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Kasuistika | Case report

High-sensitive cardiac troponin T is not always heart – Paraneoplastic systemic sclerosis simulated myocardial ischemia

Johannes Mierke[a], Stefanie Jellinghaus[a], Anna Selle[a], Hagen Schroetter[a], David M. Poitz[b], Karim Ibrahim[a]

[a] *Technische Universität Dresden, Department for Internal Medicine and Cardiology, Herzzentrum Dresden, University Clinic, Germany*
[b] *Technische Universität Dresden, Faculty of Medicine, Institute for Clinical Chemistry and Laboratory Medicine, Dresden, Germany*

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SOUHRN

Kontext: Vysoce senzitivní srdeční troponin T (hs-cTnT, Elecsys®) je vynikajícím a na celém světě využívaným diagnostickým markerem ischemie myokardu s vysokou senzitivitou. Zvýšené hodnoty hs-cTnT se však objevují i při jiných systémových onemocněních a mohou vést k chybné diagnóze. Vysoce senzitivní srdeční troponin I (hs-cTnI, ARCHITECT®) vykazuje srovnatelnou senzitivitu jako hs-cTnT, ale zároveň mnohem větší specificitu než hs-cTnT (92 % vs. 80 %, 99. percentil).
Kasuistika: U asymptomatické pacientky s karcinomem neznámé etiologie byly opakovaně zaznamenány vysoké hodnoty hs-cTnT. Elektrokardiogram, echokardiografie, srdeční magnetická rezonance ani CT angiografie koronárních tepen neprokázaly žádné patologické nálezy. Opakované klinické vyšetření odhalilo lokalizovanou sklerodermii a profil autoimunitních protilátek pomohl stanovit diagnózu paraneoplastické systémové sklerózy (paraneoplastic systemic sclerosis, SSc). Proto byla zahájena léčba rituximabem – anti-CD20 protilátkou, což snížilo aktivitu SSc a také koncentraci hs-cTnT.
Závěr: V prezentované kasuistice byla lokalizovaná sklerodermie způsobená paraneoplastickou SSc provázena zvýšenými hodnotami hs-cTnT bez přítomnosti kardiovaskulárního onemocnění. Léčba rituximabem zmírnila zánět tkáně kosterního svalstva, což vedlo ke snížení hodnot hs-cTnT. Jako první přinášíme zprávu o skrytém zvýšení hodnot hs-cTnT, které vyvolala paraneoplastická SSc.

Keywords:
Biomarkers
High sensitive troponins
Paraneoplastic syndrome
Systemic sclerosis

ABSTRACT

Background: The high-sensitive cardiac troponin T (hs-cTnT, Elecsys®) is an excellent and worldwide used diagnostic marker for myocardial ischemia with high sensitivity. However, elevated hs-cTnT levels are found in different systemic diseases and can lead to misdiagnosis. The high-sensitive cardiac troponin I (hs-cTnI, ARCHITECT®) shows comparable sensitivity. However, hs-cTnI is much more specific than hs-cTnT (92% vs. 80%, 99th percentile).
Case summary: An asymptomatic women with a cancer of unknown primary (CUP) presented constantly high hs-cTnT. Electrocardiogram, echocardiography as well as cardiac MRI and CT angiography of the coronary arteries showed no pathological findings. A repeated clinical examination revealed a localized scleroderma and autoimmune antibody pattern diagnosed a paraneoplastic systemic sclerosis (SSc). Therefore, a treatment with Rituximab – a CD20 antibody – was initiated, which reduced activity of SSc and also concentration of hs-cTnT.
Conclusion: In the present case, a localized scleroderma due to a paraneoplastic systemic sclerosis (SSc) was accompanied by elevated hs-cTnT levels in the absence of cardiovascular disease. A reduced inflammation of skeletal muscle tissue due to rituximab treatment decreased hs-cTnT levels. This is the first report of an occult hs-cTnT elevation due to paraneoplastic SSc.

