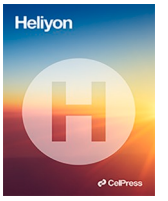
Heliyon 10 (2024) e26089

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Case report

Treatment of childhood intraneural perineurioma: A case report and literature review

Rongpei Li [a,b], Yao Zhang [a], Guanggui Li [a,c], Cuijie Wei [a], Hui Xiong [a], Xingzhi Chang [a,*]

[a] Department of Pediatrics, Peking University First Hospital, Beijing 100034, China
[b] Department of Pediatrics, Jining First People's Hospital, Shandong, 272011, China
[c] Department of Pediatrics, The First People's Hospital of Zunyi, Guizhou, 563099, China

ARTICLE INFO

Keywords:
Intraneural perineuriomas
Peripheral neuropathy
Surgical treatment
Childhood
Case report

ABSTRACT

Background: Intraneural perineurioma is a rare, benign slow-growing lesion that usually involves a single main trunk nerve during childhood and young adulthood. The treatment of intraneural perineurioma is still a subject of controversy, especially in fast-growing children. To date, there was no systemic analysis of intraneural perineurioma in children.
Method: A case of Intraneural perineurioma affecting the left sciatic nerve with 2 years of follow-up was presented. A systematic review was performed on literature published before June 2023, focusing on intraneural perineurioma diagnosed at no older than 18 years old.
Result: A 9-year-old boy presented with progressive left foot-drop and abnormal gait for 2 years. The electromyography and magnetic resonance neurography study confirmed neuropathy involving the left sciatic nerves and its branches. Pathological investigation of the left sural nerve confirmed the diagnosis of intraneural perineurioma. The boy received physical therapy, and the disease was stable during the 2 years of follow-up. Fifty-seven childhood cases were identified in literature. Five patients with oral intraneural perineurioma underwent excision of the mass with good outcomes. In the other 52 patients with peripheral nerve involvement, 25 of them received surgical treatment, with different outcomes according to different operations. Out of 33 cases with precise lesion sizes, the length of the lesion in patients without nerve resection was significantly longer than that in patients with nerve resection (12.86 ± 7.44 cm vs 4.57 ± 4.5 cm. $p < 0.05$).
Conclusions: Intraneural perineuriomas are rare benign tumors with slow progression. The options for surgery should be cautiously considered in childhood patients with long segmental peripheral nerve involvement.

1. Introduction

Perineuriomas are a group of rare benign slow-growing tumors consisting of neoplastic perineurial cells, accounting for approximately 1% of peripheral nerve sheath neoplasms [1]. According to their locations, perineuriomas are divided into intraneural perineurioma (surrounding nerve fibers) and extraneural perineurioma (localized in skin and soft tissue) [2]. Regarding intraneural

* Corresponding author.
E-mail address: changxingzhi7318@163.com (X. Chang).

https://doi.org/10.1016/j.heliyon.2024.e26089
Received 23 November 2023; Received in revised form 9 January 2024; Accepted 7 February 2024
Available online 15 February 2024
2405-8440/© 2024 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC license (http://creativecommons.org/licenses/by-nc/4.0/).

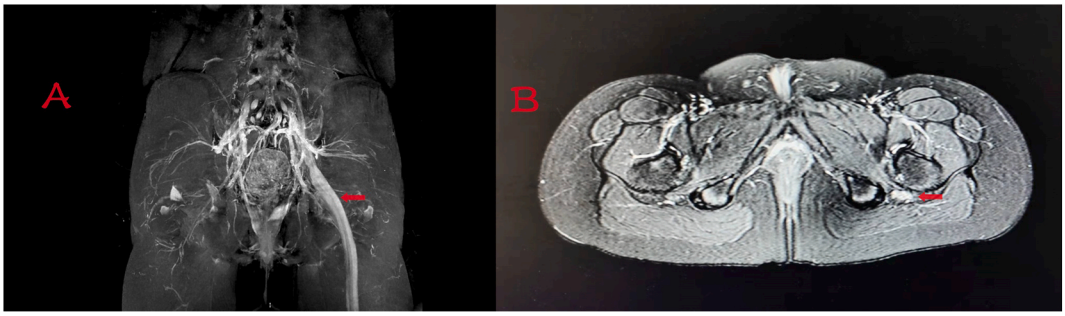


Fig. 1. MRI demonstrates enlargement of the left sciatic nerve and abnormal hyperintense signals on the coronal T2-weighted images (1A, arrow), signal enhancement on axial T1-weighted postgadolinium images (1B, arrow).

perineurioma (IP), only cases and small series have been reported. There have been no reports on incidence or prevalence of the disease due to its scarcity. In the literature, the age of onset of intraneural perineurioma is either adolescence or young adulthood [2], while infantile cases have been reported occasionally [3]. There was no systemic analysis of intraneural perineurioma in children.

