



Recurrence of carpal tunnel syndrome in isolated non-syndromic macrodactyly: DTI examination of a giant median nerve

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Abstract

Macrodystrophia lipomatosa, a hamartomatous enlargement of soft tissues leading to gigantism of a part or a whole extremity, generally affects the territory of distribution of a single nerve. In some cases, this condition may cause an entrapment neuropathy. We report the clinical, radiological, and surgical findings of a patient with isolated non-syndromic macrodactyly and giant median nerve presenting recurrent carpal tunnel syndrome (CTS). In this case, conventional magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI) supported the presence of fibrohamartomatous infiltration, determining an enlargement of the median nerve and consequently an increased susceptibility to compression damage. A 57-year-old man presenting macrodactyly of the second and third finger of the right hand showed recent onset of severe hypoesthesia of the first three fingers of the right hand. He also underwent surgery for right CTS 23 years before. The electromyography/electroneurography confirmed the diagnosis of CTS. The ultrasonography showed a massive enlargement of the median nerve within the carpal tunnel, while MRI confirmed the enlargement of the median nerve with thickened hypointense bundles and interposed tissue, with increased mean diffusivity and decreased fractional anisotropy at DTI. We discuss about the use of a relatively novel imaging technique, investigating for the first time an uncommon cause of a very common entrapment neuropathy.

Keywords Carpal tunnel syndrome · Diffusion tensor imaging · DTI · Macrodystrophia lipomatosa · Macrodactyly · Median nerve

Introduction

Macrodystrophia lipomatosa represents an hamartomatous enlargement of soft tissues that can lead to localized or generalized gigantism of a limb. It is an uncommon, non-hereditary, congenital disorder, typically affecting the territory of innervation of a single nerve [1], that can determine also enlargement of one or more fingers or an entrapment neuropathy. Due to extreme rarity of this disorder, incidence and prevalence are not estimable.

About 100 cases of lipofibromatous hamartoma of the median nerve have been documented in literature, and only one-fourth were associated with true macrodactyly in the territory of the nerve distribution, predominantly in females and young adult or children [2]. A possible relation with PI3K/AKT (cell-signaling pathway activation has been postulated [1]. PI3K/AKT is an oncogene involved in sarcomas and carcinomas but also in overgrowth syndromes, while there is no association with neurofibromatosis. In case of isolated macrodactyly, a gain-of-function mutation can determine structural abnormalities of the peripheral nerves' structure, in particular of the perineurium, with additional secondary effects on axons' size and number. From the anatomopathological point of view, macrodystrophia lipomatosa is characterized by fibro-fatty enlargement of the median nerve, mostly confined by the nerve sheath, with a massive epineural and perineural fibrosis surrounding and compressing individual nerve bundles, while nerve fibers themselves are usually normal [3]. This condition has been rarely described as etiology of carpal tunnel syndrome (CTS) [4–6]. We report the case of a patient with isolated non-syndromic macrodactyly and giant median nerve presenting with recurrent CTS, in which an advanced magnetic resonance imaging (MRI) technique, as diffusion tensor

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imaging (DTI), has been performed, to better evaluate the possible intraoperative findings.

Case description

A 57-year-old man was admitted to a neurosurgical tertiary referral center for a 5-month history of severe hypoesthesia in the first three fingers of the right hand, with impairment in fine manipulation and writing. Since childhood, he presented macrodactyly of the second and third finger of the right hand; moreover, mild clinodactyly of the third finger was noted (Fig. 1). Twenty-three years before, the patient underwent a first surgical decompression, without neurolysis, for right CTS, performed through a longitudinal carpal skin incision. A subsequent improvement of symptoms for a very long time was then achieved. After admission, the clinical examination showed reduced pinch strength and thenar muscles hypotrophy, more severe for abductor pollicis brevis muscle. Electroneurography and electromyography were performed, depicting the complete absence of compound muscle action potentials of the abductor pollicis brevis muscle. These signs and symptoms, along with neurophysiological findings, were consistent with recurrence of CTS.

