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Hereditary Neuropathy with Liability to Pressure Palsies (HNPP): A Case Misdiagnosed as Lumbar Disc Herniation and Review of Clinical Features

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1. Abstracts

1.1. Background: Hereditary neuropathy with liability to pressure palsies (HNPP) is a rare autosomal dominant peripheral neuropathy caused by PMP22 gene mutations. Its heterogeneous clinical manifestations often lead to misdiagnosis. While standard management focuses on symptom relief, integrated traditional Chinese medicine (TCM) approaches (e.g., acupuncture, tuina) may offer adjunct benefits. This case highlights diagnostic challenges and explores the potential role of TCM in HNPP management.

1.2. Case Presentation A 37-year-old woman presented with recurrent low back pain and alternating lower limb numbness, initially misdiagnosed as lumbar disc herniation (LDH). Despite two months of conservative therapy, symptoms persisted. Subsequent neurophysiological studies revealed multifocal peripheral nerve demyelination, and genetic testing confirmed a heterozygous PMP22 deletion. A multimodal regimen—combining methylcobalamin, vitamin B1, acupuncture (ST36, ST39, ST41, BL55, BL56, BL57), and tuina—led to significant symptom improvement within two weeks. At two-month follow-up, residual left lower limb numbness was noted without functional impairment.

1.3. Conclusions: Electromyographic evidence of demyelination at compression-prone sites should raise suspicion for HNPP. Early genetic confirmation and integrative therapies (neurotrophic agents combined with TCM) may mitigate neurological deficits. Multicenter studies are needed to validate TCM efficacy in HNPP.

2. Keywords: Hereditary neuropathy with liability to pressure palsies; Electromyography; PMP22; Genetic testing; Case report

3. Background

Hereditary neuropathy with liability to pressure palsies (HNPP) is an autosomal dominant disorder caused by deletions or point mutations in the peripheral myelin protein 22 (PMP22) gene [1]. Clinically, HNPP manifests as painless sensory deficits and muscle weakness at anatomical compression sites (e.g., peroneal, ulnar, and median nerves) [2]. Due to its variable presentations, HNPP is frequently misdiagnosed as radiculopathy or entrapment neuropathies. This report describes a case of HNPP initially misdiagnosed as lumbar disc herniation (LDH), emphasizing the diagnostic pitfalls and therapeutic integration of TCM.

4. Case Presentation

In August 2023, a 37-year-old woman presented to our department with persistent lumbar pain accompanied by right lower limb weakness and numbness lasting one month. Her medical history indicated prior hospitalization in September 2022 for similar left lower limb symptoms. Initial lumbar MRI at that time revealed L5/S1 disc degeneration with herniation. Electromyography (EMG) demonstrated motor axonal damage in the left lower limb, bilaterally abnormal F-waves (left-dominant), and chronic radiculopathy. A provisional diagnosis of lumbar disc herniation (LDH) was established, and conservative management—including activity modification, acupuncture, Tuina therapy, and oral methylcobalamin—yielded partial symptom relief without complete resolution.

On physical examination, bilateral tenderness adjacent to the L4/L5 spinous processes was noted, though straight-leg raise tests were negative. Left calf muscle atrophy (Fig. 1) and asymmetric dorsiflexion weakness (right: 3/5; left: 4/5) were observed. Deep tendon reflexes (knee and Achilles) were diminished, with reduced superficial sensation over the lateral calves and foot dorsum bilaterally. Cerebellar function tests (finger-nose, heel-knee-shin) and upper motor neuron signs (Babinski, meningeal irritation) were unremarkable. Routine laboratory investigations—complete blood count, metabolic panels, inflammatory markers, rheumatologic/immunologic profiles, and infectious serology (HIV/syphilis)—remained within normal limits. A preliminary diagnosis of recurrent LDH led to treatment with dexamethasone, mannitol (for nerve edema reduction), acupuncture, Tuina, and herbal hot compresses. Transient improvement in right calf numbness was observed, but left calf symptoms progressed. Repeat lumbar imaging showed L5 transverse process hypertrophy and degenerative changes (Fig. 2), while MRI confirmed a small central L5/S1 disc herniation without overt nerve root compression (Fig. 3). Subsequent EMG

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revealed multifocal peripheral neuropathy involving motor and sensory nerves, predominantly at compression-prone sites (Tables 1-4). Genetic testing confirmed hereditary neuropathy with liability to pressure palsies (HNPP) through identification of a PMP22 whole-gene deletion (Fig. 4).