Intraneural perineurioma was previously known as localized hypertrophic neuropathy, as it usually involves a single peripheral nerve, characterized by perineurial cell proliferation [4]. The etiology of intraneural perineurioma has previously been ascribed to a reactive process associated with trauma [5], and recently more researchers have described it as a true neoplasm [6,7]. Histopathological characteristics were taken as the gold standard for the diagnosis of IP, including concentric whorls of perineural cells around the nerve fibers (known as pseudo–onion bulbs), and the lamellae of the onion bulbs stain for epithelial membrane antigen (EMA), while the centers stain for S100 protein. With recent advances in magnetic resonance imaging (MRI), some researchers have proposed that the diagnosis of IP may rely on clinical and radiological factors, obviating invasive tissue diagnosis in certain circumstances [8]. The

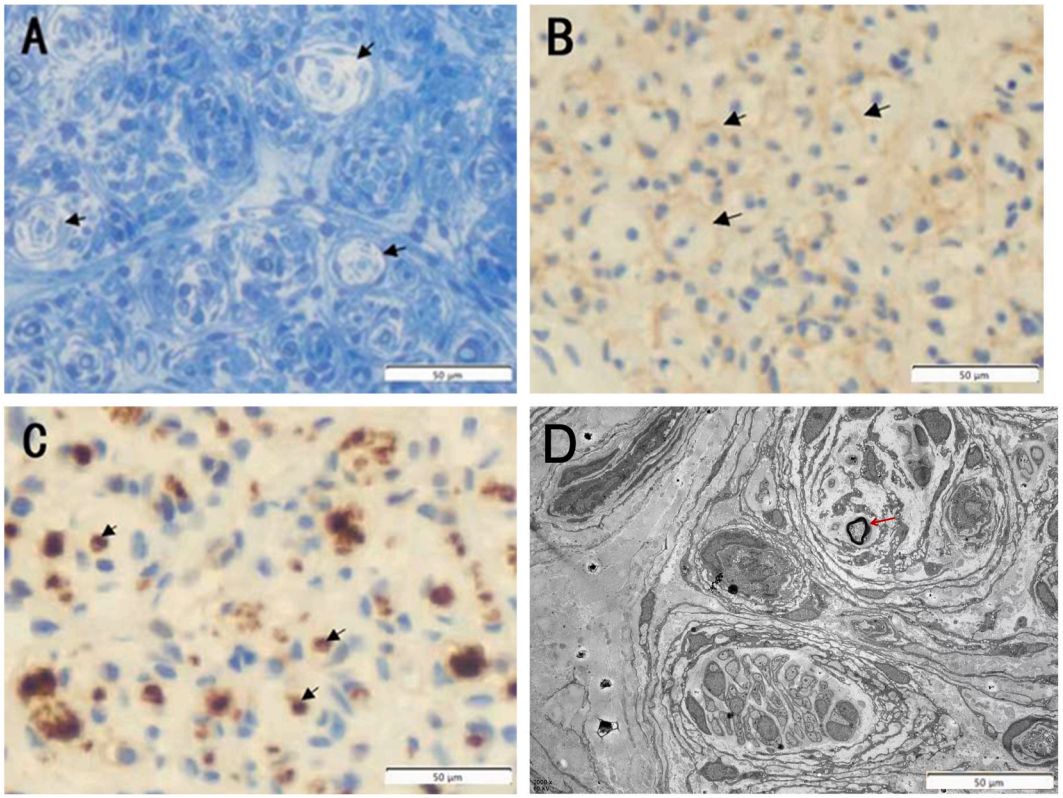


Fig. 2. Pathological features of intraneural perineurioma. The present case. (2A) Toluidine blue stain on semi-thin section demonstrates diffuse pseudo-onion bulb formation, and thinly myelinated fibers at the center of pseudo-onion bulbs (arrowheads). (2B) Reactivity of pseudo-onion bulb leaflets with epithelial membrane antigen (EMA) confirming these are of perineurial origin (arrowheads). (2C) Schwann cell preparation (S-100) demonstrates reactivity of the myelinated fibers at the center (arrowhead) and absence of reactivity of the surrounding pseudo-onion bulbs. (2D) Electron micrograph demonstrates dense concentrically arranged cellular processes around thinly myelinated axons (arrowhead).

Table 1
Clinical and MRI features of intraneural perineurioma in children.