Address: Dr. med. Johannes Mierke, Technische Universität Dresden, Department for Internal Medicine and Cardiology, Herzzentrum Dresden, University Clinic, Fetscherstraße 76, 01307 Dresden, Germany, e-mail: johannes.mierke@mailbox.tu-dresden.de
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Case report

A 62-year-old asymptomatic woman without chest discomfort or dyspnoe was referred to our department from her attending oncologist because of highly elevated hs--cTnT levels (Elecsys®, 3rd generation, Roche Diagnostics GmbH, Mannheim, Germany, 0 h 324 ng/l, 3 h 276 ng/l). The measurement was initiated to exclude any myocardial damage before a planned immunochemotherapy. A cancer of unknown primary (CUP) with metastases in the liver and lung was known for two years and showed a partial remission in response to Cetuximab/FOLFIRI regimen half a year ago. No cardiovascular risk factors or other comorbidities were existing.

Repeated measurements showed a constantly elevated hs-cTnT. Furthermore, a distinct increase in creatine kinase (CK) with only a marginally elevated MB subtype was detected (Fig.1A and B). Inflammatory parameters were only slightly increased (leukocytes 11.3 Gpt/l, CRP 20.6 mg/l). Continuous ECG monitoring revealed no rhythm disturbances. An echocardiography showed a normal biventricular systolic function without detection of wall-motion abnormalities, heart-valve defects or pulmonary hypertension. Based on the missing cardiovascular risk factors, lacking symptoms but significant elevated troponin levels a non--invasive imaging strategy was performed. The cardiac MRI showed no signs of any florid myocarditis, pericarditis or any pathologies of the myocardium (Fig. 2). The existence of a coronary artery disease was ruled out by CT angiography. Furthermore, the additional measurement of hs-cTnI (ARCHITECT®, Abbott Diagnostics, Chicago, IL, USA) showed no significant increase (hs-cTnI < 2 ng/l, Fig. 3).

A repeated clinical examination revealed a located scleroderma, which was mostly pronounced in the upper extremities and was accompanied by slightly myalgia. No symptoms of a severe rhabdomyolysis were diagnosed. Based on the clinical presentation and the tumor history, a paraneoplastic development of a systemic sclerosis (SSc) was postulated. The autoimmune antibody pattern underlined the diagnosis of a SSc (ANA 1:1280) and obviated the need for muscle biopsies.

Immunosuppressive therapy was considered as not appropriate due to the yet localized skin areas with scleroderma. During the following months the scleroderma exaggerated with systemic inflammation and restrictive ventilation disorder. Thus, an immunosuppressive treatment with Rituximab – a CD20 antibody that mainly depletes B lymphocytes – was initiated to reduce the activity of SSc. The hs-cTnT concentration constantly declined during the immunosuppressive therapy as shown in Fig. 4.

Discussion

SSc is known to be accompanied by elevated CK levels, which can be explained by the underlying myositis. Increased CK-MB and cTnT levels are described to be elevated mostly in SSc patients with cardiomyopathy or severe pulmonary hypertension [1–3]. An involvement of cardiac enzymes due to paraneoplastic genesis of SSc is not described yet in the current literature.