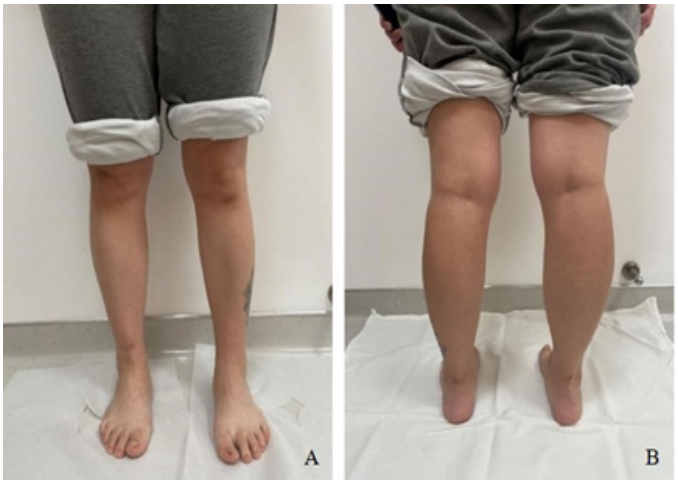

Fig.1 Atrophy of the left calf muscles

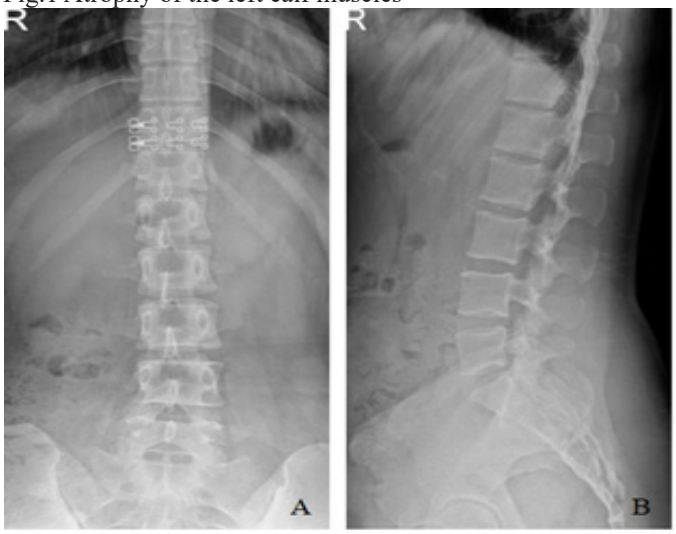

Fig.2 Lumbar spine X-ray

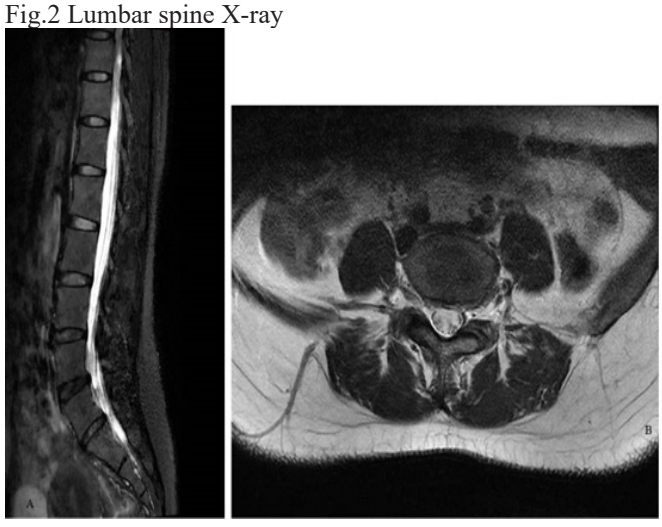

Fig.3 Lumbar spine MRI

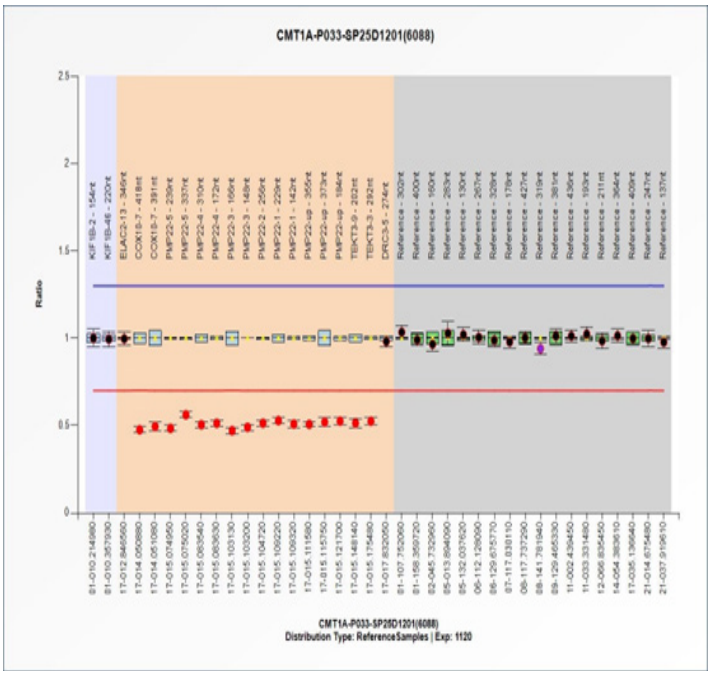

Fig.4 Genetic testing

Muscle	Insertion potentials Electromagnetic potentials MUP phase of fundraising							
	Active Fibrillation Orthostatic Bundle Other Multiphasic morphology -							
	fibrillation							
(left) Inteross dorsI	normal	-	-	-	-	-	normal	interference Phase
(left) Flex carpi rad	normal	-	-	-	-	-	normal	interference Phase
(left) Biceps	normal	-	-	-	-	-	normal	interference Phase
(left) Tibialis anterior	normal	-	-	-	-	-	partly lenient	mixed phase
(left) Gastroc caput med	normal	-	-	-	-	-	normal	interference Phase
(left) Vastus med	normal	-	-	-	-	-	normal	interference Phase
(right) Inteross dorsI	normal	-	-	-	-	-	normal	interference Phase
(right) Flex carpi rad	normal	-	-	-	-	-	normal	interference Phase
(right) Biceps	normal	-	-	-	-	-	normal	interference Phase
(right) Tibialis anterior	normal	-	-	-	-	+	partly lenient	mixed phase
(right) Gastroc caput med	normal	-	-	-	-	-	normal	interference Phase
(right) Vastus med	normal	-	-	-	-	-	normal	interference Phase

Table 1: Electromyography (EMG)

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Motor conduction velocity	Latency	Amplitude	Distance	Conduction velocity	F-wave latency
	ms	mv	mm	m/s	ms
(left) Medianus					
Wrist-APB	4.2	7.1	45		27.4
Elbow-Wrist	8.04	6.3	210	54.7	