Pt	Sex	Onset Age(y)/ diagnostic age (y)	Duration of symptom (m)	Weak-ness	Sensory loss	Location	Operation	Follow-up (m)	Outcome of motor	MRI	MRI contrast	Length of tumor (cm)	ReferencePMID
1	F	11	12	+	–	Sciatic	–	12	Progress	Fusiform	+	15	19,567,701
2	M	5.8	15	+	–	Sciatic	–	10	Progress	Fusiform	+	12	19,567,701
3	F	birth	24	+	+	Lumbosacral plexus	–	20	Progress	Fusiform	+	12	19,567,701
4	F	11.5	6	+	+	Sciatic	–	61	Progress	Fusiform	–	4	19,567,701
5	F	12	36	+	–	Sciatic	–	88	Progress	Fusiform	–	>25	19,567,701
6	F	6.5	7	+	–	Sciatic	TT	118	Improve	Fusiform	+	6.5	19,567,701
7	F	8	48	+	_	Brachial plexus	–	41	Progress	Fusiform	+	9.7	19,567,701
8	M	112.5	18	+	+	Sciatic	–	24	Progress	Fusiform	+	32	19,567,701
9	M	birth	144	+	–	Brachial Plexus	–	54	Progress	Fusiform	+	14	19,567,701
10	F	7.4	8	+	+	Peroneal	NG, TT	135	Improve	Mass	+	3.5	19,567,701
11	M	13.6	16	+	+	Median	–	33	Progress	Fusiform	–	/	19,567,701
12	F	5	72	+	+	Brachial plexus	–	/	/	/	/	/	19,567,701
13	F	11	24	+	+	Peroneal	–	56	Stable	Fusiform	–	6	19,567,701
14	M	0.5	90	+	+	Sciatic	TT	14	Stable	Fusiform	+	6.8	19,567,701
15	F	11	24	+	+	Ulnar	–	8	Progress	Fusisorm	+	7.8	19,567,701
16	M	9	36	+	+	Sciatic	–	/	/	Fusiform	+	20	19,567,701
17	F	1.8	2	+	+	Median	Resection, NG	12	Cure	Mass	+	5	11,281,674
18	F	/17	/	+	+	Brachial plexus	Excision biopsy	/	/	Enlargement	/	1.3	30,637,060
19	M	/18	/	+	–	Radial	Excision biopsy	/	/	Enlargement	/	1	30,637,060
20	F	/17	/	+	+	Brachial plexus	Excision biopsy, TT	/	/	Enlargement	/	/	30,637,060
21	M	/15	/	+	+	Brachial plexus	Excision biopsy	/	/	Enlargement	/	7.5	30,637,060
22	M	/18	/	+	+	Brachial plexus	Excision biopsy	/	/	Fusiform	/	6	30,637,060
23	F	8.3	9	+	–	Radial	Excision biopsy, NG	6	Improve	ND	–	3	16,039,379
24	M	7	12	–	–	Median	Excision	72	Cure	/	/	2.4	15,750,909
25	F	7	48	+	–	Sciatic	–	/	/	Enlargement	+	>68	20,004,070
26	M	8	48	+	+	Sciatic	–	/	/	Fusiform	+	/	29,094,786
27	M	7	36	+	+	Sciatic	–	/	/	Fusiform	+	/	29,094,786
28	M	10	36	+	+	Sciatic	–	/	/	Fusiform	+	/	29,094,786
29	M	13	48	+	+	Femoral	–	24	Stable	Fusiform	+	/	29,094,786
30	M	16	12	+	+	Sciatic	–	/	/	Fusiform	+	/	29,094,786
31	F	14	12	+	+	Sciatic	–	/	/	Fusiform	+	/	29,094,786
32	F	5	48	+	+	Sciatic	–	/	/	Fusiform	+	/	29,094,786
33	M	1.5	12	+	–	Sciatic	–	30	Progress	Enlargement	–	/	19,520,281
34	F	5	24	+	–	Ulnar	Excision	12	Stable	Mass	/	1	15,086,844
35	M	1	156	+	–	Radial Median	–	168	Progress	Enlargement	+	/	24,263,031
36	M	12	48	+	+	Sciatic	–	168	Progress	Fusiform	+	/	19,766,004
37	F	/11	/	+	–	Peroneal	Excision, NG	/	/	Fusiform	–	/	19,766,004
38	F	/18	12	+	+	Brachial Plexus	Excision biopsy	0.2	Improve	Fusiform	+	4	27,326,273
39	M	/18	/	+	–	Radial	Excision, NG, TT	11	Stable	Mass	+	5	32,529,330

(*continued on next page*)

Table 1 (*continued*)

