A failure to relax

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Case study – Mr ST

Mr ST, a caucasian man aged 31 years, presented to hospital with weakness of his arms and legs. He felt unable to cope at home. Six weeks earlier, he sustained burns to his right hand, which occurred while trying to remove the radiator cap from his car.

A review of hospital records revealed a history of hypertrophic cardiomyopathy, androgenic alopecia and abdominal pain, for which he had visited the cardiology, dermatology and gastroenterology departments respectively.

Examination disclosed a slim male with frontal alopecia and wasted facial and proximal limb muscles. Reflexes were preserved, sensation intact. Notably, hand grip relaxation was delayed (myotonia).

Haematological and biochemistry tests were unremarkable. Left ventricular hypertrophy and lateral T wave inversion were present on the electrocardiogram.

Question 1

What is the most likely diagnosis? What other clinical features would you look for?

Question 2

What other medical conditions may occur with myotonic dystrophy?

Question 3

How would you confirm the diagnosis?

Question 4

How is this condition treated?

Answer 1

A working diagnosis of myotonic dystrophy was made based on the history of muscle weakness, myotonia and cardiomyopathy, as well as the classic phenotypic appearance (*Figure 1*). It was hypothesised that the burn on the right hand was also a result of the myotonia (ie. failure to release his grip from the radiator cap).

Patients with myotonic dystrophy have a characteristic appearance typified by frontal baldness (*Figure 2*), partial ptosis, temporal recession, and a sullen, expressionless and triangular or 'hatchet' shaped face secondary to weakness and wasting of the temporalis and facial muscles. Consequently, diagnosis may sometimes be possible at first glance. Stellate shaped cataracts can arise. Myotonia may be demonstrated by percussion over the thenar eminence to reveal contraction followed by slow relaxation of thumb opposition, or by asking the patient to make a fist and relax (again delayed). Nonspecific features of myopathy such as proximal muscle weakness and wasting (*Figure 3*), as well as a waddling gait, may be elicited. Hypogonadism can occur and hence testicular atrophy may be present in male patients.

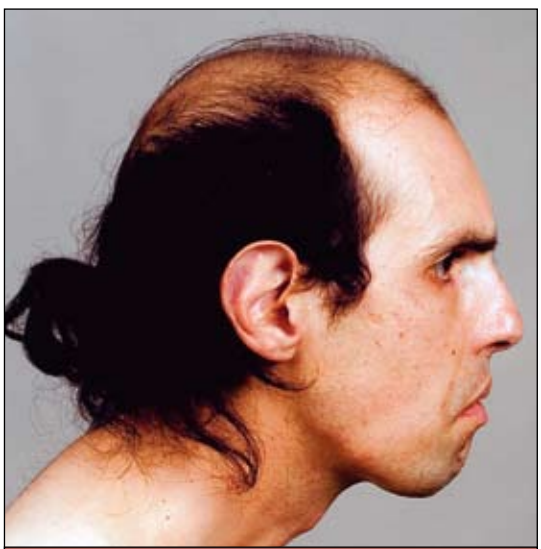

Figure 1. Classic phenotypic appearance of myotonic dystrophy

The differential diagnosis, bearing in mind the proximal weakness and expressionless face, would include other myopathic disorders, although myotonia is only found in myotonic dystrophy, myotonia congenita, and the very rare channnelopathies. Temporalis wasting can give the forehead a bossed appearance resembling Paget disease.

Myotonic dystrophy is the most common form of muscular dystrophy among caucasians, with an estimated

