Magnetic Resonance Neurography Evaluation in Children

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Abstract

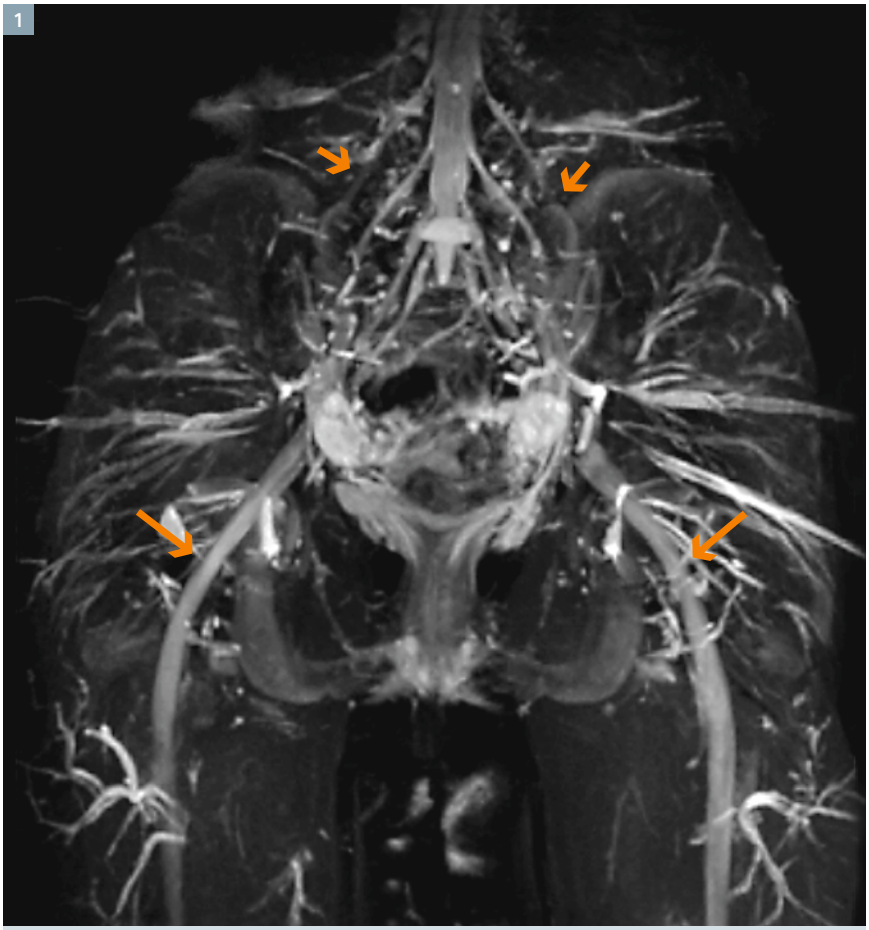
Magnetic Resonance Neurography has proven to be an excellent technique for the evaluation of peripheral neuropathies. However, its use in pediatric age group has been less well described. In this article, the authors discuss the technical considerations, various common causes of peripheral neuropathies in children* and the role of magnetic resonance neurography in their diagnosis and management.

Introduction

A wide spectrum of peripheral nerve pathologies are encountered in children, including hereditary neuropathy, traumatic birth injury and motor vehicle accident, neoplasm, infection and inflammation. Clinical features in these cases are often nonspecific and invasive electrodiagnostic tests, such as nerve conduction studies are usually uncomfortable and not feasible in the pediatric age group. Peripheral nerve imaging can therefore, be very useful in small children with strong clinical suspicion in whom the diagnosis cannot be firmly established. However, small size of the nerves and the relative lack of specific clinical features makes imaging of the nerves challenging and requires high technical skill for performance and interpretation. There is a paucity of literature describing the diagnostic role of peripheral nerve imaging in children [1-3]. Magnetic Resonance Neurography (MRN) is a non-invasive imaging technique, which enables direct visualization of the anatomy and pathology of the peripheral nerves and regional muscles, thereby aids in localizing the site of injury or tumor. It can not only help in confirming and localizing the neuropathy, but also in ruling out neuropathy by showing normal appearing nerves and regional muscles. The authors describe the MRN technique used in pediatric age group and discuss a spectrum of peripheral nerve pathologies that can be observed in children using relevant case examples.

MR Neurography technique

The currently available 3 Tesla scanners (MAGNETOM Skyra, Verio and Trio, Siemens Healthcare, Erlangen, Germany) are preferred over 1.5T systems (MAGNETOM Aera and Avanto) due to higher signal-to-noise ratio (SNR) and short imaging times on the higher field scanners. Additionally 3D imaging with fat suppression is better obtained



1 Normal LS plexus and sciatics in a young girl. MIP image from coronal 3D STIR SPACE sequence shows normal symmetrical appearance of the LS plexus nerve roots (short arrows) and bilateral sciatic nerves (long arrows).

on 3T scanners. 2D imaging can be obtained similarly on both types of scanners, although it takes a little longer on 1.5T scanners, especially when one tries to attain similar image quality on thin section (2–3 mm) scans. High resolution imaging with combined 2D and 3D isotropic spin echo type imaging is essential for optimal assessment of small peripheral nerves. The inability to stay still for infants and small children makes imaging more challenging, frequently requiring sedation or general anesthesia for adequate results and to avoid repeat acquisition [1].