Pt	Sex	Onset Age(y)/ diagnostic age (y)	Duration of symptom (m)	Weak-ness	Sensory loss	Location	Operation	Follow-up (m)	Outcome of motor	MRI	MRI contrast	Length of tumor (cm)	ReferencePMID
40	M	/10	/	+	–	Sciatic	–	/	/	Enlargement	+	/	32,529,330
41	M	/5	/	+	–	Ulnar	Excision, NG	36	Improve	Mass	+	1.5	17,824,794
42	F	/13	/	+	+	Radial	Excision, NG	10	Stable	Fusiform	+	2.5	27,086,131
43	M	/14	12	+	+	Femoral	Excision, NG	18	Improve	Fusiform	+	5	27,086,131
44	F	9	24	–	+	Ulnar	Excision	/	Cure	Mass	/	2	16,096,405
45	M	14	24	+	–	Ulnar	IFN	24	Improve	Enlargement	+	15	32,054,523
46	F	14	36	+	_	Peroneal	IFN	30	Improve	Fusiform	+	/	32,054,523
47	M	3	24	+	+	Radial	Excision, NG	/	Stable	ND	/	/	18,666,052
48	M	/10	/	+	–	Sciatic	Excision, NG	5	Stable	Enlargement	/	5	18,666,052
49	F	/8	/	+	–	Sciatic	–	/	/	Enlargement	+	/	27,001,989
50	F	/12	/	+	+	Brachial plexus	–	/	/	Fusiform	+	/	22,638,873
51	F	13	48	+	+	Femoral	Excision, NG	10	Stable	Enlargement	+	18	9,883,854
52	F	11	12	+	+	Sciatic	Excision, NG	30	Stable	Enlargement	+	12	9,883,854
53	M	7	24	+	+	Sciatic	–	12	Stable	Enlargement	+	>10	Present case
54	M	2	120	–	–	Tongue	Excision	6	Cure	/	/	0.6	16,781,350
55	M	12	24	–	–	Tongue	Excision	6	Cure	/	/	0.4	24,422,960
56	M	/16	/	–	–	Buccal mucosa	Excision	24	Cure	/	/	1.5	16,757,071
57	F	5	12	–	–	Tongue	Excision	4	Cure	/	/	1	17,824,794
58	F	/18	/	–	–	Buccal mucosa	Excision	/	/	/	–	2	17,449,293

Note: Pt, patient; NG, nerve graft; TT, tendon transfer; IFN, Interfascicular neurolysis; ND, Non-diagnostic; + , present; -, absent; >, above;/:, data unavailable.

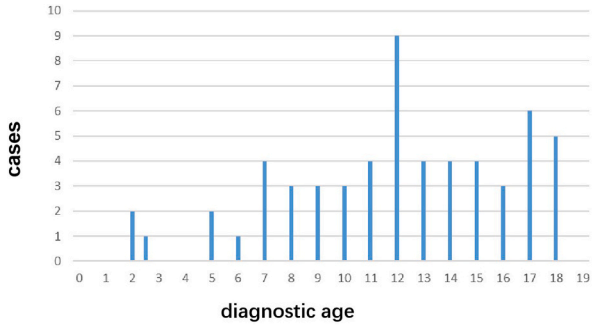


Fig. 3. Diagnostic age distribution in all reviewed patients.

treatment of IP is still a subject of great controversy. Here we present a case of IP affecting the sciatic nerve in a 9-year-old boy with 2 years of follow-up. We also review the literature in efforts to highlight the clinical features of IP in children (no older than 18 years old) and improve the treatment of this disorder in children with fast-growing limbs.