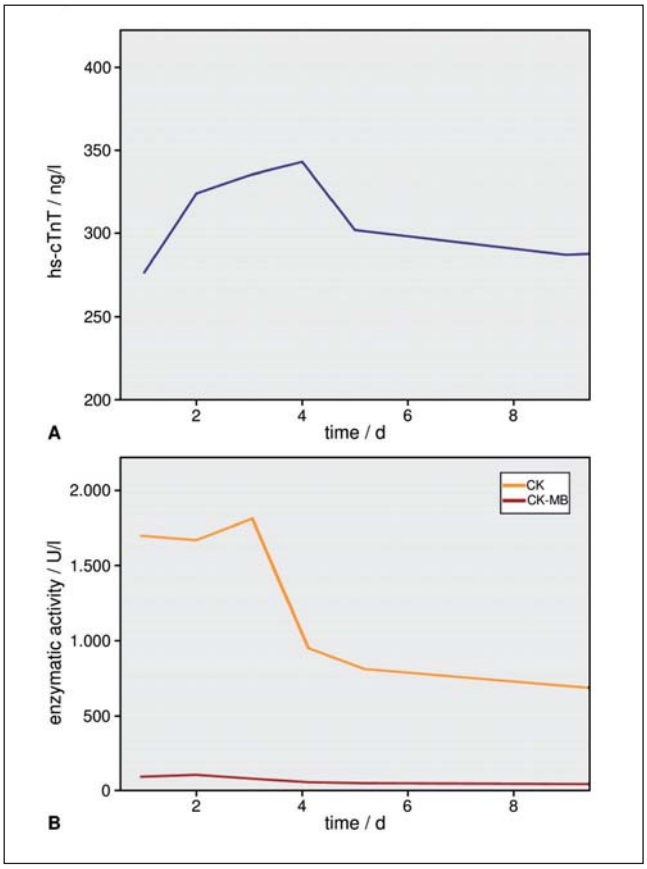

Fig. 1 – Laboratory history of hs-cTnT (A), CK and CK-MB (B).

In the present case, the elevated hs-cTnT levels could not be correlated with any signs of myocardial or coronary pathology. However, an occult increase of the normally cardiac-specific cTnT and CK-MB is known in patients with neuromuscular diseases or idiopathic inflammatory myopathies [4,5]. Skeletal muscle biopsies from patients with neuromuscular diseases proofed the expression multiple (cTnT) isoforms [6,7]. On the contrary, the hs-cTnI is exclusively expressed in cardiac myocytes. Therefore, it is eligible for exclusion of cardiomyopathy in diseases associated with chronic inflammation of skeletal muscle tissue as shown in the present case [6,8,9]. Furthermore, the hs-cTnT blood concentration was reduced after anti-inflammatory Rituximab treatment underlining the hypothesis of occult release of cTnT in diseased skeletal muscle tissue.

The present case clearly demonstrates that the additional measuring of hs-cTnI should be considered in laboratory diagnostic for myocardial ischemia in patients with underlying skeletal myopathy to avoid any unnecessary examinations. To the best of our knowledge, this is the first reported case of an occult hs-cTnT elevation caused by paraneoplastic systemic sclerosis. Moreover, elevated hs-cTnT levels might be a usable marker for the severity of skeletal muscle tissue inflammation and helpful in decision making for individual treatment strategies.

Conflict of interest
None declared.