One should use dedicated coils as far as possible. For MRN imaging around the joints, use joint specific coils, such as wrist, elbow, ankle etc. If a joint specific coil is not available, use the smallest possible flex coil to cover the expected anatomy. For contiguous imaging of the joint and extremity, e.g. wrist and forearm, use wrist coil and flex coil separately in the adolescent child to avoid excess blank (air) space around the extremity. In a child or infant, a single flex coil can suffice for such imaging due to the relatively small size of the extremity. During plexus imaging, use a combination of body array on the front and spine elements on the back to attain uniformity of magnetic signal in the field-of-view.

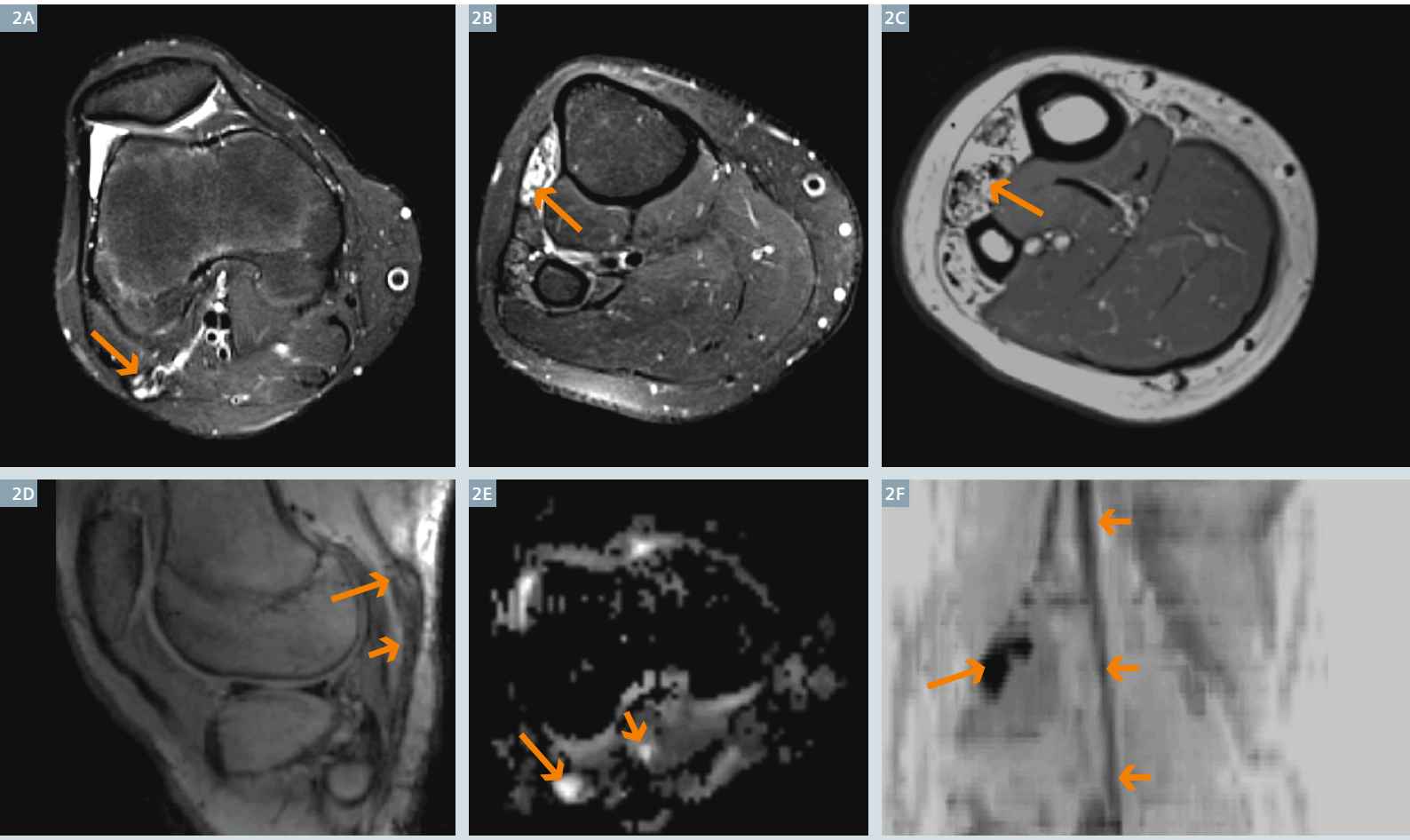
High resolution 2D (dimensional) axial T1-weighted (T1w) and T2 SPAIR (Spectral Adiabatic Inversion Recovery) sequences are useful for demonstrating regional anatomy of the nerve fascicles. Fascicular architecture of nerves is consistently seen with T2 SPAIR images in larger branches, such as femoral nerves and sciatic nerves, as well as in smaller nerves that are affected and enlarged due to neuropathy, such as lateral femoral cutaneous and genitofemoral nerves [4, 5]. Fluid sensitive sequences such as STIR (short tau inversion recovery) images have more uniform fat suppression and higher T2 contrast, especially in the presence of metal or in off-center areas [6], however STIR imaging is often marred by low SNR, pulsation artifacts and increased baseline nerve signal intensity. SPAIR produces higher SNR images and are less prone to blood flow artifacts than STIR imaging, which could be disadvantageous as peripheral nerves travel in neurovascular bundles. Use a TR/TE/TF of ~ 3800–4000/60–65/15–25 for T2 SPAIR imaging. Sagittal STIR imaging is particularly useful in brachial plexus imaging to obtain uniform fat suppression in a difficult neck area and to tease out asymmetrical or individual nerve signal intensity and caliber alterations. Dixon type fat suppression is also useful in generating uniform fat suppression.