1.1. Case presentation

The patient is a 9-year-old boy who visited us for abnormal gait for 2 years. Approximately 2 years ago, the child developed an unstable gait with a left foot drop, easily falling when running and jumping, without pain or numbness over the dorsum of the left foot. There was no history of trauma or antecedent illness.These conditions were not noticed by the family at the beginning of the illness, and his condition slowly progressed. He could not stand alone on his left foot, and his left leg became thinner than his right leg. One year ago, the boy received left peroneal tendon transfers with no improvement of abnormal gait. He had normal developmental milestones. There were no abnormalities during pregnancy or the perinatal period. Consanguinity was denied in the family. His parents and other family members were all in good health. Upon examination, his muscle strength of both upper extremities and right lower extremity was grade V; the proximal muscle strength of the left lower extremity was grade V, and the distal muscle strength of the left lower extremity was grade IV. Muscle atrophy was noticed in the distal left lower extremity. He had reduced left ankle dorsiflexion and foot eversion, with normal plantar flexion and knee jerks. He had decreased sensation to light touch and pin over the dorsum of the left foot. There was no foot size or limb length discrepancy between his lower limbs. His serum creatine kinase level was normal. In electromyography (EMG) studies, an absent sensory nerve action potential (SNAP) was observed in the left sural nerve. The compound muscle action potential (CMAP) and F-wave latency in the left tibial nerve were mildly longer than those in the right tibial nerve, with normal conduction velocity. The CMAP latency in the left common peroneal nerve was significantly longer than that in the right common peroneal nerve, with prominently decreased conduction velocity and CMAP amplitude. MRI of both lower extremities demonstrated abnormal hyperintense signals on the T2-weighted images in the lateral portion of the left sciatic nerve. The involved portion of the nerve was moderately enlarged and enhanced on the postgadolinium images (Fig. 1). The involvement of the left sciatic nerve extended from the level of the piriformis (confirmed by enhanced MRI signals) to the distal tibial nerve at the ankle level (confirmed by the sural nerve biopsy). Chromosome analysis showed a normal karyotype. Gene panel (including the PMP22, MPZ, and MFN2 genes) sequencing for hereditary neuropathies revealed no pathogenic variations. Left sural nerve biopsy was performed at the ankle level. Histology of the biopsy specimen showed concentric whorls of perineural cells around the nerve fibers (onion-bulb like), and the lamellae of the onion bulbs were highlighted by the stain for epithelial membrane antigen (EMA), while the centers were positive for S100 protein (Fig. 2). Intraneural perineurioma was diagnosed.

Because the involvement of the left sciatic nerve extended more than 12 cm, as demonstrated by MRI and EMG studies, nerve resection was not performed. The boy received physical therapy and was followed up for 2 years at our outpatient department. There was no change in symptoms and physical signs. No unanticipated events occurred during follow up.

1.2. Review of the literature

We used "intraneural perineurioma, hypertrophic neuropathy" in both Chinese and English as keywords and searched the literature for June 2023 in the following databases: the Chinese Journal Full-text Database (CNKI), Wanfang Data Knowledge Service Platform, the National Center for Biotechnology (NCBI) and biomedical literature database (PubMed). Inclusion criteria were articles published in Chinese or English presenting the clinical course, peripheral nerve location, and pathologic examination. Furthermore, all included studies were meticulously cross-referenced to ensure that patients were not included in multiple articles. The diagnosis of intraneural perineurioma was based on typical histologic manifestations. Hybrid tumors showing intraneural perineurioma combined with other tumors were excluded. Childhood cases were defined as a diagnostic age of no older than 18 years old. The search resulted in 285 articles. After analyzing the title and abstract, 259 articles were excluded. The full text of the remaining 26 articles was reviewed, comprising 57 cases (all in the English literature). Including our case, demographics, treatment and the neurological outcomes were analyzed for 58 patients (Table 1).

The diagnostic age was 11.9 ± 4.29 years (range 2–18 years, Fig. 3). The median time from symptom onset to diagnosis in patients

(43 cases with available information) was 35 ± 34.2 months (range 2 months–13 years). Most cases (39/58, 67.2%) were diagnosed after 10 years old, 24.1% (14/58) cases were diagnosed at 5–10 years old, and only 5 cases (8.6%) were diagnosed at no older than 5 years old. The ratio of males to females was 1:1 (29 males and 29 females), with no gender predilection. In most cases (53/58, 91.4%), intraneural perineuriomas affect major nerves or their branches, causing symptoms such as motor and sensory deficits. The sciatic nerve or its branches were most commonly affected in 26, followed by the brachial plexus or its branches in 23, and the lumbosacral plexus or its branches in 4. In contrast to other series reporting a predominance of the upper limb nerve [9] or equal involvement in the upper and lower limb nerves [10], a predominance of lower limb nerve involvement (30/53, 56.6%) was found in the present childhood cohort. Similar to a previous report, the location of the involved nerve was one single major nerve in most cases (43/53, 81.1%), with a few cases (10/58, 17.2%) involving more than one nerve in brachial plexus or lumbosacral plexus at the same lateral. Nagappa et al. reported a case with involvement of the radial and median nerves [9]. Only one case in Mauermann's study presented with bilateral involvement of multiple lower limb nerves [10]. In patients with major nerve involvement, limb weakness was the most frequent symptom (51/53, 96.2%), followed by mild sensory deficit (32/53, 60.4%). In one child with Beckwith-Wiedemann syndrome, IP manifested as an asymptomatic right volar wrist mass [11].A painful mass involving the ulnar nerve was reported in the other child [12].

