

SHORT REPORT

Significance of Beevor's sign in facioscapulohumeral dystrophy and other neuromuscular diseases

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An atypical presentation of facioscapulohumeral dystrophy (FSH) is described, where the presence of a positive Beevor's sign led to genetic testing and subsequent probable diagnostic confirmation. This prompted evaluation of a further 68 patients for the presence of Beevor's sign. Among these, 19/20 patients with FSH had a positive Beevor's sign, compared with 2/28 with other muscle diseases, and 0/20 in a neurological control group. Beevor's sign should be considered as an additional criterion for the diagnosis of FSH.

Facioscapulohumeral dystrophy (FSH) is a relatively common hereditary myopathy with symptom onset ranging from infancy to middle age. Typical clinical features include an asymmetrical pattern of weaknesses involving facial, humeral (biceps involved preferentially over triceps), ankle dorsiflexor, and abdominal muscles.^{1,2} However, FSH is clinically heterogeneous and many atypical presentations have been described, which may cause diagnostic difficulty.^{3–6} Beevor's sign, an upward deflection of the umbilicus on flexion of the neck, has been described in association with FSH.^{7,8} In 1990, a genetic abnormality mapped to a locus at chromosome 4q35 was reported in FSH and is seen in 95% of patients.⁹ We report an atypical presentation of FSH, where the discovery of a positive Beevor's sign was essential in reaching the correct diagnosis. In this study we report on the significance of Beevor's sign in FSH and other neuromuscular diseases.

CASE REPORT

A 79 year old man presented with a four year history of lower limb muscle cramps. He had a history of type 2 diabetes, hypercholesterolaemia, and ischaemic heart disease. There was no family history of muscle disease. He was found to have a raised serum creatine kinase (CK), at 3874 U/l (normal <300 U/l). He had been on lipid lowering drugs which were stopped, but in spite of this his CK remained persistently high (range 1974 to 2945 U/l). A muscle biopsy showed evidence of fibre necrosis and regeneration which appeared to be disproportionate to the inflammatory changes. An NADHT preparation showed lobulated fibres. Dystrophin, merosin, dysferlin, emerin, and α/γ sarcoglycan expression were normal on immunostaining. A diagnosis of polymyositis was made and immunosuppressive treatment was started but was unhelpful.

Neurological examination revealed asymmetrical weakness of shoulder abduction, elbow flexion, hip flexion, and knee flexion (MRC grade 4/5). There was no evidence of facial weakness or scapular winging. A positive Beevor's sign was documented.

Genetic testing was done and initial DNA analysis did not show the more typical *Bln* resistant fragment measuring less

than 35 kb that is seen in FSH.¹⁰ However, a *Bln* sensitive fragment measuring 29 kb was identified. Further dosage analysis with *BglII/BlnI* showed the patient to be monosomic for chromosome 4-type fragments and trisomic for chromosome 10-type repeat units. It was concluded that the *Bln* sensitive fragment was on chromosome 4, thus increasing the likelihood of FSH in our patient by a factor of 2:1.¹¹

FURTHER STUDIES

We identified 20 patients with FSH (19 had the typical gene rearrangement at 4q35, and the remaining patient had typical clinical features), 28 patients with other neuromuscular diseases, and 20 neurological patients without muscle disease.

In the FSH group, the mean age was 47.8 years with a 1.3:1 male to female ratio. In the non-FSH population, 28 patients had a variety of neuromuscular disorders including myotonic dystrophy (14 cases), limb girdle muscular dystrophy (five cases), familial tubular aggregate myopathy (two cases), Becker's muscular dystrophy, spinal muscular atrophy, Kennedy's syndrome, nemaline myopathy, tubular aggregate myopathy, Bethlem myopathy, and Emery-Dreifuss muscular dystrophy (one case each). The mean age range was 48.1 years with a 1.5:1 male to female ratio. We also examined 20 patients who attended the clinic with a range of neurological conditions but no evidence of spinal cord or muscle disease. Their mean age range was 49 years with a 1.3:1 male to female ratio.

Beevor's sign was considered positive if, when the patient was examined in the supine position, there was an upward deflection of the umbilicus on neck flexion. In our department, this forms part of the clinical work up of patients with neuromuscular disorders. We did consider "blinding" the assessor to the clinical condition of the patients but ultimately felt this was impractical.

RESULTS

Beevor's sign was positive in 19 out of 20 patients with FSH as well as in two of the non-FSH patients. The FSH patient with a negative Beevor's sign had no muscular weakness typical of that condition but had previously requested genetic screening in view of a positive family history. Genetic analysis had confirmed the presence of the classical 4q35 genetic rearrangement. This patient also had seropositive myasthenia gravis. Two of the 28 patients in the non-FSH group had a positive Beevor's sign. They were two brothers with a familial form of tubular aggregate myopathy. All 20 of the neurological control group had a negative Beevor's sign.

DISCUSSION

We report a patient with an atypical presentation of FSH. Our patient had no known family history and presented at the age of 75 with muscular cramps. Examination revealed no

Abbreviations: FSH, facioscapulohumeral dystrophy

evidence of facial weakness or scapular winging. Serum creatine kinase was higher than typically seen in FSH, and a muscle biopsy was non-diagnostic. Beevor's sign, however, was positive, raising the possibility of FSH. Although subsequent genetic analysis did not show the typical DNA rearrangement seen in FSH, it did suggest an increased likelihood for the condition.

Charles E Beevor first documented the finding of an upward deflection of the umbilicus on flexion of the neck in spinal cord injuries at or below the level of T9.¹² Beevor's sign has also been observed in patients with FSH. One study examined 30 patients with FSH and 40 with other neuromuscular diseases. The investigators found that 27 of the 30 FSH patients had a positive Beevor's sign, which was absent in all 40 controls.⁷ Genetic testing was not available at that time.

In the current study, we reinvestigated the significance of Beevor's sign now that genetic analysis is readily available. In our study, 19 of the 20 FSH patients had a positive Beevor's sign. The patient with a negative test had no clinical features of FSH. Interestingly, she also had myasthenia gravis and had received steroid treatment. Although an open label trial of steroids in FSH failed to show an improvement, we cannot comment on the impact steroids may have had in our patient.¹³

A positive Beevor's sign was seen in two of the 28 non-FSH patients with muscle disease but none of the neurological control group (0/20). Both Beevor's positive patients had a novel familial myopathy for which the genetic defect is as yet undetermined. The FSH genotype was, however, negative. We acknowledge the potential for observer bias as a consequence of our "non-blinded" approach.

The European Neuromuscular Centre workshops have established diagnostic criteria in FSH. They described the clinical findings as onset of disease in facial or shoulder girdle muscles, sparing the extraocular, pharyngeal, lingual muscles, and the myocardium.² Since genetic testing for FSH has been made available, atypical clinical presentations of the disease have been described by various groups.³⁻⁶ One group reported facial sparing in 15% of their FSH population.³ Awareness of the wide clinical spectrum in FSH is important to avoid delays in diagnosis and genetic counselling and to prevent unnecessary investigations.

Our study suggests that Beevor's sign has 95% sensitivity for FSH and 93% and 100% specificity in the neuromuscular diseases group and neurological controls, respectively. However, this sign has not been emphasised in many

previous published reports of clinical descriptors in FSH. Although not pathognomonic of FSH, Beevor's sign does appear to have a high sensitivity for that condition. It should not be overlooked in the assessment of neuromuscular conditions and we would argue that it should be included in the diagnostic criteria for FSH.

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