3D images complement information generated from 2D imaging by showing nerves in longitudinal planes. The imaging can be obtained using isotropic 3D SPACE (Sampling Perfection with Application optimized Contrasts using variable flip angle Evolutions) technique. A variety of contrasts are available on SPACE sequence, including T1, T2, PD, STIR and SPAIR. Non-fat suppressed T2 SPACE (TR/TE/TF ~ 1500–1700/110–120/42–50) is used for spine imaging, which is necessary in plexus evaluation. One can routinely obtain 0.8–0.9 mm isotropic images through the cervical or lumbar spine. In cases of suspected nerve root avulsions, one should also obtain 3D CISS imaging focused at spine for high resolution (0.6–0.65 mm isotropic) evaluation of preganglionic nerve rootlets. For post ganglionic nerve assessment in plexuses, fat suppressed 3D imaging using STIR SPACE (TR/TE/TF/SL ~ 2000–2200/70–80/50–60/1.3–1.5 mm isotropic) is most useful. There is virtually no pulsation artifact on the 3D imaging and once thick slab (8–15 mm) maximum intensity projections (MIPs) are created, the image looks smoothened and shows the high intensity nerves along their long axis or in any desired arbitrary plane, e.g. oblique sagittal planes are useful to depict femoral and sciatic nerves along their long axes (Fig. 1). SPAIR SPACE (0.9–1.0 mm isotropic) is very useful in extremity imaging due to higher SNR and similar uniform fat suppression. The nerve perpendicular plane shows cross-sectional appearance of the fascicular anatomy of the nerve. The longitudinal plane along the long axis of the nerve shows focal or diffuse nerve enlargement and mass effect of regional perineural lesions [1]. 3D imaging is helpful in localizing the lesions along the axis of the nerve, course deviations, focal neuroma, neurotmesis, etc. and for better preoperative planning. In extremities, another 3D imaging, i.e. 3D DW PSIF (diffusion-weighted reversed steady state in free precession) is extremely useful to create nerve specific isotropic images due to effective fat and vascular suppression (TR/TE/SL ~ 12/3/0.9, b-value for diffusion~60–80 ms and water selective fat suppression). Additional coronal T1w, STIR/PD SPAIR images aid in detection of lesions along the long axis of the nerves as well as allow assessment of regional joints and musculotendinous structures. These also serve as fall back sequences, in case the subject moves during the scan or if there is failure of 3D imaging for any reason. IV gadolinium contrast is not routinely used in injury cases, however is useful for differentiating types of neural hypertrophy such as suspected neoplasm, infection, inflammation, diffuse polyneuropathy, neurocutaneous syndromes, or post-operative complication [7, 8].

Normal and abnormal peripheral nerves

Normal peripheral nerves show isointense signal on T1w and T2w images. On T2 SPAIR images, minimal hyperintensity is normal, especially where the nerves curve around the joints. On 3D STIR SPACE images, the nerves appear uniformly hyperintense in the plexuses due to increased sensitivity to the endoneurial fluid. Most hyperintensity is seen at the dorsal nerve root ganglion level and the signal fades distally along the course of the nerves. Pathological nerves show one or a combination of findings, such as increasing hyperintensity approaching the signal of the regional vessels and encompassing a long segment of the nerve; focal or diffuse caliber enlargement (more than adjacent regional nerves, contralateral counterpart nerve or artery in the neurovascular bundle); internal fascicular

*MR scanning has not been established as safe for imaging fetuses and infants less than two years of age. The responsible physician must evaluate the benefits of the MR examination compared to those of other imaging procedures.



