A delayed diagnosis of stiff person syndrome

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INTRODUCTION

Stiff person syndrome is a well-described, but rare and often overlooked disorder of the neuromuscular system. This article describes a patient who had typical features of stiff person syndrome with symptoms for 7 years before a correct diagnosis was made. The report highlights the difficulties in early diagnosis of this disabling condition.

COMMENTS

Stiff person syndrome is a rare disease of the CNS first described by Moersh and Woltman (1956). The condition is characterized clinically by muscle rigidity and episodic spasms. Superimposed on the rigidity are sudden severe spasms triggered by unexpected noises or tactile stimulation. The sudden spasm can cause the patient to 'fall like a board'. Because the symptoms can be task specific, patients are often misdiagnosed as having psychogenic movement disorder.

Clinical examination often reveals no abnormality except truncal muscle rigidity and lumbar hyperlordosis (Lorish et al, 1989) but some patients have predominantly proximal limb involvement suggesting a subgroup of 'stiff limb syndrome' (Barker et al, 1998). The patient reported here had predominant shoulder and upper back rigidity and little in the way of truncal rigidity.

CASE REPORT

A 37-year-old industrial designer presented in February 2002 with a 6-week history of thirst, polydipsia and polyuria. Urine dipstick showed glucose and 3+ ketones. Diabetes was diagnosed following fasting glucose of 13 mmol/litre and glycosylated haemoglobin (Hba1c) of 10.3%. He was commenced on insulin therapy.

He had been healthy until 1995 when he described the onset of muscle spasm and pain in upper back and shoulders. There was no obvious precipitating injury. He described the muscle over his left shoulder tightening up like a knot. It subsequently spread to his neck, upper and, later, lower back, giving significant rigidity and pain. Exertion and sporting activities cause his whole back to seize up with extreme pain afterwards. The spasms spread to his legs twice in the last 7 years, but the rigidity was fortunately only short lasting. He sought advice from a chiropractor and various medical specialists including an orthopaedic surgeon, rheumatologist and pain consultant. He had many investigations including isotope bone scan and magnetic resonance imaging (MRI) scan of cervical and thoracic spine which were all normal. There was no explanation for his symptoms and no diagnosis was given. He was prescribed baclofen, which brought some relief.

Clinical examination was normal except for markedly increased tone of muscles over his left shoulder. There was no obvious truncal rigidity or exaggerated lumbar lordosis and no pyramidal or extrapyramidal signs. He was clinically euthyroid.

Antiglutamic acid decarboxylase (GAD) 65 antibody was highly elevated at 220 U/ml (normal range (NR) <1 U/ml; >100 U/ml associated with neurological disease). Thyroid function test showed normal free thyroxine of 16.3 pmol/litre (NR 10–25.0 pmol/litre) with elevated thyroid-stimulating hormone of 8.43 mU/litre (NR 0.4–4 mU/litre) and positive thyroid peroxidase (TPO) antibody at 82 IU/ml (NR <37.0 IU/ml). Nerve conduction studies showed no evidence of neuropathy. Electromyograph studies were not done because of the difficulty of excluding voluntary movement from this quite painful test. Full blood count, renal, liver and bone profile were normal. CSF was not examined.

The typical history of painful muscle spasm and strongly positive anti-GAD 65 antibody suggested the diagnosis of stiff person syndrome. The association with an autoimmune condition, in this case type 1 diabetes, and elevated TPO antibody levels further supports the diagnosis.

The association with autoimmune conditions is strong, in particular type 1 diabetes occurs in between one and two thirds of patients (Solimena et al, 1990). Autoimmune thyroid disease, pernicious anaemia and vitiligo are also common. Electromyography of the affected muscle shows continuous motor unit firing despite the patient's attempt to relax.

Differential diagnosis of stiff person syndrome includes chronic tetanus, various dystonia and extrapyramidal diseases which can be excluded on clinical examination.