Ultrasound examination was first performed, showing a massive enlargement of the median nerve and of its distal



Fig. 1 Macrodactyly of the second and even more of the third finger (yellow arrow) of the right hand, with mild clinodactyly, are clearly visible, if compared to the other fingers

branches within the carpal tunnel (cross-sectional area = 190 mm²), with diffusely thickened bundles (Fig. 2). To better clarify these findings, MRI and DTI were carried out, using a 1.5-T MR scanner (Avanto, Siemens, Erlangen, Germany). The MR examination confirmed the remarkable enlargement of the median nerve with thickened bundles and interposed tissue, which appeared hypointense in all images (Fig. 3). After DTI acquisition (slice thickness 4 mm; dist factor 30%; TR 7500 ms; TE 75 ms; FOV 350 × 350; b values = 0 and 400; diffusion directions 12; bandwidth 1698 Hz/Px), a region of interest on the median nerve was manually drawn at the flexor retinaculum. The DTI of the median nerve showed very low fractional anisotropy (FA) values (0.20), which can be secondary to fibrohamartomatous infiltration. On the basis of such ultrasonographic, MR, and DTI findings, which we presumed secondary to the presence of anatomical alterations and scar tissue surrounding the big median nerve, a carpal tunnel release was exceptionally performed under general anesthesia, with the aid of intraoperative neurophysiologic monitoring. The pre-existing longitudinal skin incision was re-opened and a subcutaneous dissection of fibrous tissue was achieved, until completing the exposure of the median nerve; it appeared diffusely malacic and uniformly enlarged (Fig. 4), but there were no neoplastic lesions. Monopolar stimulation of the median nerve did not evoke a response of the opponens pollicis muscle. The intraoperative electrophysiological monitoring was obtained through a probe that directly stimulated the exposed nerve, with compound muscle action potentials (CMAPs) recording of the target muscle. Intraoperative records were obtained by means of steel monopolar needles inserted in the subcutaneous layer at the mutual distance of two centimeters. The stimulus was a square-wave electric pulse with a voltage ranging from 0.1 to 2 mA, 0.03 ms pulse width, and 1-Hz frequency. Decompression and neurolysis were performed under microscopy magnification to better identify the epineurium that encloses nerve bundles, minimizing risks of incautious damages. At the end of the procedure, a minimal response of the opponens pollicis muscle was registered following direct stimulation. Therefore, due to the satisfactory variation of the CMAPs after decompression and neurolysis and supported by MRI and DTI findings of severe impairment of the nerve, we decided to avoid biopsy, which could have determined functional sequelae to a such compromised nerve. After surgery, the patient referred partial recovery of tactile perception in the median nerve territory. At 1-year follow-up, he showed a relevant improvement in the pinch strength test with a pinch gauge, with a residual hypoesthesia of the second and third fingers. The new EMG/ENG study demonstrated the presence of compound muscle action

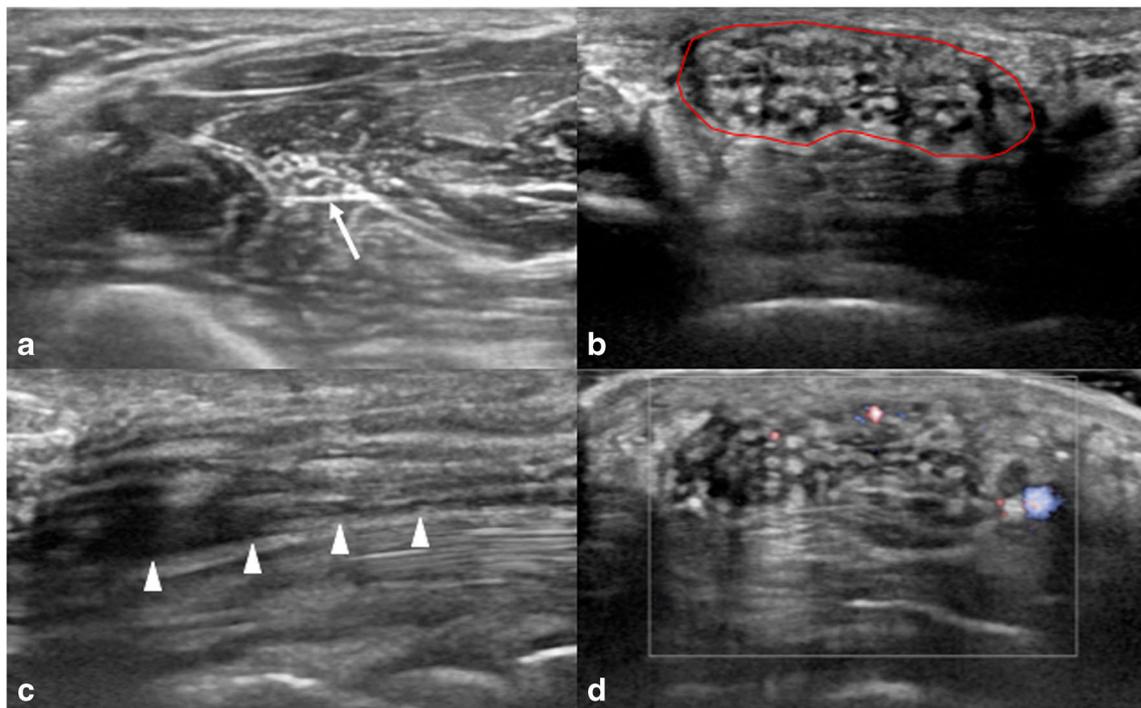


Fig. 2 Ultrasound of the median nerve shows a normal appearance of the nerve at the middle third of the forearm (**a**, *arrow*). A massive enlargement of the nerve with diffusely thickened bundles within the