(right) Medianus					
Wrist-APB	4.56	8.1	60		28.8
Elbow-Wrist	8.48	7.4	200	51	
(left) Peroneus					
Ankle-EDB	6.55	3.3	60		57.6
Bl.kee-Ankle	15.4	2.7	290	32.8	
Ab.knee-Bl.knee	17.4	2.5	80	40	
(right) Peroneus					
Ankle-EDB	5.06	2.7	70		54.3
Bl.kee-Ankle	12.9	2.7	300	38.3	
Ab.knee-Bl.knee	14.8	2.7	85	44.7	
(left) Tibialis					
Ankle-Abdhal	3.82	10.8	55		58.6
pop Fossa-Ankle	12.6	7.4	365	41.6	
(right) Tibialis					
Ankle-Abdhal	4.13	9.4	60		57.2
pop Fossa-Ankle	13	6.5	380	42.8	
(left) Ulnaris					
Wrist-ADM	2.86	7	60		30.1
Bl.elbow-wrist	6.35	6.4	190	54.4	
Ab.elbow-Bl.elbow	9.15	6.1	130	46.4	
(right) Ulnaris					
Wrist-ADM	2.5	7.6	50		31
Bl.elbow-wrist	5.98	6.6	192	55.2	
Ab.elbow-Bl.elbow	9.4	5.5	115	33.6	

Table 2: Motor conduction velocity

Sensory conduction velocity	Latency	Amplitude	Distance	Conduction velocity
	ms	uv	mm	m/s
(left) Medianus Dig III-Wrist	2.29	11.3	115	50.2
(right)Medianus Dig III-Wrist	2.13	11.3	130	61
(left) Peroneus superfic ankle-dorsum	2.5	8.1	110	44
(right) Peroneus superfic ankle-dorsum	2.56	6.3	118	46.1
(left) Radialis EPL tendon-Wrist	1.77	25.7	110	62.1
(left) Suralis Mid.lower leg-Lat.Malleolus	2	9.9	115	57.5
(right) Suralis Mid.lower leg-Lat.Malleolus	2.66	10.9	120	45.1
(left) Ulnaris DigV-Wrist	1.71	15.9	95	55.6
(right) Ulnaris DigV-Wrist	1.92	6.6	110	57.3

Table 3: Sensory conduction velocity

H-reflection			
(left)Tibialls HReflex			
	M-Lat	H-Lat	H/M Amp
	ms	ms	-
knee-Soleus	5.2	36.5	--
(right) Tibialls HReflex			
	M-Lat	H-Lat	H/M Amp
	ms	ms	-
knee-Soleus	4.9	35.5	--

