Letters to the Editor

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Non-musculoskeletal symptoms in joint hypermobility syndrome. Indirect evidence for autonomic dysfunction?

SIR, Joint hypermobility syndrome (JHS) is a chronically disabling disorder manifested as widespread pain, fatigue, multiple soft tissue lesions and fragility of skin and supportive connective tissues [1]. It is a condition that is often overlooked by clinicians [2]. Moreover, clinical experience suggests that previously unrecognized non-musculoskeletal symptoms, including pre-syncope, palpitations and bowel disturbance, are also common in JHS. Recent evidence demonstrates dysfunction of the autonomic nervous system as an explanation for these symptoms [3]. Recognition of these symptoms by clinicians is an important part of patient assessment and education, even if the pathophysiology remains unclear.

We have examined the prevalence of non-musculoskeletal complaints and explored their associations to determine whether they reflect a tendency to report multiple, non-specific concerns.

One hundred and seventy women aged between 18 and 65 yr were seen in a teaching hospital hypermobility clinic over a 2-yr period. Each was diagnosed with JHS using the 1998 Brighton criteria [4]. Individuals completed a self-reported questionnaire enquiring about symptoms experienced on a ‘regular basis’. The questionnaire was structured so that patients were unaware of any hypothesis. Fifty female hospital staff acted as controls, having been identified as non-hypermobile by the use of a five-part self-report questionnaire [5]. The symptoms explored clustered into five domains: (i) (pre)syncope (feel faint, actually faint, dizziness and light-headedness); (ii) cardiorespiratory (CR) (palpitations, chest pain and shortness of breath); (iii) gastrointestinal (GI) (nausea, stomach ache, diarrhoea and constipation); (iv) common JHS concerns (fatigue, joint pain, anxiety and depression); and (v) non-specific (migraine, allergy, rash, nocturia, dysuria, flushing, night sweats, fever, lymph gland pain and poor sleep).

Similar symptoms were combined for analysis. For example, dizziness and light-headedness were considered synonymous with pre-syncope and were not treated as mutually exclusive. They were combined, so that a person giving both in their response was only counted once within the domain.

We found that 41, 26 and 37% of individuals with JHS reported at least one symptom suggestive of a (pre)syncope, CR or GI complaint respectively. This compared with 15, 12 and 16% of controls, despite controls being older by a mean of 13 yr [32 yr (range 23–64) vs 45 yr (range 23–64)].

Pain, fatigue, anxiety and depression were, as one would expect, more common in JHS patients (91, 71, 32 and 38% respectively) than controls (30, 30, 12 and 8% respectively). Migraine, rashes and poor sleep were also over-represented amongst JHS patients. Other non-specific complaints (allergy, nocturia, dysuria, flushing, night sweats, fever and lymph gland pain) were equally distributed in cases and controls (Fig. 1).

Analysis was extended to look just at JHS patients, comparing those reporting (pre)syncopeal, CR or GI concerns (or any combination of the three domains) against those who did not. Sixty per cent of patients recorded at least one type of concern relating to (pre)syncopeal, CR or GI symptoms. Of this 60%, 28% reported concerns in one domain, 20% concerns within two domains, and 12% in all three. Those JHS patients classified as having symptoms in two or more of the three domains were found to account for 90% of all JHS patients reporting flushing or night sweats. Moreover, this group were three times more likely to complain of fatigue and anxiety [odds ratio 2.8 (95% confidence interval 1.3–6.3), P = 0.01] than their peers, fatigue and anxiety also being found to be independently associated with migraine and poor sleep (odds ratio 2.6 and 3.5 respectively). Age was not a confounder. No association was found with the other non-specific complaints (Fig. 2).

We conclude that non-musculoskeletal symptoms are common in patients with JHS and that individuals with these symptoms may express more fatigue, anxiety, migraine, flushing, night sweats...
and poor sleep than their peers. The pathophysiological basis for these symptoms needs to be explored further but may be a complication of autonomic dysfunction. Alternative explanations might include the side-effect of medications, particularly analgesics and antidepressants, or the presence of comorbidity. In our experience, however, the majority of patients seeing us for the first time are no longer taking such medications as they have often been of little benefit. We note also that very few patients have specific cardiovascular, respiratory or bowel disease.