2 Surgical failure. Axial T2 SPAIR **(2A)** image shows enlarged neuromatous common peroneal nerve (CPN) (arrow) following placement of nerve tube to bridge the resected mass of the CPN. Axial T2 SPAIR image and T1w images **(2B, C)** distally show edema like signal and fatty replacement of the muscles (arrows). Oblique sagittal 3D DW PSIF reconstructed image **(2D)** shows the findings in the long axis with neuromatous proximal nerve (long arrow) and empty nerve tube (short arrow). DTI tensor image **(2E)** and corresponding inverted scale MIP image **(2F)** show the normal continuous normal tibial nerve (small arrows) and discontinuous CPN with end bulb neuromas (long arrows).

enlargement, effacement or atrophy; intra-epineural fat deposition; epineurial or perineurial thickening; perineural fibrosis with or without nerve entanglement; nerve displacement due to mass lesion; heterogeneous nerve thickening suggesting a neuroma in continuity or end bulb neuroma from complete rupture or failure of nerve regeneration (Fig. 2); and finally, regional muscle denervation changes, which by definition are distal to the site of the entrapment [2, 4-6].

Indications

Hereditary neuropathy is the most common etiology in children. Acquired cases can be seen due to infection, inflammation, neoplastic and trauma causes. On the other hand, adults usually suffer from neuropathies secondary to entrapment, toxic insult or systemic disease, such as diabetes. It is thus important to understand the differing etiology in adults and children in order to make a proper diagnostic plan for evaluation of peripheral neuropathies in pediatric age group. MR Neurography is indicated in children with suspected but unclear underlying hereditary or acquired pathology that may cause neuropathy, known neuropathy without any identifiable underlying cause, and to characterize neuropathy in cases of infection, inflammation or trauma.

Advantages of MRN

MRN is particularly useful in children due to frequent inability of electrodiagnostic studies (EDS) to yield diagnostic information. Moreover, MRN is not operator dependent and can localize the exact site of nerve pathology. It provides useful data for preoperative planning and postoperative response to surgical treatment even before clinical and functional improvement is noticeable [1]. The EDS give vital physiologic information about the nerve pathology by evaluating nerve conduction velocity or muscle action potentials using electromyography [9]. On the other hand, imaging studies primarily evaluate the anatomy and results of nerve pathology. Both these modalities

are used to complement information gained from one another to reach a correct diagnosis. Although ED tests are good for systemic conditions causing peripheral neuropathies, they are highly dependent on clinical and technical expertise of the examiner and are not practical in infants or small children, since patient cooperation is imperative to their success [10]. Imaging of the nerves as such is of vital importance in children for evaluation of neuropathies.

Non-invasive imaging of nerves can be done using ultrasonography (US) or MRN. US is cost effective, portable and allows dynamic assessment of the extremity nerves. Large segments of the nerves can be seen along their entire course in the extremities. It does require considerable technical skill and cannot depict subtle changes in signal intensity as with MRN in cases with mild neuropathy without fascicular enlargement. Deep nerves are difficult to interrogate using US and muscle denervation changes are not apparent till late stage. MRN can evaluate the nerves, their innervated muscles and regional soft tissue structures. With its combined 2D and 3D imaging capabilities, it can illustrate neuromuscular anatomy and pathology in multiple planes for better interpretation by the radiologist and localize the pathology for preoperative planning for the referring physician.

Spectrum of peripheral neuropathies in children

The causes of neuropathies differ between adults and children. More than 70% of neuropathies in children are related to inherited causes, while most cases of neuropathy in adults are acquired (60%). Adults with acquired neuropathy are mostly related to trauma, entrapment or chronic injury from sports or occupation. In children, acquired neuropathies are more likely secondary to infection and inflammation [11]. Clinically, neuropathy results in numbness, pain, paresthesia and weakness of the innervated muscles. In small children these symptoms may be less noticeable, and thus reflex testing is of vital importance. Following is a discussion of various common causes of peripheral neuropathies.

