Nerve Lipomatosis

see also Brachial plexus lipomatosis.

Nerve Lipomatosis commonly presents with neurologic dysfunction due to massive fibro-fatty enlargement of the peripheral nerves. It is uniquely associated with adipose tissue proliferation in the subcutaneous tissue and muscle in the innervated territory, along with osseous abnormalities.

Most frequently involves the median nerve, and manifests clinically as a compressive neuropathy. However, 30-60% of cases are associated with tissue overgrowth within the affected nerve's territory (e.g., macrodactyly for lipomatosis of nerve in the distal median nerve). Somatic activating PIK3CA mutations have been identified in peripheral nerve from patients with lipomatosis of nerve with type I macrodactyly, which is now classified as a PIK3CA-related overgrowth spectrum disorder. However, the PIK3CA mutation status of histologically confirmed lipomatosis of nerve, including cases involving proximal nerves, and cases without territory overgrowth, has not been determined. Fourteen histologically confirmed cases of lipomatosis of nerve involving the median (N = 6), brachial plexus (N = 1), ulnar (N = 3), plantar (N = 2), sciatic and superficial peroneal nerves (N = 1 each) were included. Ten cases had nerve territory overgrowth, ranging from macrodactyly to hemihypertrophy; and four cases had no territory overgrowth. Exome sequencing revealed “hotspot” activating PIK3CA missense mutations in 6/7 cases. Droplet digital polymerase chain reaction for the five most common PIK3CA mutations (p.H1047R, p.H1047L, p.E545K, p.E542K, and p.C420R) confirmed the exome results and identified an additional six cases with mutations (12/14 total). PIK3CA mutations were found in 8/10 cases with territory overgrowth (N = 7 p.H1047R and N = 1 p.E545K), including two proximal nerve cases with extremity overgrowth, and 4/4 cases without territory overgrowth (p.H1047R and p.H1047L, N = 2 each). The variant allele frequency of PIK3CA mutations (6-32%) did not correlate with the overgrowth phenotype. Three intraneural lipomas had no detected PIK3CA mutations. As PIK3CA mutations are frequent events in lipomatosis of nerve, irrespective of anatomic site or territory overgrowth, we propose that all phenotypic variants of this entity be classified within the PIK3CA-related overgrowth spectrum and termed “PIK3CA-related lipomatosis of nerve” [1].

A 10-year-old boy for lipomatosis of the median nerve at the wrist noted shortly after birth. He underwent median nerve resection accompanied by sural nerve grafting at another institute. They reviewed the literature on nerve lipomatosis and the efficacy of nerve grafting.

Clinically, he made a good recovery, with mild loss of thenar function and relatively preserved sensation. Serial magnetic resonance imaging over 5 years has revealed progression of the nerve lipomatosis at both coaptation sites, fibrofatty proliferation within the nerve grafts as well as distal digital nerves, and enlargement of a fibrous scar at the coaptation sites. This has never been reported in the 9 decades of study of this disease.

They the first medium-term follow-up of a patient who underwent nerve sacrifice to attempt to cure the nerve lipomatosis alongside a historical review of treatment. We believe that macroscopic gross total resection (i.e., microscopic subtotal resection) is insufficient in stopping the potential progression of this hamartomatous lesion because of the persistent effect of trophic factors. [2].

1)

Blackburn PR, Milosevic D, Marek T, Folpe AL, Howe BM, Spinner RJ, Carter JM. PIK3CA mutations in lipomatosis of nerve with or without nerve territory overgrowth. Mod Pathol. 2020 Mar;33(3):420-430. doi: 10.1038/s41379-019-0354-1. Epub 2019 Sep 3. PMID: 31481664.
2)

Mahan MA, Amrami KK, Niederhauser BD, Spinner RJ. Progressive nerve territory overgrowth after subtotal resection of lipomatosis of the median nerve in the palm and wrist: a case, a review and a paradigm. Acta Neurochir (Wien). 2013 Jun;155(6):1131-41. doi: 10.1007/s00701-013-1707-z. Epub 2013 Apr 25. PMID: 23615799.