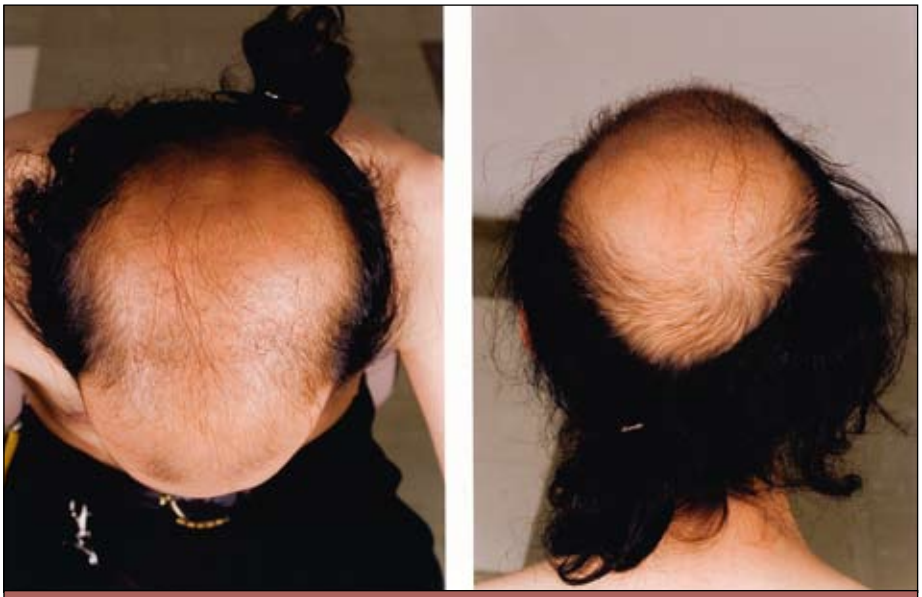

Figure 2. Appearance typified by frontal baldness

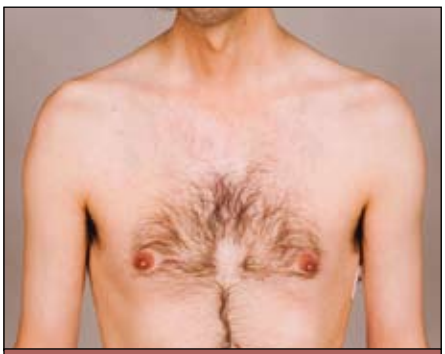

Figure 3. Proximal muscle weakness

incidence of 1 in 8000.[1] Transmission is autosomal dominant with variable penetrance. Myotonic dystrophy can also occur as a result of a sporadic mutation – this is termed 'classic' myotonic dystrophy.

The mutation underlying myotonic dystrophy is an expansion of the cystosine thymidine-guanine (CTG) repeat in the 3 untranslated region of the myotonic dystrophy protein kinase gene on chromosome 19q13.3. Asymptomatic individuals have 50–99 repeats, whereas affected individuals have 100–2000 or more copies.[2] Amplification of the number of repeats has been proposed as the explanation for the clinical phenomenon of anticipation, ie. the increasing severity of disease in successive generations.[2]

Answer 2

Myotonic dystrophy is a progressive multisystem disorder which usually manifests in adolescence or early adulthood. Other clinical features include:

- hypogonadism
- cataracts
- diabetes mellitus
- peripheral neuropathy (independent of diabetes)
- cardiomyopathy and conduction defects[3]
- low intelligence
- abnormal gastrointestinal motility.

Answer 3

Diagnosis had until recently rested upon an accurate physical examination, possibly supplemented with an electromyogram. The discovery of the underlying genetic defect has enabled DNA testing to be applied to patients and their relatives.

In this patient's case, blood was taken for DNA analysis and the diagnosis was confirmed by southern blot (*Figure 4*). The patient and his family were informed of the diagnosis and were referred for genetic counselling. Cardiology and neurology opinions were sought.

Answer 4

Treatment of myotonic dystrophy is largely symptomatic.[4] Patients frequently develop peripheral weakness, therefore braces for an associated foot drop may be useful. The myotonia may respond to medications such as class IA-IC anti-arrythmics or the anticonvulsants

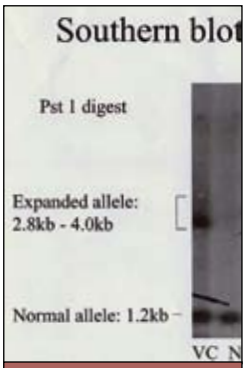

Figure 4. Southern blot analysis demonstrating expanded trinucleotide repeat

valproate or carbamazepine. Specialist respiratory and cardiovascular opinion could be sought regarding the treatment of respiratory muscles weakness or the cardiomyopathy respectively. Referral to an ophthalmologist is indicated for cataracts and intraocular lens implants if indicated. There are reports of the successful use of noninvasive ventilation and cardiac pacemakers, although specific guidelines do not exist.[3] Prognosis is variable, although the lifespan of many patients is reduced. Negative prognostic factors include a young age at disease onset, cardiovascular and respiratory involvement, and a large number of trinucleotide repeats.[5]

As myotonic dystrophy is a disease with severe consequences, a high level of clinical suspicion is necessary so that genetic counselling and symptomatic treatment may be provided.

Conflict of interest: none declared.

References

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