LETTERS TO THE EDITOR

Serum skeletal troponin I in inflammatory muscle disease: relation to creatine kinase, CKMB and cardiac troponin I

The measurement of serum creatine kinase (CK), which is used widely in the diagnosis and management of polymyositis and dermatomyositis lacks both sensitivity[1–7] and specificity,[7–9] leading to potential problems if the serum total CK concentration is interpreted as a direct measure of muscle disease activity. Furthermore, in those cases where the total CK is raised reliance on an analysis of the CK isoforms is an unreliable means of determining the presence of myocardial involvement. This is because in chronic inflammatory muscle diseases, regenerating striated muscle contains up to 50% of the CKMB isoform.[6 10 11] This often results in an increase in the CKMB/total CK ratio by more than the 3% threshold commonly used to imply myocardial damage.[6 8 9 11 12]

The need for more sensitive and specific serum markers of striated and myocardial inflammation has led us to a study of the troponins. Skeletal troponin I (sTnI) has been found to correlate with total CK in exercising athletes[13 14] and to be increased in a small series of patients with polymyositis[13] but has not previously been studied in detail in relation to total CK in inflammatory muscle disease. Cardiac troponin I (cTnI) is a highly specific marker of myocardial injury[15] in contrast with CKMB, which is expressed both in myocardial and striated muscle. The behaviour of cTnI has not been reported in the inflammatory muscle diseases.

We report the relation between serum sTnI and total CK in patients with polymyositis and dermatomyositis. In the assessment of myocardial disease the use of serum cTnI has been compared with serum CKMB and the CKMB/total CK ratio.

Serum samples were collected from 43 healthy control subjects (23 female) and 16 patients with polymyositis or dermatomyositis. Patients with inflammatory muscle disease were recruited from the Muscle Clinic at St George's Hospital between 1994 and 1997. Table 1 gives details of the patients. Diagnoses were established according to the criteria of Bohan and Peter[16] from clinical features of proximal muscle weakness with or without rash, serum total CK, EMG, muscle histology and in addition muscle magnetic resonance imaging. Evidence of myocardial involvement was assessed from clinical examination, ECG and echocardiography. Patients were treated with standard immunosuppressants including prednisolone, azathioprine, cyclosporin A and IV immunoglobulin according to clinical and biochemical assessment of disease activity, including serial muscle strength of deltoid and hip abductors using a hand held myometer[17] and serum total CK. In the myositis group between one and six samples were collected per patient

Table 1 Demographic details and CK, CKMB, skeletal and cardiac Troponin I values in patients with polymyositis and dermatoyositis

Case	*Sex*	*Age*	*Race*	*Diagnosis*	*CK (U/l)*	*CKMB (μg/l)*	*sTnI (μg/l)*	*cTnI (μg/l)*
1	F	50	W	PM	89	1.3	<1.6	0.1
2	F	74	W	PM	103		2	
3	M	75	A-J	DM	117	3.5	4.7	1.39
4	M	46	W	PM	123	2.5	1.6	0.03
5	F	56	A	PM	172	2.1	<1.6	0.03
6	F	30	A-C	PM	213	0.8	1.6	0.03
7	F	54	A	PM	227	1.8	<1.6	0.03
8	F	34	W	PM	231	5.1	3.4	0.03
9	F	56	I	DM	333	4.8	3.3	0.03
10	M	24	W	DM	413	17.9	10.4	0.08
11	F	63	A-C	PM	456	12.6	8.2	0.03
12	M	25	W	PM	734		18.5	
13	F	72	W	PM	2089	132	17.5	0.03
14	F	27	I	PM	2165	1183	990	0.03
15	M	40	A-C	DM	8341	294	73.6	<0.01
16	F	45	W	DM		1.7	<1.6	<0.01

sTnI: skeletal Troponin I, cTnI: cardiac Troponin I, M: male, F: female, DM: dermatomyositis, PM: polymyositis, A: African, A-C: Afro-Caribbean, A-J: Anglo-Japanese, W: white, I: Indian. Reference ranges: CK 30–250 U/l (male), 30–180 U/l (female), CKMB <5 μg/l, sTnI <7.5 μg/l, cTnI <0.1 μg/l.

