XMPMA: acute on chronic ventilatory failure managed successfully with non-invasive ventilation

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X-linked myopathy with postural muscle atrophy (XMPMA) is a recently described myopathy; it may cause symptomatic sleep disordered breathing which can be managed with non-invasive ventilation.

Introduction

Many myopathies involve the respiratory muscles, both inspiratory and expiratory muscle groups. Inspiratory muscle weakness results in problems ranging from mild dyspnoea, orthopnoea, sleep-disordered breathing and nocturnal hypoventilation through to diurnal ventilatory failure. Expiratory muscle weakness manifests with poor cough and airway clearance resulting in difficulty with secretion management and respiratory tract infections. Respiratory complications are the major cause of morbidity and mortality in many progressive neuromuscular disorders.1

The benefit of long-term non-invasive ventilation (NIV) on both symptoms and survival across a range of causes of chronic respiratory failure is well established.2 The provision of this service has led to close links between respiratory medicine and neurology departments and the need for respiratory physicians to remain up to date with the expanding number of disorders that are covered by the label ‘muscular dystrophies’.

Here we present the first reported case of the need for long-term nocturnal NIV in a patient with XMPMA. This disorder has only been identified recently and there remain just a handful of families worldwide diagnosed with this type of myopathy.

Case report

A 58-year-old man was admitted acutely unwell to his local hospital Emergency Department. In the preceding weeks he had become bed-bound due to progressive weakness, increasingly breathless at rest and described clear orthopnoea. His concentration was poor and in the days immediately before admission family members reported excessive daytime sleepiness and hallucinations. Blood tests were unremarkable and chest radiograph showed small lung volumes with no evidence of consolidation. An arterial blood gas revealed acute on chronic ventilatory failure (pH 7.18, pCO2 16.3 kPa, pO2 10.5 kPa and serum bicarbonate 44 mmol/L). He was established on to NIV acutely and when stable transferred to our regional long-term ventilation service.

He had first presented to medical services over 25 years previously due to mild lower limb weakness and moderately elevated serum creatine kinase. Despite extensive tests including nerve conduction studies, electromyography and muscle biopsy, no diagnosis was reached though the label ‘muscular dystrophy’ was later given in clinic letters. His symptoms progressed slowly and he declined regular clinic appointments. Three years before this admission he had been diagnosed with XMPMA. A male family member had been diagnosed with the disease at a specialist neuromuscular centre and the patient attended there for review. Causative mutation in the four and a half LIM domain gene (FHL1) on the X chromosome was confirmed. At that time he was still mobile with crutches, had no symptoms of nocturnal hypoventilation and a sitting vital capacity of 2.43 L (63% predicted) with no...
significant fall when supine. He was not seen again by secondary care services until this admission to his local acute hospital.

Clinical examination showed clear paradoxical abdominal breathing, vital capacity was 0.83 L and maximal inspiratory pressures were reduced consistent with diaphragm weakness (<30 cmH₂O). He was established on long-term nocturnal NIV via a face mask with 1 L oxygen entrained. Arterial blood gas taken in the morning prior to discharge was much improved (pH 7.41, pCO₂ 6.1 kPa, serum bicarbonate 26.7 mmol/L) and overnight oximetry confirmed that less than 30 min spent with saturation <90% as is our local protocol.

Cough peak flow was low (<100 L/min) and maximal expiratory pressures were consistent with expiratory muscle weakness. He required one course of intravenous antibiotic for hospital acquired pneumonia and had been issued with a cough-assist machine on discharge.

When most recently seen in clinic by our physiotherapy team he had remained well with no symptoms suggestive of inadequate ventilation and good compliance with NIV.

Discussion

Myopathies are muscle disorders typified by weakness and atrophy of skeletal muscle. Many will involve both respiratory and cardiac muscle though the degree is variable between and within individual disorders. Several myopathies have an X-linked recessive mode of genetic transmission, the most common is Duchenne muscular dystrophy, and others include Becker muscular dystrophy and Emery Dreifuss muscular dystrophy.3

A new and phenotypically distinct late onset X-linked myopathy, named X-linked myopathy with postural muscle atrophy (XMPMA) was described in 2008 after genetic study of a large Austrian family spanning several generations which was affected by an uncharacterized myopathy.3 The main clinical features were atrophy of some postural muscles combined with a generalized hypertrophy of others.

Linkage studies and haplotype analysis suggested candidate genes and the four and a half LIM domain gene (FHL1) at Xq26.3 was identified as key. Further tests identified a missense mutation within the FHL1 gene with marked decrease in expression of FHL1 protein as responsible for this myopathy. FHL1 protein was not reduced in either Becker muscular dystrophy of limb girdle muscular dystrophy. The exact role of FHL1 is not known, it is more common in oxidative muscle fibres and is suggested to play a role in sarcomere synthesis and assembly.3,4 FHL1 is expressed in skeletal and cardiac muscle. In the initial Austrian family the cause of death was uncertain, many were diagnosed with heart failure of unknown cause. In the initial description a second family from the United Kingdom was demonstrated to have XMPMA and it was confirmed by genetic testing. Many of these were previously labeled with Becker muscular dystrophy and documented to have died from respiratory failure.3 Our patient had an echocardiogram which showed no significant structural, valvular or ventricular function abnormalities.

Summary

XMPMA is a new and rare disorder, it is clear that in addition to peripheral muscles it can affect both inspiratory and expiratory respiratory muscles. If significant then it may present with ventilatory failure and the symptoms and signs of nocturnal hypoventilation and poor cough as it did in our patient. These symptoms and disordered physiology can be stabilized, controlled and reversed by the use of NIV and cough-assist techniques as you would expect from other neuromuscular conditions.1 The case presented here is the first one reported of XMPMA treated successfully with NIV in the published literature.

We hope this report informs the general reader about XMPMA and that it should join the ever-growing list of neuromuscular conditions of which a respiratory physician involved in long-term ventilation should be aware. With an identified genetic cause it is likely to become more common in clinical practice as many patients and families with a myopathy of uncertain cause are reassessed. The basic principles of assessment and treatment are as for all neuromuscular disorders affecting respiratory muscles and it is clear that NIV is an effective therapy.
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