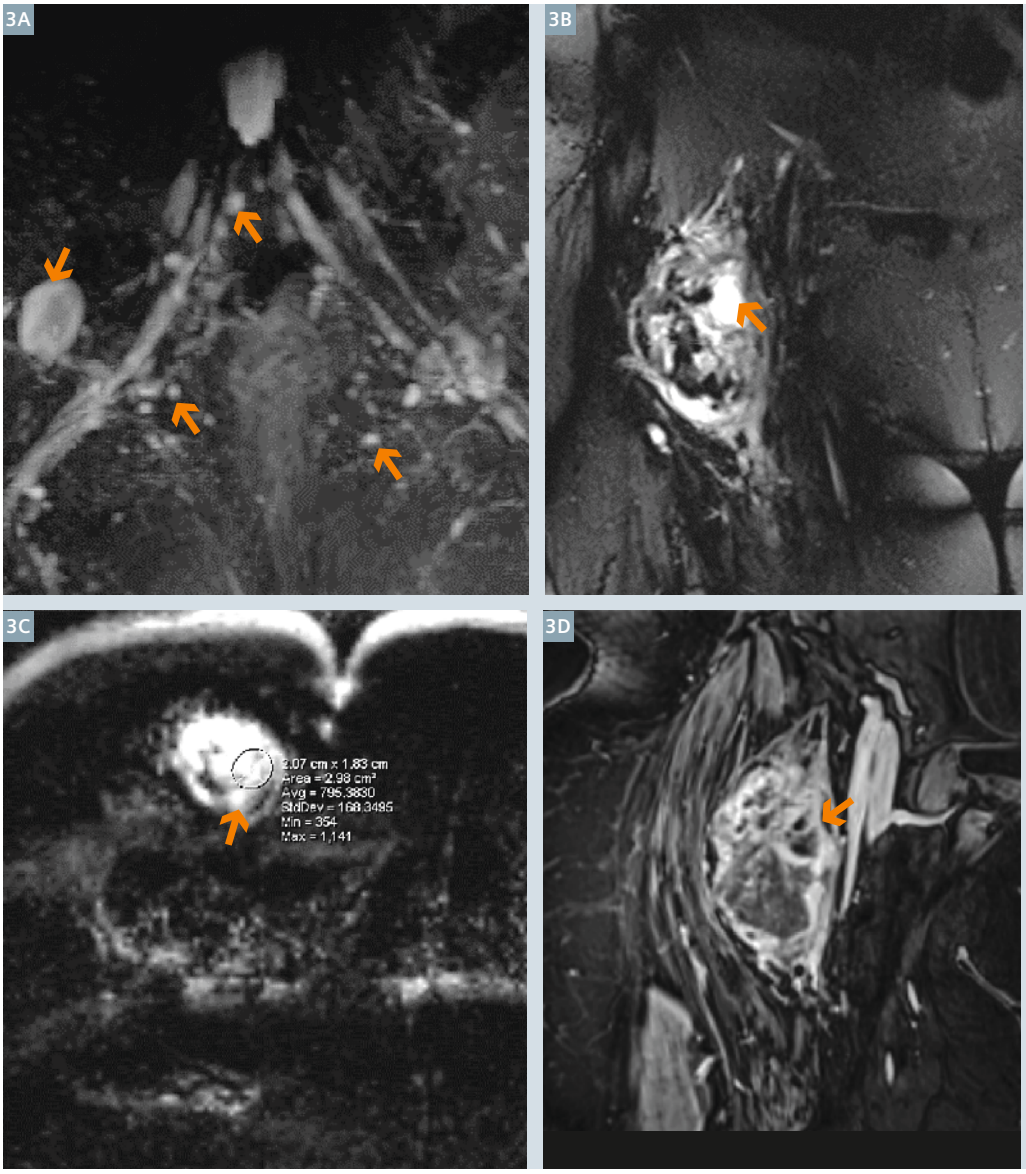
Hereditary Neuropathies

Inherited Neuropathies are a heterogeneous group of pathologies in which neuropathy is either the primary presentation of the disease (such as Charcot Marie Tooth disease; CMT) or a part of a more generalized or systemic disorder. The latter group encompasses a large group of rare disorders such as familial amyloid polyneuropathy (FAP), porphyria, ataxia telangiectasia and many other syndromes. The most common of hereditary neuropathies is CMT, which is classified into various types based on pathogenesis – demyelination or axonal degeneration. Clinical features include muscle denervation changes (weakness, atrophy), high plantar arches, impaired sensation and diminished deep tendon reflexes [12, 13]. The most common form of CMT is autosomal dominant demyelinating CMT (CMT type 1A), which is seen in 70% cases. MR imaging is a useful adjunct to clinical and electrodiagnostic suspicion of the neuropathy. One would see diffuse enlargement of bilateral peripheral nerves with abnormally increased signal intensity and/or fascicular prominence in a symmetric fashion. Most enlargement is observed in CMT type 1A. No significant enhancement is seen on post-contrast imaging. Whole-body MR Neurography (WBMRN) is likely to be useful in future to assess the disease burden in these diffuse polyneuropathy cases [14]. Nerve biopsy is the most accurate test to diagnose CMT, however it is rarely necessary these days.

Neoplastic

The most common peripheral nerve sheath tumors (PNSTs) in children are neurofibromas (NF) and schwannomas [15]. These are benign tumors arising from the Schwann cells, with additional non-neoplastic cells including neurons, perineurial cells and endoneurial fibroblasts [16]. NFs may be described as localized, diffuse or plexiform. Most of NFs are of localized variant seen as small (< 5 cm) fusiform masses involving a superficial or major peripheral nerve. Plexiform NF, on the other hand, comprises proliferation of cells in the nerve sheath spreading along the length of the nerve and involving multiple nerve fascicles. They are more commonly associated with neurofibromatosis type 1 (NF-1; 90% cases) than localized variants and have a higher propensity to develop malignant PNSTs later in life. Schwannomas are commonly solitary slow-growing subcutaneous lesions < 5 cm in size. They can occasionally be multiple and associated with several hereditary neurocutaneous syndromes, most well defined of these being neurofibromatosis type 2 (NF-2) and Schwannomatosis [17].