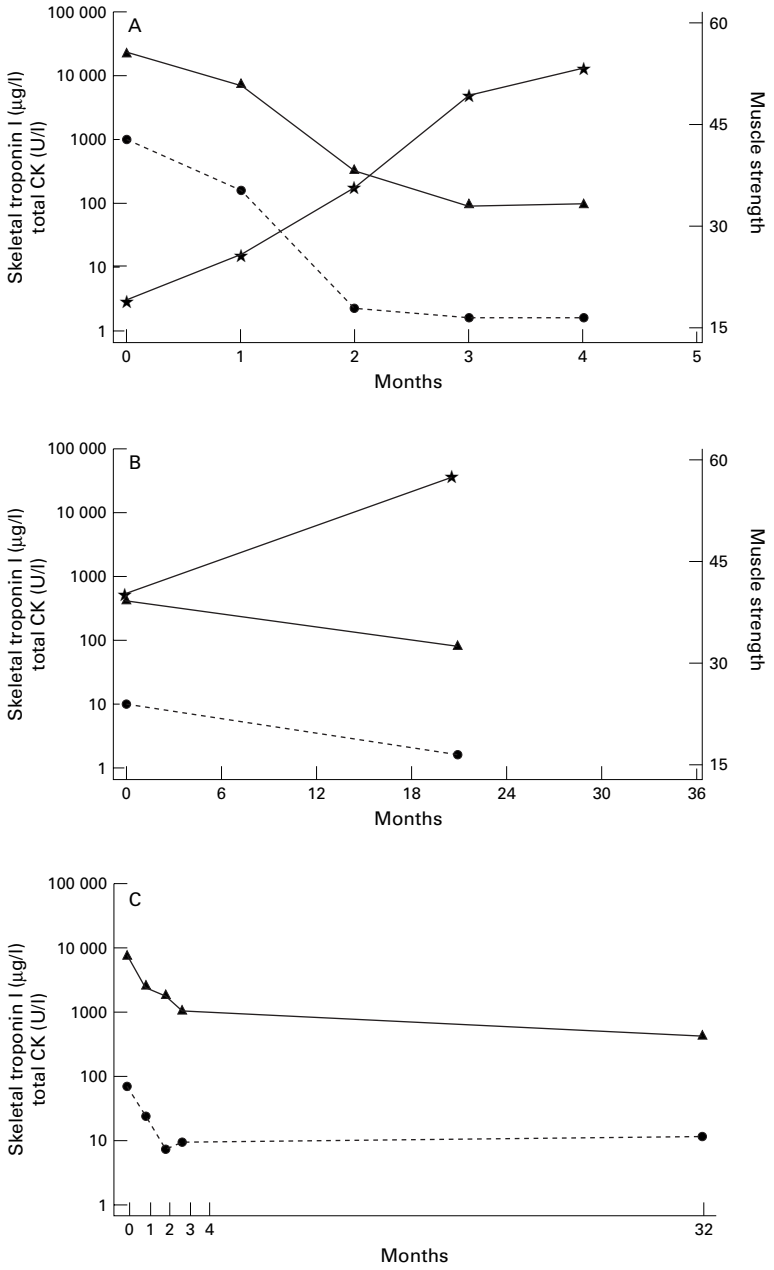

Figure 1 Serial serum skeletal troponin I (filled circles μg/l), total CK (filled triangles U/l) and muscle strength (asterisks, arbitary units) in patients with polymyositis (A) and dermatomyositis (B) and (C).

giving a total of 48 samples in which sTnI results were available.

Fast sTnI was measured by time resolved fluorimmunoassay using a modification of an enzyme immunoassay.[13] Cardiac troponin I and CKMB mass were measured on an automated analyser (Sanofi Access) according to the manufacturer's instructions (Beckman, High Wycombe, UK).

RELATION BETWEEN SERUM STNI AND TOTAL CK

In 43 control subjects the serum sTnI concentration was skewed despite log transformation (range: undetectable 12.7 µg/l, median: undetectable). The reference range, based on 95% of values for sTnI, was estimated to be less than 7.5 µg/l. Total CK values were available on 40 control subjects and correlated well with sTnI values. There were four outliers: three male subjects (CK 277 U/l, sTnI 5.2 µg/l; CK 404 U/l, sTnI 2.9 µg/l; CK 673 U/l, sTnI 5.2 µg/l) and one female subject in whom CK was normal (91 U/l) but the sTnI was increased (12.7 µg/l).

In 15 myositis patients there was a highly significant correlation between sTnI and total CK, Spearman $r = 0.95$ (95% CI 0.86, 0.98, $p < 0.0001$). In four cases the serum total CK was slightly raised in the presence of a normal sTnI. There were no cases of a raised sTnI with a normal total CK (see table 1).