The association of stiff person syndrome with type 1 diabetes prompted investigations into the potential pathogenic association between the two entities, leading to identification of antibodies against glutamic acid decarboxylase (GAD) by Solimena et al (1988). GAD catalyzes the conversion of glutamate to gamma aminobutyric acid (GABA). It is selectively concentrated in GABA-producing neurons. Outside the nervous system, it is present in pancreatic beta cells.

Anti-GAD antibody is thought to play a pathogenic role by decreasing the level of GABA in the inhibitory neurons leading to uninhibited discharges of excitatory neurons to the muscle spindles and therefore increase stiffness. The anti-GAD antibody level is much higher in stiff person syndrome than in type 1 diabetes (Kim et al, 1994). The antibody also exhibits a very distinct cellular and humoral response in the two conditions (Lohmann et al, 2000). This may explain why many individuals with one condition do not have the other.

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Treatment relates to the aetiology. Drugs that enhance GABA activity, for example diazepam, vigabatrin, tiagabine and intrathecal baclofen, have been tried with success. The presence of autoantibodies and its associations with other autoimmune conditions support an immune pathology. Intravenous immunoglobulin infusion has been tried with encouraging results by Dalakes et al (2000).

CONCLUSION

This case is reported to remind the reader of this disabling condition, which may remain undiagnosed for many years. Stiff person syndrome is clinically elusive but potentially treatable and should be considered in patients with unexplained stiffness and spasm. **HM**

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IN THE PUBLIC'S VIEW...

Blame for blame's sake?

Brits love nothing better than self-flagellation. The Rugby Union World Cup was a bit of an upset, at least to Brits south of the Scottish and east of the Welsh borders, but at the end of January it re-emerged in one of the standard winter news stories: brought to a halt by a bit of snow.

The media have pre-prepared editions for inevitable events. The death of the Queen Mother required nothing more than pressing the appropriate buttons and inserting the date and time as required. So it is with 'Phew, wot a scorcher!' if the temperature goes above 28°C for more than 1 day in summer (roll out pics of toddlers with ice cream and déshabillé couples in Hyde Park), and 'Britain slithers to a standstill' when it snows. People tut and shake their heads, and complain that a bit of snow stops everything working here, whereas countries that have buckets of the stuff every winter simply shrug their shoulders and move it out of the way before proceeding about their normal daily business.

This analysis is wrong. First, at least in southern Britain, we don't get much snow. As a cross-country skier, I wish we had more. In the 20 years that we've had our own skis, we've managed to ski in and around Bristol just three times. Even if it does snow, it's usually unskiable in 24 hours, and gone in 3 days. Stay in an Alpine village, and the local farmers have snow-ploughs on their tractors. They are out on the streets as soon as it snows. But they use their ploughs every year, and for most weeks if not days in January and February.

Who will pay for enough ploughs in Bristol for snow that causes problems 1 day a year? Council tax is set to rise more than inflation this year, and the local newspapers are complaining, but how else will we teach our children and clear the rubbish? Councillors would have some difficulty buying a fleet of snow ploughs, to rust in their depots during the usual wet British winter.

The analysis is also wrong because snow causes great problems even in countries that are used to it. Birmingham ground to a halt in January because it rained and froze on already gritted roads that were full of skidded cars: nowhere would that have been easily cleared. At the same time, in Zurich, the late arrival of delayed flights coincided with heavy snow, and there were 24-hour delays getting luggage dispatched. I know because our luggage was in there. A 17-vehicle pile-up just south of Zurich brought the motorways to a standstill. There were similar stories from elsewhere in northern continental Europe. The stories were reported, but without blame. These things happen; they are newsworthy but not blameworthy.

And what has all this to do with medicine? The Labour government has put a lot of money into the NHS. While the NHS's biggest problems still stem from the shortage of staff and the inexorable rise of medical emergency admissions, there have been real improvements. We must not let a media that likes nothing better than blaming ourselves for incompetence mislead the public when praise is due. **HM**

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