

Discussion

This is the first reported case of methotrexate-induced pericarditis and pericardial effusion. The syndrome of methotrexate pleural toxicity is invariably of pleuritic pain with normal chest X-ray and ventilation/perfusion scan. X-Ray changes if present are non-specific and diagnosis may require bronchoscopy and lavage^{3,7} or lung biopsy.⁷ The differential diagnosis is infection, pulmonary infarction and tumour-related complications. Pleural effusions after methotrexate therapy are most likely to be due to cancer; in this case the fluid should be drained and therapy changed. This patient had methotrexate chemotherapy followed by two episodes of pleurisy, the second being associated with pericarditis and a large pericar-

dial effusion. As in the majority of cases with pleural toxicity there was no peripheral eosinophilia; however, eosinophils were present in the pericardial fluid. An unrecognised viral infection or a reaction to an unsuspected allergen remains a possible cause; however, we believe that the pericardial effusion was most likely a complication of methotrexate chemotherapy and that, as with methotrexate pneumonitis, this is likely to be an immune-mediated serositis.⁷ The possibility of pericarditis and significant pericardial effusion should be considered as a potentially severe complication of methotrexate therapy. The regular use of echocardiography could provide information on the incidence of isolated asymptomatic pericardial effusion and that concomitant with methotrexate pneumonitis/pleurisy.

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The association of hereditary neuropathies and heritable skeletal disorders

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Summary

We describe two patients with associations of hereditary neuropathies and heritable skeletal disorders not previously reported. The first patient had Marfan's syndrome and hereditary motor and sensory neuropathy Type 1. The second patient had Ehlers-Danlos syndrome, Klippel-Feil syndrome and tomaculous neuropathy.

Keywords: hereditary neuropathy, heritable skeletal disorders, Marfan's syndrome, Ehlers-Danlos syndrome, Klippel-Feil syndrome

There are occasional reports of the association between a peripheral neuropathy and Marfan's syndrome, Ehlers-Danlos syndrome, or Klippel-Feil syndrome.¹⁻⁵ We report two patients with associations not previously described.

Patients

Case 1

A 19-year-old man presented with progressive difficulty in walking. He had no sensory symptoms. He was of thin build. His paternal grandmother, father and sister were said to

have a similar build. On examination, he had bilateral pes cavus and decreased tendon reflexes. He also had arachnodactyly, a high arched palate and bilateral lens dislocations. A diagnosis of Marfan's syndrome and a probable hereditary neuropathy was made.

Echocardiography showed mitral valve prolapse. Nerve conduction studies showed marked slowing of motor conduction velocity in the median nerve (15 m/s; lower limit of normal 48 m/s) and absence of sensory action potentials (median, ulnar, radial and sural). Electromyographic examination showed neuropathic changes in tibialis anterior. The findings thus showed a severe demyelinating and degenerating neuropathy consistent with hereditary motor and sensory neuropathy Type I.

Other family members were not available for clinical or electrophysiological examination.

Case 2

A 16-year-old boy presented with tingling in the distribution of the median nerve in the right hand. He had previously complained of tingling in the little finger of the left hand which was subsiding. On examination, he had blunting to pin prick sensation in the right median

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Table Associations of peripheral neuropathies and heritable skeletal disorders

Connective tissue or skeletal disorder	Neuropathy
Marfanoid features	Neuropathy ? motor (also UMN signs and myopathy) ¹
Marfan's syndrome	Tomaculous neuropathy ²
Klippel-Feil syndrome	HMSN Type I ³
Ehlers-Danlos syndrome	Tomaculous neuropathy ⁴
Ehlers-Danlos syndrome	Neuropathy (not specified) ⁵
Marfan's syndrome	HMSN Type I*
Ehlers-Danlos syndrome and Klippel-Feil syndrome	Tomaculous neuropathy*

UMN = upper motor neuron; HMSN = hereditary motor and sensory neuropathy; * = present report

nerve distribution. He was also noted to have several other abnormalities. He had a low hairline, webbed neck, thoracic kyphosis, hyperextensible joints and lax skin. Radiological examination showed bony abnormalities including mild basilar invagination, deficient anterior arch of the atlas, the first and second cervical vertebrae shared one spinous process and their laminae were fused, posterior arch defects of the fifth and sixth cervical vertebrae and rudimentary cervical ribs. The findings thus provided strong evidence of the co-existence of Klippel-Feil syndrome and Ehlers-Danlos syndrome in this patient. There was no family history.

Neurophysiological examination showed bilateral carpal tunnel syndromes and a right ulnar nerve lesion at the level of the elbow. There was also generalised slowing of motor conduction in both peroneal nerves (24 and 25 m/s; lower limit of normal 38 m/s) providing evidence for a background peripheral neuropathy. Nerve conduction studies were also done in asymptomatic family members. The patient's father and paternal grandmother had strikingly similar nerve conduction abnormalities with evidence of compression lesions of the median and ulnar nerves and a background peripheral neuropathy. Normal results were obtained from the patient's mother and maternal great aunt.

Sural nerve biopsy showed tomacula consistent with a diagnosis of hereditary neuropathy with liability to pressure palsies (tomaculous neuropathy).

Discussion

Our two cases are reviewed in the context of those reported in the literature.

Case 1 We can find only two reports mentioning the association of either Marfan's syndrome or Marfanoid features and a peripheral neuropathy.^{1,2} A 46-year-old man has been described with Marfanoid features and, amongst other things, proximal muscle weakness, upper and lower motor neuron signs and impaired vibration sense.¹ An electromyogram showed 'a mild denervation neuropathy with some slowing of conduction'. A muscle biopsy showed a non-specific myopathy. Lack of precise electromyographic findings in the report makes comparison difficult. However, this patient had a combination of myopathic and neuropathic features and there was no suggestion of the neuropathy being hereditary. Our patient had clear evidence of a severe demyelinating and degenerating neuropathy consistent with a hereditary neuropathy.

An association between Marfan's syndrome and tomaculous neuropathy, thought to be fortuitous, has also been described.² However, the report also suggested that ligamentous hyperlaxity in Marfan's syndrome may predispose to pressure palsies. Association with a myopathy has also been reported.⁶

Case 2 Our second patient had Ehlers-Danlos syndrome, Klippel-Feil syndrome and tomaculous neuropathy. We found two reports of the association between Ehlers-Danlos syndrome and a peripheral neuropathy.^{4,5} In one, the neuropathy was tomaculous in type,⁴ while the other report mentioned the presence of a neuropathy (without characterising it further) in two siblings of consanguineous parents and grandparents. An association between Klippel-Feil syndrome and Charcot-Marie-Tooth disease has also been described.³

Thus there are rare reports, including our own, describing associations between hereditary neuropathies and heritable skeletal disorders. These are summarised in the table.

It is possible that two or more of these disorders have been associated incidentally. On the other hand, these may represent rare manifestations or newer subtypes of recognised genetic syndromes.

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