Between two and six serial samples were taken from 14 patients over a three year period. All patients were receiving immunosuppressive treatment. In eight patients the disease was in remission throughout this time and the total CK and sTnI values remained within the normal range in all samples. In the remaining six patients serial samples were taken during the induction of remission and throughout subsequent follow up. In three patients changes in the total CK were mirrored synchronously by similar changes in the sTnI and in two cases were inversely related to the mean muscle strength in deltoid and hip abductors measured by a hand held myometer (see fig 1). In the other three patients there was insufficient variation in either serum marker to draw firm conclusions (not shown).

RELATION BETWEEN TOTAL CK, CKMB AND CTNI

There was a highly significant correlation between the total CK and CKMB (n = 13), Spearman $r = 0.99$, $p < 0.0001$; and also between sTnI and CKMB (n = 14), Spearman $r = 0.98$, $p < 0.0001$. There was no correlation between cTnI and CKMB (n = 14), Spearman $r = -0.11$.

Serum cTnI was increased in one case (1.39 µg/l, see table 1). There was no evidence of myocardial involvement at the time of the sample and the total CK, CKMB and CKMB/total CK ratio were normal. Intriguingly the patient had been treated for malignant hypertension three months earlier and this is the most probable explanation. A repeat cTnI sample two years later was normal.

In 6 of 13 patients (46%) the CKMB/total CK ratio was > 3%. There was no evidence in any of these patients of myocardial involvement and the serum cTnI was < 0.1µg/l in all six cases (see table 2).

Histological evidence of myocarditis has been found in 30% of patients with polymyositis[19] and non-specific evidence of myocardial disease reported in as many as 76%.[19 20] Our series concurs with others who also report a raised CKMB/total CK ratio in patients with inflammatory muscle disease.[8 9 12] However, although a ratio >3% is usually interpreted as indicative of myocardial disease in adults, in inflammatory muscle disease this is more likely to reflect striated muscle damage alone.[6 10 11] In this situation the cTnI is of particular use in distinguishing between a striated and myocardial origin of a raised CKMB/total CK ratio as cTnI is expressed only in cardiac muscle.[15] In our cross sectional study the CKMB correlated with sTnI but not with cTnI, suggesting striated muscle was the source of the CKMB. Furthermore the serum concentration of cTnI was normal in all patients where the CKMB/total CK ratio was >3%, supporting the clinical impression of no myocardial disease. This interpretation concurs with that of others.[12]

Table 2 Cardiac and skeletal troponin I in six patients with a CKMB/CK ratio >3%

Patient	CKMB/ CK %	cTnI (µg/l)	sTnI (µg/l)	CK (U/l)
1	4.2	0.03	<3	110
2	4.8	0.03	4.7	117
3	4.3	0.08	10.4	413
4	6.2	0.03	7.6	1 487
5	8.5	<0.03	26.4	2 813
6	5.5	0.03	990	21 000

In summary the concentrations of sTnI and both total CK and CKMB were significantly correlated in 15 patients with polymyositis or dermatomyositis in a cross sectional analysis and longitudinally during induction of remission of active disease. On grounds of tissue distribution, sTnI should be the preferred marker in skeletal muscle disease but further studies will be required to determine its clinical utility. A CKMB/total CK ratio >3% is more likely to reflect the presence of regenerating striated muscle than myocardial disease. cTnI is a specific tool for distinguishing between striated and myocardial damage in situations where myocardial involvement is suspected or where the CKMB or CKMB/total CK ratio is increased.

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Enlarged spleen detected by abdominal ultrasonography in patients with RA

Rheumatoid arthritis (RA) is a systemic, chronic inflammatory disease of unknown cause. Approximately 5–10% of patients with RA have an enlarged spleen on manual palpation[1] or on isotope scanning.[2]

We measured the size of the spleen in 50 patients with RA (nine men, 41 women; average age 55.8 years (range 25–78)) and 14 healthy control subjects (no men, 14 women; average age 47.8 years (range 25–80)) by abdominal ultrasonography (Aloka, Japan). This examination was done by one skilful examiner (TD) in all cases, and comparisons were made with clinical profile and disease activity. The patients with a diagnosis of Felty's syndrome, categorised as the triad, RA, leucopenia, and splenomegaly, and patients with complications of any viral or bacterial infections were excluded from this study. Mean (SD) disease duration was 6.2 (6.6) years. The disease stage was I (13 patients), II (11), III (nine), IV (17) and the functional class was I (seven patients), II (40), III (three), IV (0), assigned according to Steinbrocker criteria.[3] The following treatment was being used when the sonographic examination was performed: non-steroidal anti-inflammatory drugs (50 patients); gold treatment (12); sulfhydryl compounds (D-