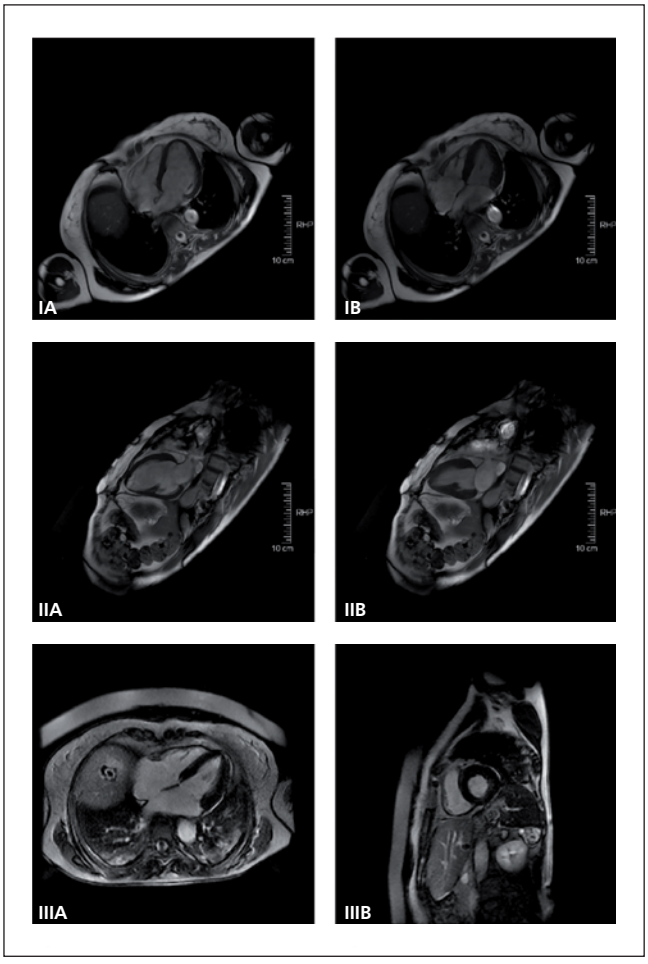

Fig. 2 – FIESTA MRI sequences in four chamber (I) and two chamber view (II). The left panel (A) points to the diastolic and the right panel (B) to the systolic phase. The left ventricle shows a regular diameter and a normal ejection fraction. (III) MRI in apical four chamber view (A) and parasternal short axis (B) view with LGE sequence. No abnormal myocardial or pericardial LGE was detected excluding a relevant perimyocarditis or myocarditis. FIESTA – fast imaging employing steady-state acquisition; LGE – late gadolinium enhancement

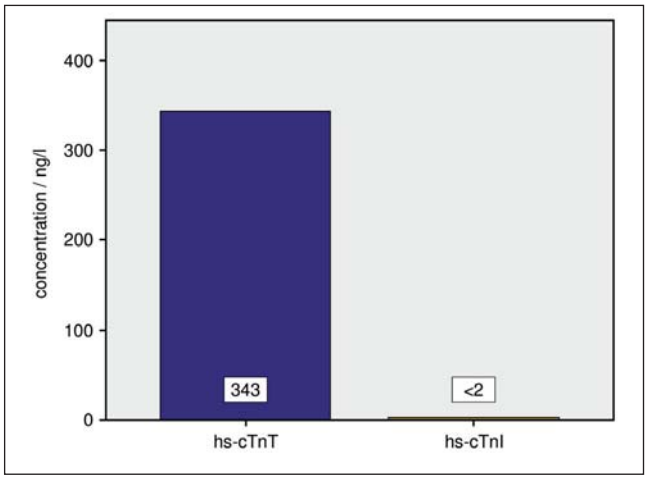

Fig. 3 – Increased hs-cTnT (blue) concentration, whereas hs-cTnI (yellow) was not detectable.

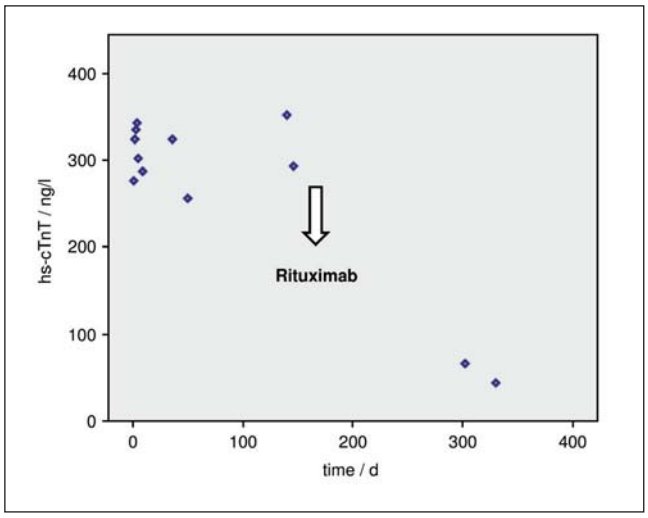

Fig- 4 – One-year history of hs-cTnT: Decreased hs-cTnT concentration after Rituximab treatment.

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Ethical statement
Authors state that the research was conducted according to ethical standards.

Informed consent
Informed consent for anonymized publishing was given.

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