Apart from the typical location on limbs, a few cases (5/58, 8.6%) of IP were identified in the oral cavity (tongue 3, buccal mucosa 2), involving unknown terminal nerves or facial nerve branches. IP in oral regions is extremely rare. Only 17 cases have been reported in the literature [13]. Clinically, most intraoral IPs were painless, slow-growing nodules in the tongue or in the buccal mucosa [14–16]. As most of these oral IPs were asymptomatic at the beginning, some cases could go undiagnosed as long as 10 years [17]. In contrast to a previous report that the patients in this group were older at the onset of symptoms (median 23 years), and nerve enlargement was found in most cases [18], our analysis identified infantile oral IP. No MRI was performed in these five patients.

In patients with major nerve involvement, electrophysiological studies were performed in most (48/53, 90.6%) to confirm the conduction block of the nerve. Though IP diagnosed only by the clinical and radiological features was excluded from the present analysis. Nearly all (51/53, 96.2%) patients with major nerve involvement received MRI. Enlargement of the affected nerve was noted in most patients (49/51, 96.1%), with no abnormal findings in two patients [19,20], and fusiform enlargement of the nerve was identified in one patient by operational exploration [20]. Fusiform enlargement of the involved nerve was identified in 29 patients, and a mass was identified in 6 patients. The involved nerve was isointense on T1-weighted images, hyperintense on T2 fat-saturated images, and with avid enhancement on postcontrast imaging in 35 (35/51, 68.6%) patients, consistent with the typical MRI characteristics of IP [21].

All 5 patients with oral IP received excision of the mass, 4 of whom were followed up for 4 months to 2 years, with no recurrence of the mass. Twenty-five out of 53 patients with peripheral nerve involvement received surgical treatment. Outcomes according to different operations were as follows: ① Eleven patients received nerve resection and nerve graft, one of whom also received tendon transfer. Ten of them were followed up for 38.2 ± 48.3 months (ranged from 5 months to 10 years). No motor improvement was observed in 5 patients (the length of the involved nerve was 2.5 cm, 5 cm, 12 cm, 18 cm, unknown length, respectively), mild improvement was observed in 5 patients (the length of the involved nerve was 3.5 cm, 3 cm, 5 cm, 1.5 cm, 5 cm, respectively). ② Nine patients received lesion excision without nerve graft, 2 of whom also received tendon transfer. Only two cases were followed up. One patient showed no motor function improvement 12 months after surgery [20]. Another patient was asymptomatic before surgery and was followed up for 6 years without recurrence of the mass. ③ Three patients underwent biopsy and neurolysis. One patient had improved hand strength on follow-up evaluation one week after surgery [22]. Two cases showed improvement of the motor function of the involved nerve on follow-up examination 24 months and 30 months after surgery [23]. ④ Two patients received only palliative tendon transfer, one had mild improvement in motor function, and one had no changes. Sixteen out of 28 patients without surgery were followed up for 50.56 ± 51.51 months (ranged from 8 months to 14 years). Motor function in three out of these patients was stable and declined in 13 patients. Out of 33 cases with precise lesion sizes in the report, the length of the lesion in patients without nerve resection (16 cases) was 12.86 ± 7.44 cm, and in patients with nerve resection with/without nerve graft or tendon transfer (17 cases), it was 4.57 ± 4.5 cm. A significant difference was noted between the two groups ($p < 0.05$, *t*-test).

2. Discussion

To date, nearly 200 cases of intraneural perineurioma have been documented both in children and in adults [18]. The median age of onset was different in different cohorts, and none of these cohorts were focused on children. It was 14 years (range 6 months–55 years) in the Mauermann et al. cohort of 32 patients [10], while the mean age (±SD) at imaging in the Wilson et al. cohort was 47 (±20) years [8]. Infantile cases of IP have occasionally been reported [3,24]. The prevalence of intraneural perineurioma in children is unknown. Considering its rareness and delay in diagnosis, the prevalence of intraneural perineurioma may be underestimated. Our review represents the largest collection of cases of IP in children. We confirmed that most childhood IP occurred in school-age children and teenagers, and only a few cases were diagnosed before 5 years old.

Compared to intraneural perineurioma in adults, congenital abnormalities seem to be more frequently encountered in children with IP, which sometimes makes the precise onset of symptoms difficult to ascertain. Chen et al. reported an IP in a child with Beckwith-Wiedemann syndrome, and with café au lait spots on the neck and left shoulder [11]. Lequit et al. reported an IP of the right brachial plexus in a 12-year-old girl with congenital torticollis [25]. Siponen et al. described a case of multiple orofacial intraneural perineuriomas in a patient with hemifacial hyperplasia [26]. Brock et al. reported an intraneural perineurioma in an eleven-year-old girl with an abnormal karyotype: 46, XX, add (2) (q11.2), add (3) (q12) [12]. Pendleton et al. reported two cases of IP with NF2 gene variations [27]. Together with chromosome 22 abnormalities [28] and TRAF7 mutations [29] reported in patients with IP, it is

reasonable to suggest that genetic background underlies the pathogenesis of IP.