Table 4: H-reflection

Following a two-week regimen combining B vitamin supplementation (methylcobalamin and vitamin B1) and acupuncture sessions administered every other day, the following acupoints were targeted: Zusanli (ST36), Xiajuxu (ST39), Jiexi (ST41), Zhibian (BL55), Chengshan (BL56), and Weizhong (BL57). Sterile 0.25 mm × 40 mm needles were inserted and retained for 20 minutes per session. Concurrent 30-minute Tuina therapy sessions emphasized acupressure along the Foot-Taiyang Bladder Meridian and Foot-Yangming Stomach Meridian. After two weeks, the patient exhibited significant improvement in both lower limb numbness and weakness, leading to hospital discharge. At the one-month post-discharge follow-up, no recurrence of right lower limb symptoms was observed. Subsequent outpatient acupuncture and Tuina therapy (twice weekly) further alleviated symptoms. Although the patient developed intermittent numbness in the left lower limbs two months after discharge, it is advised that she wear knee padding during activities, avoid prolonged sitting, undergo family screening for HNPP, and adhere to long-term neurology follow-up.

5. Conclusions

Hereditary neuropathy with liability to pressure palsies (HNPP) is an autosomal dominant disorder characterized by recurrent, painless mononeuropathies or polyneuropathies at common entrapment sites. While the peak age of onset is approximately 30 years, cases with earlier or later presentations have been documented, with no significant sex predominance [1]. Epidemiological data from Finland estimate a prevalence of 16 per 100,000 individuals [3];

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however, comparable population-based studies in China remain scarce. Clinically, HNPP predominantly manifests as transient motor or sensory deficits following minor trauma or compression, with the peroneal (36%), ulnar (28%), brachial plexus (20%), and radial (13%) nerves most frequently affected [4]. Although spontaneous recovery typically occurs within weeks to months, residual deficits may persist after repeated insults. Notably, 10% of patients develop pes cavus deformity, mimicking peroneal muscular dystrophy [5], while atypical presentations such as chronic ulnar neuropathy, carpal tunnel syndrome, or Guillain-Barré-like syndromes further complicate diagnosis [6].

Electrophysiological evaluation remains a cornerstone of diagnosis, revealing diffuse demyelinating features, particularly prolonged distal latencies and slowed conduction velocities at compression-prone sites[4]. Pathologically, HNPP is associated with focal myelin thickening interspersed with normal segments ("sausage-like" tomacula); however, this finding is not pathognomonic, as similar features occur in chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), Charcot-Marie-Tooth disease (CMT) subtypes, and paraproteinemic neuropathies [7,8]. Genetic testing confirms the diagnosis in most cases, with 80% of patients harboring a 1.5 Mb PMP22 gene deletion on chromosome 17p11.2. Reciprocal PMP22 duplication causes Charcot-Marie-Tooth type 1A (CMT1A) [9,10], underscoring the critical role of molecular analysis in differentiating these allelic disorders.

The present case illustrates diagnostic challenges in HNPP. A middle-aged woman presented with bilateral peroneal neuropathy, lumbar pain, and lower limb numbness, initially suggestive of lumbar disc herniation (LDH). However, electromyography demonstrated multifocal demyelination at typical entrapment sites, inconsistent with imaging findings. Subsequent PMP22 deletion analysis confirmed HNPP, highlighting the necessity of integrating genetic testing when clinical-electrophysiological discrepancies arise. Management focuses on preventive measures to avoid nerve trauma, coupled with supportive therapies. Although spontaneous recovery is typical, residual deficits may necessitate rehabilitative interventions. Traditional Chinese Medicine (TCM) attributes HNPP to Qi-blood stagnation in the meridians. Preliminary studies suggest that acupuncture at Yangming meridians (e.g., ST36) may enhance peripheral nerve regeneration by modulating inflammatory markers [11]. While current evidence remains largely anecdotal, the observed clinical improvement in this case suggests potential therapeutic benefits, warranting further investigation to validate these findings and explore underlying mechanisms.

In summary, HNPP requires a high index of suspicion, particularly in cases of recurrent neuropathy with atypical features. Clinicians should prioritize genetic testing in patients with unexplained multifocal neuropathy. Further studies are warranted to standardize integrative protocols combining TCM and Western medicine for HNPP management.

6. Limitations

This study has limitations. Single-case reports cannot establish causality, and the short follow-up period (2 months) precludes assessment of long-term TCM efficacy. Multicenter trials with extended follow-up are needed.

Abbreviations: HNPP = hereditary neuropathy with liability to pressure palsies, LDH = lumbar disc herniation, PMP22 = peripheral myelin protein 22, TCM= Traditional Chinese medicine, EMG =Electromyography, CIDP = chronic inflammatory demyelinating polyradiculoneuropathy, CMT = charcot marie tooth disease, CMT1A =Charcot-Marie-Tooth type 1A

7. Authors contributions

Zhen Li wrote the manuscript, Xilin Zhang revised the paper, Wuquan Sun supervised the study, Wei Zheng and Tianjie Wang collected the data. All the authors have read and approved the final version of the manuscript.

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