LETTERS TO
THE EDITOR

An inherited dystrophin deletion without muscle weakness

Deletions of the dystrophin gene are known to be present in approximately 60 to 70% of Duchenne (DMD) and Becker (BMD) patients. We describe a family with no history of congenital muscle weakness who both have raised creatine kinase levels and an identical deletion including exons 14–18 of the dystrophin gene but no muscle weakness. Muscle histology is normal in the boy.

A previously well 5 year old boy presented with a three year history of occasional muscular cramps in his legs after exercise. On examination he had no calf hypertrophy or muscle weakness and Gower’s sign was negative. However, his creatine kinase (CK) was grossly raised at 7854 IU/l (NR 1–220 IU/l) and a diagnosis of DMD was suspected. Examination by a paediatric neurologist confirmed a normal neurological examination, including reflexes, and muscle bulk. Two further CK measurements were also raised at 6253 IU/l and 11 800 IU/l (NR 25–180 IU/l). A Gower’s sign and muscle biopsy were histologically normal with little variation in fibre size and no evidence of fibre regeneration or degeneration, or fibre type differentiation and no evidence of denervation or congenital myopathy. Immunochemistry for dystrophin and G418 antibody was abnormal in both parents.

The boy’s mother had no muscle related symptoms and a normal CK (101 IU/l) but reported that her father suffered from occasional muscular pains when young. Clinical examination revealed a normal examination and his legs as a child and still had aching of his limbs after exertion. However, he had coped with physically demanding jobs throughout his life. A creatine kinase level in him was also raised at 520 IU/l (NR 1–220 IU/l). DNA analysis by Southern blotting using standard techniques was carried out using DNA probes specific to dystrophin gene exons. Both the proband and his grandfather who both had raised creatine kinase levels and an identical deletion including exons 14–18 of the dystrophin gene. Exons 13 and 19 were present. Such a deletion would not be expected to disrupt the reading frame. Western blot analysis of a muscle biopsy from the proband using antibodies containing exons 20–35 did show a deletion (by autoradiography) whereas, a sample from a control of this age group without dystrophin deficiency showed a full band (exons 21–40). Western blot analysis of a muscle biopsy from the proband using antibodies containing exons 21–35 showed a mild reduction in dystrophin levels (by densitometry) compared to a sample from an age-matched control. Exon 21, containing fragments of normal dystrophin, was also present in the family.”

We are very grateful to Tim Sherratt for performing the Western blotting.

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Genital anomalies detected in patients with LPHAS

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The newly recognised skeletalgenital syndrome

I read with great interest the comments of Teebi on the newly recognised skeletalgenital syndrome (MIM 276820). All nine reported cases (five females and four males) in five unrelated families (from Jordan, Brazil, Israel, Kuwait, and Italy) showed the characteristic phenotype of the Al-Awadi-Richieri-Costa-Raas-Rothschild limb-pelvis-hypoplasia aplasia syndrome (LPHAS).

We recently reviewed the syndrome and discussed inter- and intramural variability of expression of its pleiotropic gene affecting both the skeletal and genital systems.

In 1988, Raas-Rothschild et al called this syndrome LPHAS and recently Teebi proposed a new nomenclature for this syndrome ("limb-pelvis-hypoplasia aplasia syndrome") (LPHAS). The first term (LPHAS) ignored all genital anomalies and the second (LPHAS) focused only on the urethral anomalies (40%). Three of the four affected males had inguinal testes (75%), two had a hypo-plastic scrotum (50%), and one had hypospadias (25%). Displaced external genitalia was a common feature in both females and males (7, 98% and 9, 78%).

I would argue against the nomenclature of Raas-Rothschild et al focusing on the major skeletal anomalies alone and on the nomenclature of Teebi (LPHAS) focusing on urethral anomalies (40%). Both ignored the associated genital anomalies (89%) and the displaced external genitalia occurring in seven males and females (table).

Syndromologists are invited to enrich the scientific discussion of the best nomenclature for this newly recognised skeletal genotype syndrome.