carpal tunnel is observed on short (**b**, *circle*) and long axis (**c**, *arrowheads*). Power Doppler analysis of nerve vascularity displays a mild intraneural flow (**d**)

potentials of reduced amplitude (0.19 mV) registered at the abductor pollicis brevis muscle.

Discussion

There is no consensus on the diagnosis and treatment of macrodystrophia lipomatosa. Different conditions can mimic its typical features, in case of medial nerve involvement, as Dejerine–Sottas disease (a subtype of Charcot–Marie–Tooth disease), Klippel–Trénaunay–Weber syndrome, but also ganglion cyst, pure lipoma, and traumatic neuroma. Moreover, tumors with low malignant potential, such as neurofibromas

and schwannomas, may present in a similar fashion. Finally, it is very important to exclude malignant peripheral nerve sheath tumors [6]. Ultrasonography represents a well-established, first-choice imaging technique in peripheral neuropathies, in particular for CTS [7]. Klauser reported a maximum and mean CSA in control patients of 12.85 and 10.12 mm², but CSA of the median nerve can present a wide range of values, also according to age, height, and weight [8]. A comparative report between an Indian cohort and a Dutch cohort showed a significant difference in mean value of CSA for normal volunteers (7.0 ± 1.1 mm² in the Indian cohort and 8.3 ± 1.9 mm² in Dutch cohort), also after normalization for demographic details [9]. MRI can instead be helpful for the evaluation of neoplastic lesions or anatomical variants, besides being useful

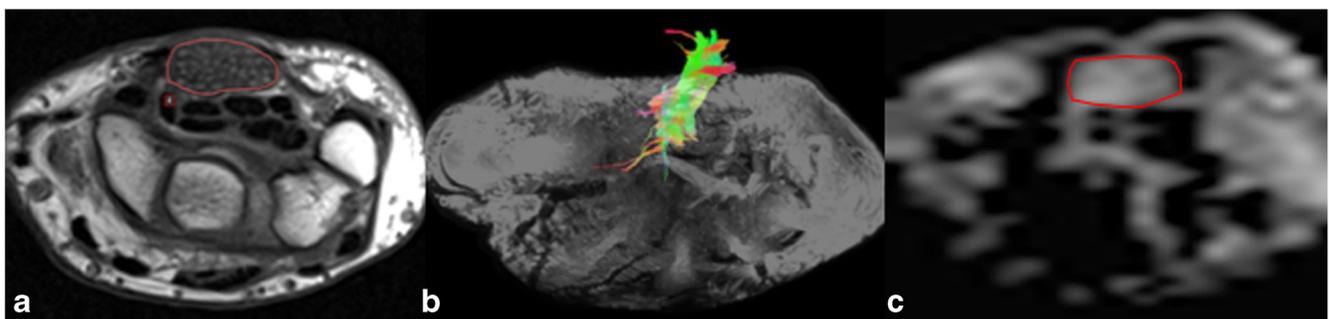


Fig. 3 Axial T1-weighted MR image (**a**) confirms the remarkable enlargement of the median nerve with thickened bundles and interposed hypointense tissue. The 3D fusion image (**b**) with the corresponding tractography image depicts a median nerve with disorganization of its

fibers probably due to diffuse fibrohamartomatous infiltration. Region of interest placement on the pertinent axial ADC map for DTI calculation (**c**)



Fig. 4 After re-opening the pre-existing longitudinal carpal skin incision, the intraoperative image showed a diffusely enlarged, malacic right median nerve surrounded by fibrous tissue (arrows)

