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CASE REPORTS

Idiopathic thrombocytopenic purpura and neuropathy: A case report and review

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Abstract

Mononeuropathy multiplex is a rare disorder associated with idiopathic thrombocytopenic purpura. Extrinsic compression due to hematoma, intraneural bleed and immune mediated nerve injury are reported mechanisms of neuropathy. We report of a case of a girl with recurrent idiopathic thrombocytopenic purpura with mononeuropathy multiplex, along with a brief review of the mechanism of neuropathies in asscociation with idiopathic thrombocytopenic purpura.

INTROUDUCTION

The development of peripheral neuropathy in hemorrhagic disorders have been reported and these are typically due to the formation of hematoma in neighbouring structures leading to extraneural compression. Intra-neural hemorrhage and immune mediated neuropathy are rarely reported as a cause of neuropathy in these disorders. In this report we describe a young girl with recurrent idiopathic thromobocytopenic purpura (ITP) and mononeuropathy multiplex (MM).

CASE REPORT

A 25-year-old girl was previously diagnosed as having acute ITP 5-years ago. She improved with platelet transfusion and a short course of oral steroids. She remained symptom free until the current presentation when she developed a second episode of ITP manifested by generalised petechial rash all followed by spontaneous nose bleeds and menorrhagia. On day 3 of her relapse, she noticed an acute onset of burning paresthesia and weakness in the ulnar aspect of her right hand and similar sensory symptoms over the left leg and dorsum of her left foot. Her symptoms progressed over the next 2-3 days and plateaued thereafter. On examination, she had stable vital signs with generalised petechial rash with no signs of hepatosplenomengaly, lymphadenopathy, ecchymosis or subcutaneous swelling. Her neurological deficit was restricted to the right ulnar nerve (affecting the small muscles of hand and finger flexors) and the left common peroneal nerve (affecting foot dorsiflexion, foot eversion and toe extension) along with sensory deficits in the distribution of the corresponding nerves. Her deep tendon reflexes were intact and plantar reflexes were flexor.

Investigations showed normal peripheral blood smear with low platelet count (10,000/mm^3). Bone marrow aspiration and biopsy revealed normal marrow apart from an increased megakaryocytes. Bleeding time was prolonged but the rest of the coagulation profile, including D-dimer was normal. Other investigations including serum chemistry, urine analysis, stool for occult blood, thyroid function test, serum-vitamin B12, and serum-lactate dehydrogenase were within normal limits. Serum protein electrophoresis, C-reactive protein, cryogobulins, antinuclear antibodies, anti doublestranded DNA, antineutrophil cytoplasmic antibodies, complements C3 & C4, anti phospholipid antibodies, antibodies against HIV-1 and HIV-2, hepatitis B virus and hepatitis C-virus were unremarkable.

Nerve conduction studies revealed reduced compound muscle action potential in the right ulnar nerve (4.3 mV, normal >5 mV), and in the left common peroneal nerves (0.7 mV; normal >2.0 mV), with relatively preserved motor conduction velocities (CV) and distal motor latencies (DL). The F latencies waves were unrecordable and both ulnar and superficial peroneal sensory nerve action potential were absent. Ulnar nerve was also

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stimulated using the inching method till above elbow to detect any focal entrapment/lesion but there was no evidence of a conduction block. However, the ulnar nerve was not recordable on proximal stimulation at Erb's point/axilla. There was no electrophysiological evidence of peroneal nerve entrapment at head of fibula respectively. Needle examination (EMG) was not done due to the patient's low platelets and prolonged bleeding time.

Magnetic resonance imaging of the involved extremities was performed with the 1.5 tesla Siemens scanner. T1 weighted, T2 weighted, short T1 inversion recovery and post contrast T1 weighted images were obtained in coronal, sagittal and axial planes using specific limb coils. The scan did not reveal any intrinsic signal abnormalities in the affected nerves or abnormal contrast enhancement. There was also no radiological evidence of an extrinsic nerve compression in the course of the nerve or entrapments at common entrapment sites (ulnar groove or cubital tunnel and neck of fibula).

The patient received platelet transfusion and a short course of steroids. Her strength improved significantly over the next four months and was only left with minimal sensory deficit.

DISCUSSION

Extraneural compression resulting from bleeds in the adjacent structures is the most common cause of neuropathy in hemorrhagic disorders.[1] However, intraneural bleeding[2-5], immune mediated neuropathy[6-9] and vasculitis[10,11] are other suggested mechanism of neuropathies in the ITP. At autopsy, intraneural bleeding was documented in the cavernous portion of the oculomotor nerve in a 52 year man with ITP and acute oculomotor palsy.[2] Autopsy of another patient with ITP and right median and peroneal nerve weakness revealed multiorgan hemorrhages, along with intraneural haemorrhages at multiple sites in the right median nerve without extraneural hemorrhage.[5] However, Ijichi *et al* did not find any hemorrhage in the sural nerve biopsy of a patient with ITP and MM and they proposed a proximally situated intraneural hemorrhage as a cause of MM, which could not be detected by sural nerve biopsy.[4] Intraneural hemorrhage as a cause of neuropathy is also described in secondary thrombocytopenia (unrelated to ITP) due to rupture of precapillaries and capillaries of the peripheral nerve.[12]

