Racial variation in serum creatine kinase levels

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INTRODUCTION

Serum total creatine kinase is most often used in clinical practice in the diagnosis of acute myocardial infarction where the rise and fall in serum creatine kinase activity follows a well-recognized pattern. Serum creatine kinase may also be used in the diagnosis and monitoring of rheumatological conditions which affect skeletal muscle such as polymyositis, some types of muscular dystrophy and rhabdomyolysis where levels of creatine kinase above the quoted reference range may be found. Exercise or intra-muscular injections may also cause transient rises in serum creatine kinase levels[1]. It is less well recognized, however, that there are racial differences in the distribution of creatine kinase. We now report on four separate cases which illustrate the difficulties in using serum creatine kinase in the diagnosis of acute myocardial infarction and in the diagnosis and monitoring of skeletal muscle disease.

Case 1. Racial variant: sustained high activity of serum creatine kinase

A 29-year-old Afro-Caribbean man rose during the night to go to the toilet, felt warm and dizzy, and had difficulty breathing leading to transient loss of consciousness. SWH, his general practitioner (GP) was called out, examined him and diagnosed micturition syncope. A blood sample was sent to the laboratory with the clinical details section of the request card reading 'breathlessness': the card was not marked as urgent. Some hours later the hospital laboratory telephoned SWH with a serum creatine kinase of 670 U/l (reference range in men < 210 U/l) and the comment that this was consistent with a diagnosis of acute myocardial infarction. SWH tried to contact the patient as a matter of urgency but had to enlist the help of the police and social services before he was found and sent to the local hospital. The receiving physician agreed with the diagnosis of micturition syncope: an electrocardiogram was normal and a repeat of the serum creatine kinase was 555 U/l. Serum aspartate transaminase, hydroxybutyrate dehydrogenase and thyroid function tests were within the reference ranges. The patient was otherwise asymptomatic and the biochemical findings were ascribed to a racial variant in creatine kinase level. No further investigations were ordered. The final diagnosis was micturition syncope.

Case 2. Racial variant: sustained high serum activity of creatine kinase plus ST elevation on the electrocardiogram

A 42-year-old Afro-Caribbean man was referred to the accident and emergency department by SWH with a 3 h history of chest pain. The chest pain had settled by the time of his arrival. An electrocardiogram (ECG) showed ST elevation in the anterior chest leads (Figure 1). A chest X-ray was normal. Serum creatine kinase activity was 385 U/l. The receiving physician was aware that ST elevation in the anterior chest leads can be found as a racial variant: moreover he was not convinced that the history was that of an acute myocardial infarct and repeated the serum creatine kinase after 4 h when it was found to be 360 U/l. Since the creatine kinase level had not risen and a repeat electrocardiogram did not show any change from the first, the diagnosis of an acute myocardial infarct was no longer considered. The findings were ascribed to racial variations in both creatine kinase level and ST segment. The patient was discharged with follow-up and the cause of his chest pain was never found. This case illustrates that care should be taken not only in interpreting the serum biochemistry results but also in assessing the electrocardiogram in Afro-Caribbean

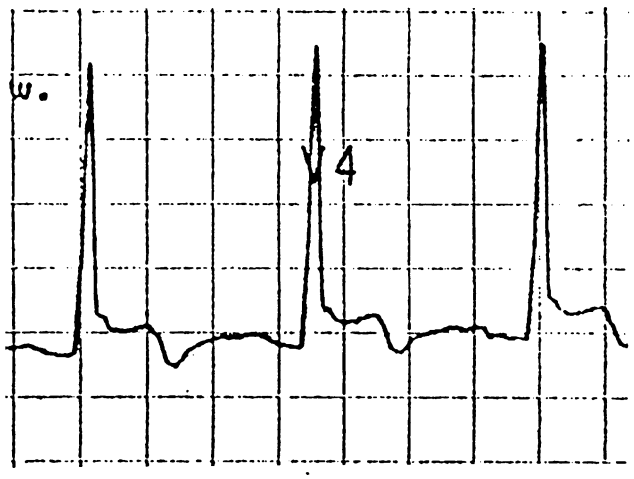

Figure 1 **Lead V4 from an electrocardiogram obtained from case 2, showing ST elevation and T wave inversion as a normal racial variant**

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patients since the ECG may also differ on a racial basis[2]; in fact, we find that every permutation of normal ECG/ST elevation in the chest leads 'normal' creatine kinase/high creatine kinase is found in the Afro-Caribbean population. This emphasizes the need for a proper history and examination and, if possible, access to previous laboratory results when assessing patients of Afro-Caribbean extraction.

Case 3. Racial variant: raised serum creatine kinase activity in the presence of skeletal muscle disease

A 44-year-old African woman with a history of proximal muscle weakness was diagnosed as having polymyositis and was started on oral steroids. Her condition deteriorated and she was referred to the rheumatology department with marked muscle weakness. Electromyography and muscle biopsy confirmed the diagnosis of polymyositis. Serum creatine kinase (which had not been measured before the onset of her illness) was 11 600 U/l (upper reference range quoted for women is 180 U/l). She was treated with high dose steroids and immunosuppression and over the next 3 months her clinical condition improved. Her serum creatine kinase fell to 210 U/l, just above the quoted reference range, and we were unsure whether this represented residual disease activity or racial variation. Management was therefore based on her clinical status and the results of myometry rather than the serum creatine kinase results.