Currently, the treatment of intraneural perineurioma is still a subject of controversy, especially when a single major nerve is involved. Management options may include lesion resection with or without nerve graft repair, nerve transfer, tendon transfer, or conservative management. Uerschels et al. retrospectively analyzed the neurological outcome of 77 patients who received surgical treatment. The neurological outcome was unchanged in 35 cases (45.5%) and worsened in 16 cases (20.8%), and the results were similar between the different surgical treatment options [23]. Intraneural perineurioma is a rare benign tumor with a slow progression. As at least 2 years of clinical and radiologic follow-up of patients showed that intraneural perineuriomas only rarely grew in length, and did not grow to involve new nerves or nerve divisions, and growth did not correlate with clinical progression, Alkhaili et al. suggested that the surgical decision should be made in relation to patient age, functional deficit and the size of the lesion, and patients may receive excision biopsy and/or palliative treatment for their motor deficit [30]. Although no consensus exists, it is widely accepted that nerve resection should be restricted to shorter lesions, as the length of lesions in patients who undergo nerve resection is significantly shorter than that in patients who do not undergo nerve resection in our analysis. Decompression and neurolysis were successfully performed in patients with lesions as long as 15 cm, and whether it is a more suitable surgery type for improving the neurological deficits of patients with long nerve involvement requires further study [23]. For short involvement at terminal branches of a single major nerve, complete surgical removal may prevent proximal progression and eventual loss of nerve function, similar to terminal nerves involved in oral intraoral perineurioma. All 5 intraoral perineuriomas in our review received complete surgical excision with satisfactory outcomes.

Limitations of the present review. First, this is a review on a rare tumor. Apart from several large cohort studies from the Mayo Clinic, we were only able to review case reports and small case studies. The focus of each case report was different, which resulted in missing information in some individuals, such as the precise size of the lesion, the onset time of symptoms, and the follow-up information. Second, the evaluation of outcomes was different in different reports; some focused on the clinical or radiological progress, some focused on motor or sensory function, and some focused on the recurrence of the lesion.

3. Conclusions

In conclusion, we presented a typical intraneural perineurioma in a teenager and reviewed 57 cases diagnosed in children no older than 18 years old. Intraneural perineurioma can occur in infancy but is most common in children over 10 years old. Most intraneural perineuriomas involve a single peripheral nerve, of which sciatic nerve is the most common, followed by brachial plexus. Occasionally intraneural periuneuriomas occurr in other locations, most commonly in the oral cavity. Congenital abnormalities are more frequently encountered in children than in adults. Oral intraneural perineurioma may be excised with satisfactory outcomes, while excision of intraneural perineurioma involving major nerves should be performed with caution.

Ethics Declarations

This study was reviewed and approved by the Ethics Committee of Peking University First Hospital (Beijing, China). Written informed consents were obtained from the parents of the patient for the publication of their anonymised case details and images.

Fundings

Not applicable.

Data availability statement

Data will be made available on request.

CRediT authorship contribution statement

Rongpei Li: Writing – original draft, Conceptualization. **Yao Zhang:** Data curation. **Guanggui Li:** Resources, Data curation. **Cuijie Wei:** Supervision, Data curation. **Hui Xiong:** Writing – review & editing. **Xingzhi Chang:** Writing – review & editing, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

Not applicable.