do detect osteoarthritic changes. In macrodystrophia lipomatosa, MRI can depict fusiform enlargement of the median nerve on coronal section, with displacement of the flexor retinaculum, with low-intensity nerve bundles embedded within abundant adipose material and fibrous tissue septa along the median nerve [10]. The adjunct of DTI allows examining tissue microarchitecture by measuring water molecules diffusion along multiple directions [11]. DTI has been used to track nervous pathway of the central nervous system, while more recently different papers investigated its potential role in the peripheral nerve system. This particular MRI sequence allows evaluating the favorite spatial pathway of diffusion of water molecules by calculating FA. In physiologic conditions, the nervous myelin sheath forces the molecules to move in a specific direction, determining high FA values. In case of pathologic structural alterations, water molecules tend to move in multiple directions, with subsequent reduction of FA values [12, 13]. Nerves normally present a high degree of anisotropic diffusion of molecules, which is generally reduced in CTS [11]. Previous studies have shown that FA decreases in CTS, ranging from 0.36 to 0.64, due to extra-cellular matrix edema [8, 13]. Moreover, FA values of the median nerve have shown the highest accuracy for diagnosis of CTS when

compared to other imaging techniques [14]. Thus, a significant reduction of FA values can be considered a helpful tool for achieving CTS diagnosis. It has also been demonstrated that both single- or multiple-level assessment can be applied, with the former approach clearly being more time saving [8]. In our case, the median nerve showed a much lower reduction of FA values; median nerve entrapment alone was not enough to explain these results. We can postulate that fibrohamartomatous tissue interposed between the nerve bundles might have led to fiber disorganization increasing perpendicular diffusivity of water molecules, demonstrated by the very low FA values. It should be taken into account that the low FA values that we encountered could be related to the inclusion of fat-voxels of the median nerve and, since the DTI is a fat-suppressed sequence, the ROIs would have included dark fat-saturated fat voxels which might have affected FA calculation. Nevertheless, as shown by Ponrartana et al. [15], fatty infiltration has been proven to paradoxically increase the FA values. Also, Qi et al. [16] and Williams et al. [17] have reported a paradoxical increase of FA values with increasing fatty infiltration of the muscles in myopathies, with the authors having postulated probably due to error from random noise because of the signal loss from using a fat-suppressed echoplanar imaging technique of predominantly fat-replaced tissue. Moreover, although probably there would be microscopic fat components within the nerve, there were no macroscopic fatty areas in the interposed tissue between the nerve bundles, as demonstrated by the diffusely low signal intensity of the nerve on T1-weighted images. Figure 3a shows relatively high signal of the bundles in comparison with the low signal of interposed fibrohamartomatous tissue. Clearly, there is still much to say on this issue and larger cases series are needed. Furthermore, in previous studies, the evaluation of the median nerve through DTI sequences has been performed on both 1.5- and 3-T MR units, but there is poor knowledge on the comparison between the two different field strength scanners [18]. Nevertheless, previous studies have reported that FA and ADC values on DTI of human brain are not significantly affected by the field strength [19]. At our institution, we use a 1.5-T MR scanner for both daily clinical practice and research studies.

In our case, the median nerve, which was malacic and much larger than usual, seemed to be very suffering and damaged under microscopic view, so we preferred to avoid further trauma by obtaining a bioptic sample that could determine adjunctive damage. The satisfactory variation in the amplitude of the CMAPs after decompression and neurolysis supported us in the choice to not perform other surgical manipulation such as a biopsy. Also supported by MRI and DTI findings, which showed severe changes of the nerve structure, we decided to avoid biopsy that, although diagnostic, could have determined functional sequelae to a such compromised nerve. So, even if biopsy and histopathological examination are the

only definitive means of a certain diagnosis, different authors suggest to avoid routine nerve biopsy, due to the risks of neurological deficit, if MRI provides features that exclude alternative diagnoses, in particular of potentially malignant tumors, and to apply a dedicated follow-up protocol for each single patient.

To our knowledge, this is the first case of CTS recurrence related to intraoperative findings of a diffusely enlarged median nerve, without mass lesion or signs of segmental compression in a patient with isolated macrodactyly. The considerable size of the nerve, along with its structural intrinsic changes, is probably a predisposing factor for compression due to repetitive trauma and subsequent fibrous tissue growth. Consequently, this condition may be recognized as a risk factor for relapse of median nerve compression after carpal tunnel surgery. Even though our patient has shown a progressive recovery, a new relapse is still possible for the anatomical predisposition of the median nerve to damage. The nerve enlargement determined an increasing vulnerability to damage. Thus, the patients have to be informed about the need of periodic clinical evaluations and a long follow-up. In such rare cases, in selected patients, the use of advanced imaging techniques such as DTI might be helpful in the pre-operative assessment of the median nerve. In conclusion, we report clinical, radiological, and operative findings of an uncommon cause of a common entrapment neuropathy as CTS, investigated with a relatively novel imaging technique, which could be relevant for clinical and surgical treatment. However, the meaning of our results should be further investigated in larger cases series.

Compliance with ethical standards

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Conflict of interest The authors declare no conflict of interest.

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