Immune mediated neuropathy has also been reported in patients with ITP. Interestingly, most of them were diagnosed with an acute inflammatory polyneuropathy (AIDP)- like acute polyneuropathy rather than MM.[6,7,9] MM due to immune mediated mechanism was recently reported by Nakamura *et al*.[8] However, there was a considerable time gap between the hemorrhagic phase of ITP and the onset of neuropathy. Giampolo *et al* reported vasculitis as a probable mechanism in a patient who presented with progressive mixed sensorimotor polyneuropathy, who went on to develop ITP after 1½ -years.[10] Table 1 shows a brief review of the various reported cases of ITP and its relation to onset, extent and mechanism of neuropathy. These observations suggest that immune mediated neuropathies in ITP are usually symmetrical polyneuropathies which develop after a considerable time period of about one month or more. Intraneural bleed is a likely etiology in patients with acute mononeuropathy multiplex which develops during the active bleeding phase of ITP. All reported patients except one patient who developed neuropathy were adults, despite the fact that ITP is more common in the paediatric age group.

Our patient developed MM during her second episode of ITP, temporally related with its active hemorrhagic phase. Most of ITP patients have a monophasic illness, but about 3-5% of patients may develop recurrent episodes. The time interval between the two episodes is variable (3 to 96 months).[13] In the present patient, nerve conduction studies were suggestive of axonal neuropathy of right ulnar nerve and left common peroneal nerve. Others also reported axonal type neuropathy in patients with ITP.[4] The possible mechanisms of MM in an ITP patient with active bleeding are extrinsic nerve compression or intraneural hemorrhage. There was no evidence of extrinsic nerve compression on imaging of the extremities. We postulate that intraneural hemorrhage was the cause of MM in our patient as, it was an acute onset MM, temporally related with the active hemorrhagic phase of ITP. There was no evidence to suggest an autoimmune disorders or other common causes of mononeuropathy multiplex on detailed evaluation. Although there was no evidence of intraneural bleeding on imaging, it is possible that small intraneural lesions can be missed. Nerve biopsy could not be done due to the active bleeding and low platelets. In any case, her sural nerve was not involved and the yield of unaffected nerve biopsy is not high as shown by Ijichi *et al*.[4] Intraneural hemorrhage in the

Table 1: A summary of reported cases of ITP with neuropathy showing relationship between type of neuropathy and its onset with its mechanism

Referance	Patient (age/sex)	Neuropathy	Onset	Mechanism
Gross (1980)[6]	30/F	AIDP like sensorimotor	Acute	Immune mediated
Kura *et al* (1980)[11]	Not available	MM	Not available±	Vasculitis
Fukayama *et al*. (1983)[14]	32/F	AIDP like sensorimotor	Acute	Immune mediated
Khaldi *et al*. (1990)[7]	3/F	AIDP like motor	Acute	Immune mediated
Combarros *et al*. (1991)[15]	75/F	AIDP like sensorimotor	Acute	Immune mediated
Greenberg *et al*. (1991)[5]	47/M	MM Right ptosis	Acute	Intraneural bleed
Vashista *et al*. (1992)[16]	50/F	AIDP like motor	Acute*	Immune mediated
Giampolo *et al*. (1993)[10]	70/M	Chronic sensorimotor	2-years before onset of ITP	Vasculitis
Miyao *et al*. (1993)[2]	52/M	MM (Oculomotor Nerve)	Acute	Intraneural bleed
Corbanese *et al*. (1998)[17]	50/F	AIDP like sensorimotor	Acute	Immune mediated
Yalçin *et al*. (1998)[3]	21/M	MM	Acute	Intraneural bleed†
Gaur *et al*. (2003)[18]	73/M	AIDP like motor	Acute	Immune mediated
Ijichi *et al*. (2003)[4]	61/M	MM	Acute	Intraneural bleed†
Sato *et al*. (2005)[9]	67/M	AIDP like sensorimotor Ophthalmoplegia Bulbar palsy	Acute	Immune mediated
Yilmaz *et al*. (2007)[19]	56/M	Chronic sensorimotor	1 month	POEMS syndrome
Nakamura *et al*. (2010)[8]	78/M	MM	1 month	Immune mediated
Present Case	25/F	MM	Acute*	Intraneuroal bleed†

* Onset during second episode of ITP
† Nerve biopsy is either normal or could not be done
± Article in Japanese, abstract not available in Pubmed
Acute onset (simultaneous or within 1 week)
AIDP: Acute inflammatory polyneuropathy; MM: mononeuropathy multiplex

affected nerves has been documented at autopsy in other similar cases (Table 1).

In conclusion, MM is not a common complication in ITP. Thrombocytopenia- related hemorrhage may involve any tissues including the peripheral nerves. Intraneural bleeding should be considered in cases of asymmetrical neuropathy during active hemorrhagic phase of ITP. In cases where the pattern of neuropathy is an AIDP- like polyneuropathy or if there is a significant time gap between the onset of ITP and the development of neuropathy, an immune -mediated mechanism may be more likely.

DISCLOSURE

Conflict of interest: None

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