presentation may have other associated findings that should be investigated, particularly neuro-muscular symptoms, as they may be displaying a representation of MERRF syndrome.

REFERENCES

1. Enzi G, Busetto L, Sergi G, et al. Review: Multiple symmetric lipomatosis: a rare disease and its possible links to brown adipose tissue. Nutr Metab Cardiovasc Dis. 2016; 25(4):347-353.
2. Chong PS, Vucic S, Hedley-Whyte ET, Dreyer M, Cros D. Multiple symmetric lipomatosis (Madelung’s disease) caused by the MERRF (A8344G) mutation. A report of two cases and review of the literature. J Clin Neuromusc Dis. 2003;5:1-7.
3. Olsen AB, Grebe TA, Joganic E, et al. Multiple symmetric lipomatosis as a genetic disorder: a review. Eur J Plast Surg. 2012;35:413-419.
4. Holme E, Larsson NG, Oldfors A, et al. Multiple symmetric lipomas with high levels of mtDNA with the rRNALysA-G8344 mutation as the only manifestation of disease in a carrier of myoclonus epilepsy and ragged-red fibers (MERRF) syndrome. Am J Hum Genet. 1993;52:551-556.