Case 4. Racial variant: exaggerated rise in serum creatine kinase activity in response to exercise

A 26-year-old Afro-Caribbean man was referred to the rheumatology department by SWH, his GP, for investigation of an 18-month history of low back pain. He was a keen athlete. He did not give a history of anabolic steroid or other drug abuse. On examination, he was a well-muscled man with clinically normal muscle power and tender sacro-iliac joints. Irregular sacro-iliac joints were seen on X-ray and an isotope bone scan showed increased uptake in both sacro-iliac joints. Serum creatine kinase activity was 572 U/l. The patient was reviewed 1 month later and a repeat creatine kinase was requested which was 20 000 U/l. On further questioning, the patient admitted to strenuous exercise in the days before his clinic appointment but there was concern that he might have underlying myositis. Electromyography, muscle biopsy and an autoantibody screen were all normal. One month later the patient was reviewed and his serum creatine kinase activity was 300 U/l. He was followed up for some months. He continued to exercise intermittently and serum creatine kinase levels varied from just within the reference range up to 2000 U/l. There was no evidence of muscle weakness.

DISCUSSION

The above cases illustrate some of the diagnostic dilemmas and inconveniences posed to physicians who try to apply Caucasian reference values in patients of Afro-Caribbean origin. The reference range for serum creatine kinase has been constructed from data obtained from healthy Caucasian volunteers with the upper limit of the reference range being set to include 97.5% of that population (equivalent to two standard deviations above the mean). This means that 2.5% of a normal, healthy Caucasian population will have a serum creatine kinase activity above the upper limit of the reference range. The distribution of serum creatine kinase in an Afro-Caribbean population is shifted towards higher values. Thus, whilst it is uncommon to find a healthy Caucasian with a serum creatine kinase of, say, 300 U/l, this is commonplace in those of Afro-Caribbean origin and we have found Afro-Caribbeans with serum creatine kinases as high as 1200 U/l as a normal finding. The racial difference in distribution of serum creatine kinase was first described by Meltzer[3,4] who studied psychiatric inpatients and found that serum creatine kinase levels were significantly higher in Afro-Caribbeans than Caucasians. Meltzer[4] also found that the level of creatine kinase was related to the degree of skin pigmentation: this curious association has been confirmed in two further studies[5,6] where Hispanics had serum creatine kinase levels intermediate between those of Afro-Caribbeans and Caucasians. Wong[6] constructed three different creatine kinase reference ranges for the population based on racial origin and sex: the high serum creatine kinase group were black men with values up to 520 U/l; the intermediate serum creatine kinase group were non-black men and black women who had values up to 340 U/l and the low serum creatine kinase group comprised non-black women with values up to 140 U/l.

The differences in serum creatine kinase between racial groups may not necessarily be benign. Thus, the American Marines became alarmed when a disproportionate number of Afro-American recruits suffered exercise-induced rhabdomyolysis, myoglobinuria and renal failure[7]: these investigators found that not only did Afro-Americans have higher baseline levels of serum creatine kinase than their Caucasian counterparts but also that the increase in serum creatine kinase in response to exercise was much greater[7]. We have also found that the day-to-day variation in serum creatine kinase is greater in the Afro-Caribbean population than in the Caucasian population irrespective of exercise. This can make assessment of response to treatment in myositic illnesses particularly difficult in Afro-Caribbeans and, for this reason, some rheumatologists advocate formal myometry as a more useful means of assessing disease. Corticosteroid-induced

myopathy is not associated with raised serum creatine kinase activities[1] but anabolic steroid misuse may be suspected in young men presenting with vague myalgic symptoms[8]. There was no evidence for this in case 4.

Racial differences are not just confined to the serum level of creatine kinase. Afro-Caribbeans have different reference ranges for serum amylase activity[9], liver function tests[10], neutrophil counts, pulmonary function tests[11] and electrocardiographic findings[2] (as illustrated in case 2 above). In order to avoid inconvenience to both the patient and the physician these differences need to be borne in mind: easily available laboratory tests should not be allowed to supplant a good history and examination.

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Delayed puberty and reversible pituitary enlargement in a girl

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INTRODUCTION

The combination of hyperprolactinaemia, amenorrhoea and enlargement of the pituitary in a young woman usually suggests a prolactinoma. We describe the case of a girl who presented with primary amenorrhoea and growth delay associated with hyperprolactinaemia and suprasellar enlargement of the pituitary, whose underlying diagnosis was not a prolactinoma as initially thought but primary hypothyroidism.

CASE HISTORY

A 15-year-old girl was referred to the gynaecologists for investigation of primary amenorrhoea. She had a cyclical vaginal discharge but no definite per vaginam (PV) bleeding. She was an only child and had had a normal delivery with a birth weight of 8lb 4oz (3.75 kg). Her parents were alive and well and there was no family history of endocrine disorders. On examination, she was pre-pubertal with absent pubic and axillary hair and no breast development. In addition she was below the third percentile for height. Chromosomal analysis showed she was 46XX. She had a normal pelvic ultrasound. Luteinizing hormone (LH) was 1.0 IU/l and follicle stimulating hormone (FSH) was 7.1 IU/l. However her prolactin was raised at 1858 mU/l. A skull radiograph and formal visual field testing were normal.

Her delayed puberty was thought to be due to hyperprolactinaemia causing suppression of the hyperthalamo-pituitary-ovarian axis and she was started on bromocriptine 2.5 mg daily. Subsequently her prolactin fell to within the normal range (449 mU/l) and she began to menstruate normally and to develop secondary sexual characteristics. However, after 6 months on bromocriptine there was no growth in stature and she was referred for further endocrine investigation. No further history was available and there was no clinical abnormality apart from

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