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LETTER TO THE EDITOR - PERIPHERAL NERVES

Lipomatosis of nerve and overgrowth syndrome: an intriguing and still unclear correlation

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Dear Editor,

We read with great interest the paper by Marek and co-authors entitled "Lipomatosis of nerve and overgrowth: is there a preference for motor (mixed) vs. sensory nerve involvement?" which recently appeared as "Online First Articles" in *Acta Neurochirurgica* [4].

Based on their extensive experience in this field [2, 3, 7], the authors present a summary literature review along with their Institutional cases of nerve lipomatosis (LN). This intriguing and in many ways still unclear condition consists of a fibroadipose epineurial proliferation, frequently associated with bone and soft-tissue enlargement. Due to the epineural and perineural fibrosis, nerve bundles can be strongly compressed, leading to an entrapment neuropathy [6]. Gigantism and overgrowth as asymmetric macrodactyly generally interest a part or a whole extremity, usually corresponding to the territory of distribution of a single nerve. Marek and coworkers analyzed the prevalence of overgrowth syndrome and nerves lipomatosis according to motor/sensitive (mixed) or purely sensitive nerves. Their analysis was performed on 44 Institutional cases plus 329 other cases retrieved from the review. Among them, there was an extremely high prevalence of median nerve lipomatosis, with 225 cases in the motor/sensitive group (106 with overgrowth and 119 without overgrowth) and 20 cases in the sensitive group (3 with overgrowth and 17 cases without overgrowth).

We greatly appreciated the attempt to find a correlation between the different types of nerves, sensitive or motor/sensitive, and unknown aspects of nerve lipomatosis. However, in our opinion, some clarifications would be necessary. For detailed literature review, the authors refer to another paper (Marek et. al. "Strengthening the association of lipomatosis of nerve and nerve-territory overgrowth: a systematic review." *J Neurosurg* 2019 - In Press) that, at date, is not available in PubMed or at journal website, even as "online first." This makes harder to exactly support some of their findings. As a matter of fact, lipomatosis of nerves have been reported in literature with a variety of definitions, as macrodystrophia lipomatosa, fibrolipoharmartoma, lipofibromatous hamartoma, fibrofatty tumor, lipofibroma, or lipofibromatous hamartoma. Due to this variety, the literature review in extenso would also help in better understanding the present article.

The authors also asses that "statistical analysis comparing overgrowth status in the mixed and sensitive nerve groups showed a statistically significant difference in overgrowth, favoring the mixed group for overgrowth ($p < 0.0001$)." However, due to the extreme imbalance between median nerve and all other nerves, the lack of details about which statistical analyses were performed makes the conclusion not so robust. Median nerve, comprising distal sensitive branches, accounts for 259 cases on a total of 373 cases. According to their findings, there is a strong relation between mixed motor nerves and territory overgrowth. Nevertheless, it seems that only the median nerve is strictly related to overgrowth syndrome. Again, one can postulate that, due to the predominance of mixed nerves in such enlargement syndromes respect to sensitive ones, there should be a greater presence of purely motor nerves determining an overgrowth disease. On the contrary, according to authors' findings, the correlation with motor nerves as posterior interosseous nerve is purely anecdotal: only two radial nerves are retrieved in the review, and no one in their institutional series.

This article is part of the Topical Collection on *Peripheral Nerves*

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Correctly the authors recognize the difficulty in retrospectively "determining the true longitudinal extent" of lipomatous lesions. They recommend that evaluation of LN should be based on MRI imaging comprising all the nerve course. Certainly, MRI represents a pivotal tool, because LN can present a pathognomonic appearance on conventional pulse sequences. However, more advanced MR techniques may provide additional information. We recently presented a case of a 57-year-old patient with isolated non-syndromic macrodactyly with giant median nerve presenting recurrent carpal tunnel syndrome (CTS) after twenty years, in which conventional MRI was supported by the use of diffusion tensor imaging (DTI) [1]. These techniques stayed the presence of fibrohamartomatous infiltration that determined an enlargement of the median nerve and consequently an increased susceptibility to compression damage [8]. MRI confirmed the remarkable enlargement of the median nerve with thickened bundles and interposed tissue. DTI instead showed an increase of mean diffusivity values and very low fractional anisotropy values, secondary to the fibroadipose degeneration. Also, newer techniques, such as elastography, may potentially add some clinical value to the diagnosis of peripheral neuropathies [5]. In conclusion, adding newer imaging techniques to conventional MRI pulse sequences may provide newer insights on still unanswered questions about nerve lipomatosis.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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