On MR imaging, the lesions appear isointense on T1w images and show homogenous to heterogenous increased signal intensity to muscle on T2w images. PNSTs have classically been described using several imaging signs on MRI. The 'tail sign' describes a tail forming at the superior and/or inferior margin of the nerve lesion. The 'target sign' is central hypointense tissue due to collagenous stroma with peripheral increased signal intensity on T2w images due to more myxomatous tissue. It is observed in NF more commonly than Schwannoma. The 'split fat sign' means prominent fat around the slowly growing lesion. The 'fascicular sign' depicts prominent fascicular neurogenic appearance within the margin of the lesion. The 'bag of worms' sign is seen in superficial plexiform NFs [17, 18]. While NF may show multifascicular involvement of the nerves, schwannoma shows one or two fascicular continuity with the mass lesion. It is difficult to differentiate between benign and malignant PNSTs on conventional MRI. Diffusion tensor imaging showing low minimum apparent diffusion coefficient (ADC) value ($< 1.1 \times 10^{-3}$ mm^2/s) is useful to find most cellular areas that may suggest malignancy and can be directed for biopsy. In underlying neurofibromatosis, there is increased chance of malignancy and it may develop at an earlier age in life as compared to the isolated forms of malignant peripheral nerve sheath tumors. New onset of severe pain, neurologic deficit, rapid increase in size, heterogeneous appearance and low ADC value can



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Young girl with NF type I and MPNST. MIP images from coronal 3D STIR SPACE **(3A, B)** show numerous peripheral nerve sheath tumors and nodular thickening of the sciatic nerves (arrows in 3A) and a large heterogeneous MPNST arising of the right femoral nerve (arrow in 3B) in this known case of NF type I. ADC image **(3C)** from DTI shows a low value of 0.7×10^{-3} mm²/s in keeping with high cellularity. Contrast fat suppressed T1w VIBE image shows heterogeneous nodular enhancement with central necrosis (arrow).

serve as important signs of incipient malignancy (Fig. 3). Perineurioma is another classic benign tumor, seen in young children in their adolescence showing uniform fascicular thickening and nerve thickening over a long segment, usually in a sciatic distribution. Due to compact fascicular thickening, it may show ADC values in the range of $1.0–1.2 \times 10^{-3}$ mm²/s, however, the clinical symptoms of slow motor loss and MRN imaging appearance are classic findings (Fig. 4).

Trauma

Traumatic peripheral nerve injuries are common in both children and adults, albeit the causes are different. About 80% peripheral nerve injuries in children occur in the upper extremity, and the most common causes include obstetric lesions (46.78 %) (Fig. 5) and iatrogenic (16.95 %), with predominant involvement of the brachial plexus and sciatic nerve [19].

Sunderland classified peripheral nerve injuries into five grades of increasing severity [20].

- Neurapraxia (Sunderland Grade I) is a mild form of neural insult leading to temporary impulse conduction block along the affected nerve segment. It is reversible and muscle denervation changes do not occur.
- Axonotmesis (Sunderland Grade II) is more severe than neuraplaxia involving physical disruption of the axon with preservation of outer covering layers of endoneurium, perineurium and epineurium. Wallerian degeneration follows such an insult, which later results in regeneration of the axon along its original course as the nerve coverings are preserved. Although the duration and severity of symptoms is worse, it usually carries an excellent prognosis similar to neurapraxia.
- Neurotmesis (Sunderland Grade III) refers to complete disruption of the axon and supporting connective tissue structures. There is loss of continuity of the nerve fibers, and the regenerating nerve fibers are no longer confined to the endoneurium.