Potential manifestations of autonomic pathology include cardiac dysrhythmias, postural orthostatic tachycardia syndrome, orthostatic hypotension and orthostatic intolerance. Mechanisms leading to such phenomena in JHS patients may include weakened vascular tissue elasticity and impaired peripheral vasoregulation as a consequence of adrenoceptor or neuronal abnormalities. Similar symptoms are found in chronic fatigue syndrome [6]. Consequently, these disturbances might also be secondary and reflect a degree of physical deconditioning rather than a primary autonomic or connective tissue pathology. Further studies are required. In the meantime, clinical assessment should include an enquiry as to the presence of such symptoms, and health professionals should acknowledge that they are often encountered among patients with JHS.

Ethical approval for the use of a general questionnaire identifying features of JHS both in clinical and epidemiological studies was gained from Guy’s Hospital, London. Verbal consent was deemed sufficient.

The authors have declared no conflicts of interest.

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The mobile phone as an imaging tool in SLE

Sir, I recently reviewed a patient with SLE at out-patients. Over many years she had described a recurring but always transient rash, which sometimes lasted for just a few hours but which had never been seen or properly documented by a physician.

On this occasion she brought with her a mobile phone, one of the newer models with an inbuilt digital camera. Stored on the database were several images of her rash, which had appeared on a shopping trip and lasted for about 3 h before vanishing. It appeared as a typical urticarial rash, as she had described, and not a photosensitive manifestation, as had sometimes been suspected on account of its distribution.

I believe this is the first report of a mobile telephone being used as diagnostic imaging technique in rheumatology.

The author has declared no conflict of interest.

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Pregnancy in a rheumatoid arthritis patient on infliximab and methotrexate

Sir, A lady was diagnosed with rheumatoid arthritis at the age of 29. She was initially treated with sulphasalazine (3 g/day) and then azathioprine (eventually 250 mg/day) was added. This failed to control her disease, so hydroxychloroquine (400 mg/day) was added. On this combination of drugs (with 5 mg prednisolone and diclofenac 150 mg/day) her disease appeared to be coming under control.

At this point the patient decided she would like to try for a baby. The hydroxychloroquine and sulphasalazine were stopped and the prednisolone was increased to 7.5 mg/day, and she continued on the azathioprine 250 mg/day (with diclofenac 150 mg/day). She tried to conceive for 9 months but was unsuccessful. The infertility clinic found she was not ovulating. Her antiphospholipid antibodies were negative. Her diclofenac (150 mg/day) was stopped and she was commenced on clomifene for infertility. After 2 months of treatment she became pregnant. The baby was stillborn at 36 weeks due to an acute hypoxic event. After several months she again became pregnant on clomifene but miscarried at 15 weeks. She very quickly became pregnant again on clomifene and this time her azathioprine was eventually stopped and her prednisolone was reduced during pregnancy. She gave birth to a healthy boy at 34 weeks. Six months later she became pregnant again on clomifene and gave birth to a girl at 35 weeks. She was restarted on the azathioprine (with prednisolone 7.5 mg/day and diclofenac 150 mg/day) after each pregnancy. The azathioprine (250 mg/day) failed to control the arthritis after her second pregnancy, so it was stopped and she was commenced on methotrexate (eventually at 20 mg/week with folic acid 5 mg/week) in addition to prednisolone 7.5 mg/day and diclofenac 150 mg/day for 12 months. This was ineffective, so infliximab (3 mg/kg) every 8 weeks (after the loading doses) was added to this regime.

Prior to commencing infliximab she was counselled again about avoiding pregnancy and using adequate contraception. Once on infliximab, her disease activity score improved from 6.43 initially to 4.24 at 6 months and her prednisolone was reduced to 5 mg/day. After 9 months on infliximab she became pregnant, which was unplanned. They had been using only

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