References

[1] L.M. Wang, et al., Intraneural perineurioma affecting multiple nerves: a case report and literature review, Int. J. Clin. Exp. Pathol. 7 (6) (2014) 3347–3354.
[2] L. León Cejas, et al., Intraneural perineuriomas: diagnostic value of magnetic resonance neurography, J. Peripher. Nerv. Syst. 23 (1) (2018) 23–28.
[3] D.T. Alfonso, A. Sotrel, J.A. Grossman, Carpal tunnel syndrome due to an intraneural perineurioma in a 2-year-old child, J Hand Surg Br 26 (2) (2001) 168–170.
[4] Z. Simmons, et al., Localized hypertrophic neuropathy: magnetic resonance imaging findings and long-term follow-up, Muscle Nerve 22 (1) (1999) 28–36.
[5] H. Mitsumoto, et al., Perineurial cell hypertrophic mononeuropathy manifesting as carpal tunnel syndrome, Muscle Nerve 15 (12) (1992) 1364–1368.
[6] M.E. Heilbrun, et al., Intraneural perineurioma of the common peroneal nerve. Case report and review of the literature, J. Neurosurg. 94 (5) (2001) 811–815.
[7] C.E. Restrepo, et al., The almost-invisible perineurioma, Neurosurg. Focus 39 (3) (2015) E13.
[8] T.J. Wilson, et al., Clinicoradiological features of intraneural perineuriomas obviate the need for tissue diagnosis, J. Neurosurg. 129 (4) (2018) 1034–1040.
[9] M. Nagappa, et al., Intraneural perineurioma of unilateral radial and median nerves manifesting with long-standing focal amyotrophy in a 14-year-old-boy, J. Clin. Neuromuscul. Dis. 15 (2) (2013) 52–57.
[10] M.L. Mauermann, et al., Longitudinal study of intraneural perineurioma–a benign, focal hypertrophic neuropathy of youth, Brain 132 (Pt 8) (2009) 2265–2276.
[11] L. Chen, Y. Li, J.H. Lin, Intraneural perineurioma in a child with Beckwith-Wiedemann syndrome, J. Pediatr. Surg. 40 (2) (2005) E12–E14.
[12] J.E. Brock, et al., Cytogenetic aberrations in perineurioma: variation with subtype, Am. J. Surg. Pathol. 29 (9) (2005) 1164–1169.
[13] C.M. Schadel, et al., Perineurioma of the tongue: a case report and review of the literature, J. Oral Maxillofac. Surg. 77 (2) (2019) 329.e1–329.e7.
[14] M. Hirano, et al., Intraneural perineurioma arising in the lateral border of the tongue, Pathol. Int. 63 (12) (2013) 619–621.
[15] P. Dundr, et al., Intraneural perineurioma of the oral mucosa, Br. J. Oral Maxillofac. Surg. 45 (6) (2007) 503–504.
[16] B.L. Boyanton Jr., et al., Intraneural perineurioma: a systematic review with illustrative cases, Arch. Pathol. Lab Med. 131 (9) (2007) 1382–1392.
[17] D.E. da Cruz Perez, et al., Intraneural perineurioma of the tongue: a case report, J. Oral Maxillofac. Surg. 64 (7) (2006) 1140–1142.
[18] K.A. Lenartowicz, et al., Clinical features, Natural history, and outcomes of intraneural perineuriomas: a systematic review of the literature, World Neurosurg 154 (2021) 120–131.e8.
[19] C. Scheller, et al., Intraneural perineuriomas; a rare entity. Clinical, surgical and neuropathological details in the management of these lesions, Zentralbl. Neurochir. 69 (3) (2008) 134–138.
[20] W. Cortes, J. Cheng, H.S. Matloub, Intraneural perineurioma of the radial nerve in a child, J Hand Surg Am 30 (4) (2005) 820–825.
[21] A. Salvalaggio, et al., Nerve ultrasound and 3D-MR neurography suggestive of intraneural perineurioma, Neurology 86 (12) (2016) 1169–1170.
[22] E.S. Lavi, et al., MRI of intraneural perineurioma of the brachial plexus, Radiol Case Rep 7 (1) (2012) 649.
[23] A.K. Uerschels, et al., Modern treatment of perineuriomas: a case-series and systematic review, BMC Neurol. 20 (1) (2020) 55.
[24] J.R. Østergaard, T. Smith, B. Stausbøl-Grøn, Intraneural perineurioma of the sciatic nerve in early childhood, Pediatr. Neurol. 41 (1) (2009) 68–70.
[25] T. Lequint, et al., Mini-invasive robot-assisted surgery of the brachial plexus: a case of intraneural perineurioma, J. Reconstr. Microsurg. 28 (7) (2012) 473–476.
[26] M. Siponen, et al., Multiple orofacial intraneural perineuriomas in a patient with hemifacial hyperplasia, Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod. 104 (1) (2007) e38–e44.
[27] C. Pendleton, et al., Association of intraneural perineurioma with neurofibromatosis type 2, Acta Neurochir. 162 (8) (2020) 1891–1897.
[28] J. Kurihara, et al., Intraosseous intraneural perineurioma derived from the inferior alveolar nerve with an abnormality of chromosome 22 and expression of the BCR-ABL fusion gene: report of a case and review of recent literature, World J. Surg. Oncol. 16 (1) (2018) 189.
[29] C.J. Klein, et al., Genomic analysis reveals frequent TRAF7 mutations in intraneural perineuriomas, Ann. Neurol. 81 (2) (2017) 316–321.
[30] J. Alkhaili, A. Cambon-Binder, Z. Belkheyar, Intraneural perineurioma: a retrospective study of 19 patients, Pan Afr Med J 30 (2018) 275.