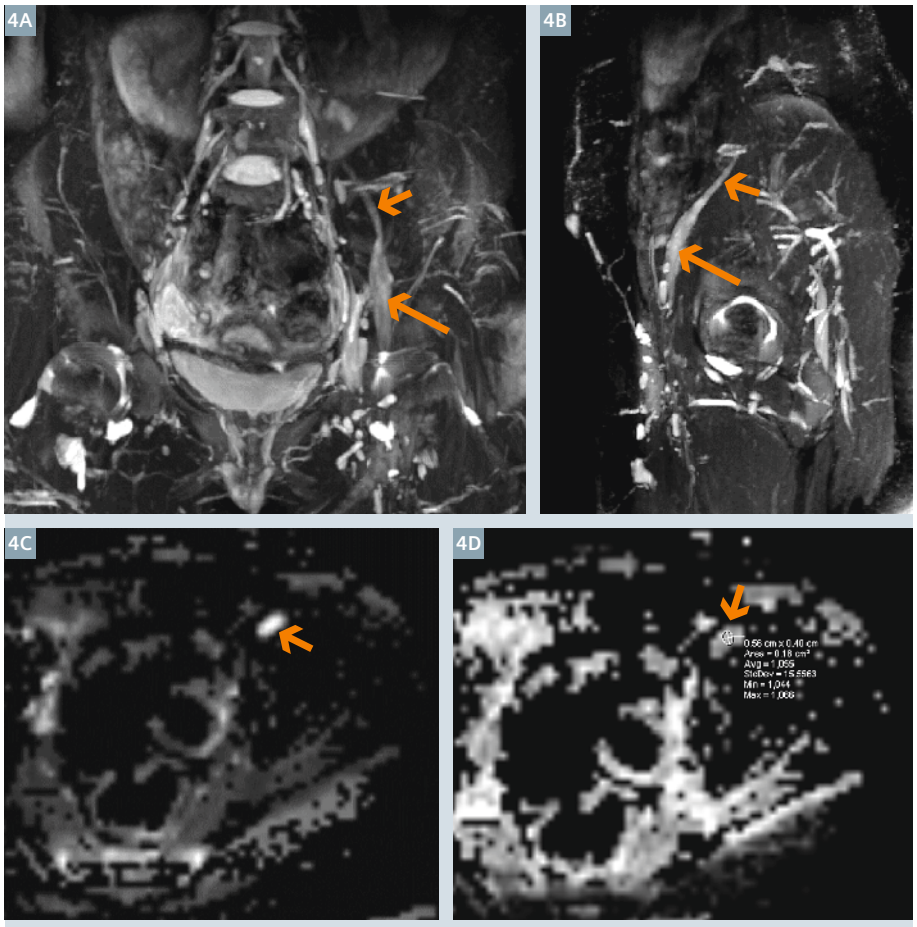
This complicates the regeneration process and may lead to dysfunctional distal end of the nerve.

- Grade IV injury results in neuroma -in-continuity (NIC), which encompasses perineurial disruption and entangled disorganized mass of regenerating nerve fibers.
- Sunderland grade V injury leads to end-bulb neuroma, also called stump neuroma with underlying discontinuity with the nerve (Sunderland Grade V) [17, 21].

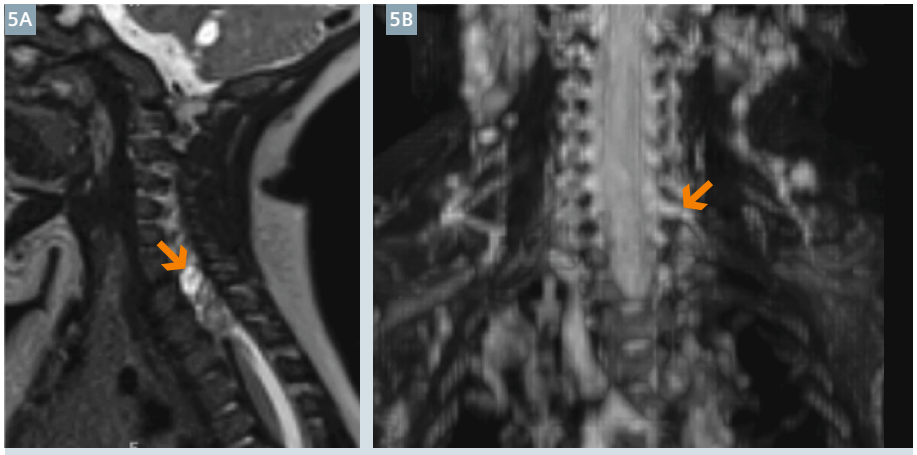
On MR imaging, NIC appears as a heterogeneous mass with 'tail sign' which does not show enhancement on contrast administration (differentiating it from neurogenic tumor, which shows enhancement). Stump neuromas are seen as fusiform masses with an irregular outline showing decreased signal intensity on T1w images and increased signal intensity on T2w images [21]. MRN can clearly show abnormal nerve hyperintensity and/or enlargement with otherwise underlying nerve continuity in Grade I-III injuries, which undergo medical management, except that one might release superimposed nerve entrapment. Grade IV and V injuries show a focal neuroma and these can also be distinguished based on the presence of nerve continuity or discontinuity.

Infection / Inflammation

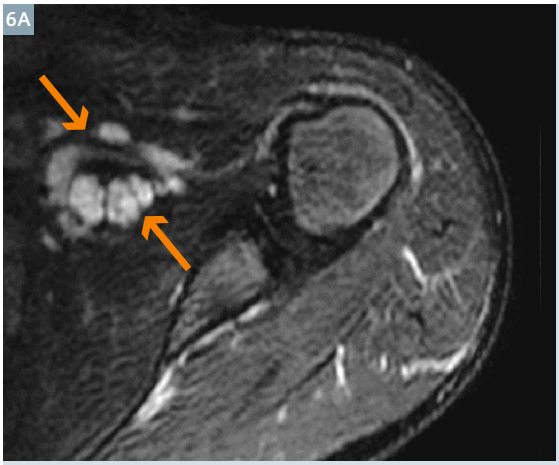
Infectious neuropathy may result from direct nerve involvement or immunologic response of the body towards the infectious agent. The most common and important of these is the Guillain-Barre Syndrome (GBS), also known as acute inflammatory demyelinating polyneuropathy (AIDP). Various microorganisms have been implicated as the trigger for the immune response in GBS (Campylobacter jejuni, Cytomegalovirus and Ebstein Barr virus, etc.). GBS is a clinical diagnosis classically presenting in the child after a recent mild infection with weakness, sensory loss, pain, and hypoflexia in the lower extremities. MR imaging is usually ordered in such cases to confirm the diagnosis and more importantly to rule out other spinal cord or nerve root pathologies that mimic AIDP. MRI findings may be normal in pediatric patients. Hyperintensity and nerve thickening

