Recurrent isolated alternating phrenic nerve palsies: a variant of brachial neuritis?

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Abstract

A 40 year old man presented with three episodes of shoulder pain. This is likely to be a variant of brachial neuritis.

We report a patient who experienced three episodes of shoulder pain followed by respiratory embarrassment. Investigations on each occasion suggested an isolated phrenic nerve palsy, initially affecting the right hemidiaphragm, then the left, and subsequently the right again.

Case report

A previously healthy manual labourer first presented at the age of 26 with orthopnoea and exertional dyspnoea. This had followed a week of severe neck and shoulder pain, which resolved spontaneously. There had been no recent trauma or vaccinations. There was no relevant family history. Examination disclosed no weakness of the shoulder girdle, and no sensory deficit. A chest radiograph showed elevation of the right hemidiaphragm with paradoxical movement shown by screening. After six weeks the dyspnoea resolved and he was able to resume playing football. One year later a repeat chest radiograph was normal and screening showed the diaphragm to be moving normally.

He remained well until the age of 35, when he had a similar short lived episode of pain. After this he was again aware of difficulty in breathing when lying flat, especially after a heavy meal, and also in lifting when leaning forward. Once again there were no abnormal signs in either shoulder or arm. On this occasion radiography showed elevation and paralysis of the left hemidiaphragm with normal movement on the right. Over the next six months his symptoms improved, though he was unable to resume playing football. His chest radiograph once again returned to normal.

He presented to this unit at the age of 40 years. With no obvious precipitant he developed the same pain, which kept him awake for five nights. He found it impossible to sleep supine and on several occasions noticed early morning headache and hypersomnolence. He had discovered that he could fall asleep more easily when sitting by rocking himself backwards and forwards. Examination showed nothing abnormal apart from inward movement of the abdomen during inspiration in the supine position.

He was investigated three months after the third episode, by which time there had been some spontaneous improvement. Routine laboratory studies gave normal results. Screening of the diaphragm showed complete paralysis on the right with paradoxical movement during deep breathing, coughing, and sneezing. Movement was normal on the left. A cervical spine radiograph showed minor degenerative changes with no encroachment on the foramina or cervical canal.

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sory neuropathy after high dose (>2 g daily) pyridoxine. Sensory neuropathy was also reported in 23 of 58 women taking pyridoxine daily for premenstrual tension.1 Our patient was treated with the recommended dose (150 mg daily) of pyridoxine.1,2 

Pyridoxine is a pyridine, one of a group of chemicals known to be neurotoxic. Neurotoxicity might occur through various mechanisms. The vitamin depends on a limited and easily saturated enzyme system to cross the blood-brain barrier and is not known to be centrally neurotoxic. The cell bodies of the peripheral sensory nerves, mainly located in the dorsal ganglia, are outside the blood-brain barrier and are subject to pyridoxine toxicity.

Vitamin B6 exists in three interconvertible forms—pyridoxal phosphate, pyridoxamine, and (the least active) pyridoxine. Excess of the latter may saturate the activating enzymes pyridoxal kinase and pyridoxine phosphate oxidase, resulting in paradoxical vitamin B6 deficiency by competitive inhibition of the more active form, pyridoxal phosphate.

The dose of pyridoxine recommended by the British National Formulary for prophylaxis against isoniazid induced neuropathy, 10 mg daily, should not cause peripheral neuropathy and may be recommended, particularly in poorly nourished patients. Our case calls into question current recommendations1 2 that doses in the range of 100–200 mg daily of pyridoxine should be used in patients with established peripheral neuropathy due to isoniazid.

This case has been reported to the Committee on Safety of Medicines.

His vital capacity (VC) was 3.5 litres when he was standing and 1.9 l when he was supine. Balloon manometry showed a maximum change in transdiaphragmatic pressure (ΔPdimax) of 15 cm H2O when he inspired from resting lung volume to total lung capacity, half the minimum predicted value for ΔPdimax of 30 cm H2O (Pdi at functional residual capacity (FRC) 0 cm H2O and at total lung capacity (TLC) 15 cm H2O). Neurophysiological examination showed no evidence of generalised neuropathy, and no evidence of denervation in shoulder girdle or upper arm muscles. Phrenic nerve stimulation by standard techniques showed no response to the right diaphragm, and a small response on the left of 100 µV, with a normal latency of 5-8 milliseconds. An ear oximeter sleep study showed no appreciable oxygen desaturation during a night’s supine sleep.

He was assessed again one year after the third episode, by which time he had symptoms only during heavy exertion or lying flat after a heavy meal. No change was observed in the radiographic screening of his diaphragms. His standing VC had improved to 4.071 and his supine VC to 2.441. His transdiaphragmatic pressure change had increased to 20 cm H2O (Pdi at FRC 0 cm H2O and at TLC +20 cm H2O and the maximum sniff pressure change was 40 cm H2O (predicted >90 cm H2O). Again no response was obtained from stimulation of the right phrenic nerve and no appreciable change was seen in the response on the left.

Discussion
Radiographic screening suggested that each episode could have affected one of the phrenic nerves independently, but normal hemidiaphragmatic movement does not exclude some weakness. The amplitude of the diaphragmatic muscle action potential is not a good quantitative measure of phrenic nerve palsy, but the results did suggest that the cumulative deficit was bilateral after the third episode. Manometry and spirometry provide the best measure of total diaphragmatic function, and they showed spontaneous improvement after one year.

The aetiology of our patient’s recurrent painful alternating phrenic nerve palsies is not clear. The time course, the bilateral nerve palsy, and the spontaneous recovery exclude the commonly recognised causes of isolated phrenic nerve paresis. Osteoarthritis of the cervical spine is a rare cause, but is improbable in our patient. In our view the severe pain followed by diaphragmatic paralysis and subsequent improvement suggests recurrent brachial neuritis, selectively affecting the phrenic nerve, as the only plausible explanation.

The term brachial neuritis was first coined in 1941, and since then various other names have been used, such as neuralgic amyotrophy and brachial plexus neuropathy. Paresis of the phrenic nerve was first recognised in 1951 after administration of tetanus antitoxin. A further 26 cases have subsequently been reported. Cape and Fincham described a typical case of brachial neuritis with paralysis of a hemidiaphragm, with subsequent recurrence on the contralateral side. About 10% of patients have weakness confined to muscles supplied by a single peripheral nerve, and Mumenthaler and Gunzel have described patients with isolated paresis of the phrenic nerve.

The usual recurrence rate of idiopathic brachial neuritis is about 5%. A second recurrence is very unusual and raises the possibility of the familial form of brachial neuritis. This is inherited in an autosomal dominant manner, so the lack of family history in our case makes this unlikely. The disease has 60% penetrance and theoretically non-affected parents may carry the gene and bear affected children, but this phenomenon has not been recorded. None of our patient’s episodes was preceded by vaccination, trauma, or infection, which may provoke an episode of weakness in either type. Even after one year the patient still has evidence of bilateral phrenic nerve damage. Improvement might be expected to continue over the next two years. Should he have a further episode he is clearly at risk of severe respiratory embarrassment. The condition may be immunologically mediated, and if his symptoms recur we plan to treat him immediately with high dose intravenous methylprednisolone in an attempt to limit further phrenic nerve damage.

We wish to thank Dr CJ Glynn for referring this patient.