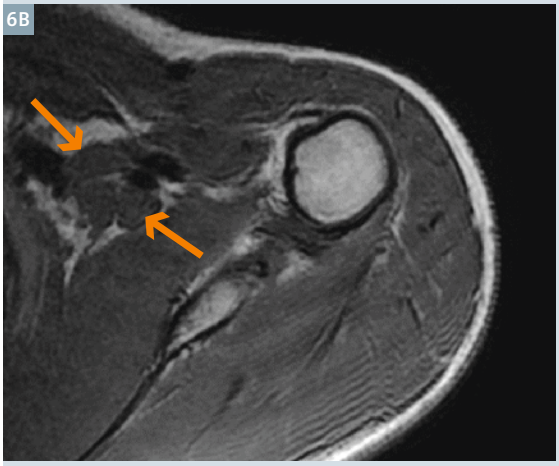


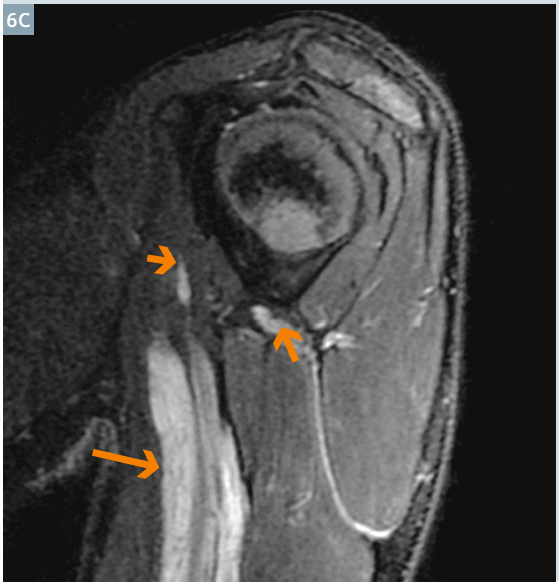
4 Young girl with gradual left leg weakness caused by a Perineurioma. MIP images from coronal and oblique sagittal reconstructed 3D STIR SPACE **(4A, B)** images show left femoral nerve (small arrows) fusiform enlargement by a perineurioma (long arrows). DTI images show ADC value of 1.1×10^{-3} mm²/sec.



5 Left C7 nerve root avulsion in an infant from birth injury. Sagittal T2w SPACE **(5A)** image and MIP image from coronal 3D STIR SPACE **(5B)** show pseudomeningocele of the left C6-7 neural foramen with left C7 nerve root avulsion (arrows).







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CIDP. Young boy with left arm weakness and mild sensory changes. Axial T2w SPAIR **(6A)** and T1w **(6B)** images show multifocal thickening and prominent fascicular appearance of all brachial plexus peripheral branch nerves (arrows). Sagittal fs PDw **(6C)** image shows most thickening of median nerve (long arrow) and less pronounced thickening of the musculocutaneous nerve (small arrow) and axillary nerve (medium arrow).

on MRN images may be seen in spinal nerve roots as a result of the inflammatory process, showing enhancement on contrast imaging. The anterior nerve roots show enhancement more frequently than posterior nerve roots, which is suggestive of GBS [22, 23].

Chronic inflammatory demyelinating polyneuropathy (CIDP) is also an immune mediated condition which presents similar to GBS and is differentiated from GBS on basis of course of the disease (progressive worsening for more than 2 months, while GBS is self-limiting, lower limb involvement > upper limbs and high CSF protein). MR imaging findings in CIDP are nonspecific showing mild to moderate diffuse enlargement with increased cross sectional area of the nerve, as with other hereditary neuropathies such as CMT. However, family history is generally insignificant, the lesions may be asymmetrical or unilateral (Fig. 6) as compared to CMT type IA [4, 24]. Multifocal motor neuropathy is another condition that affects the motor function predominantly and is more common in upper limbs as compared to the lower limbs. Multiple conduction blocks are noted on electrodiagnostic examinations and MRN of the extremity or plexus shows diffuse nerve thickening and/or enlargement, not limited to the entrapment sites. There is generally good response to IVIG treatment or cyclophosphamide therapy.

Conclusion

Imaging of nerves in children is challenging due to their small size and comparative rarity of neuropathies affecting them. MR Neurography is a powerful diagnostic tool even in pediatric population. With proper communication between the referring physician and the radiologist, the diagnostic value of MRN is enhanced leading to early diagnosis and proper patient care.

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