


Transthyretin amyloidosis with macro-creatine kinase

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DESCRIPTION

A man in his 70s with no other significant medical history presented with a 2 month history of dyspnoea on exertion. He was the eighth of ten siblings and had a remarkable family history for heart diseases: his mother, oldest brother and seventh oldest sister had died of heart failure. Physical examination revealed a mild peripheral oedema without any murmur or crackles. He denied any muscle pain. An ECG revealed a sinus rhythm with low voltage complexes and a pseudoinfarct pattern. Chest radiography showed cardiomegaly without pleural effusion. His echocardiogram indicated a left ventricular ejection fraction of 42%, thickening of the ventricular walls and an impaired diastolic function. Laboratory findings showed an elevation of creatine kinase (CK) of 823 U/L (normal, 59–248 U/L), CK-MB of 9.5 ng/mL (normal, <5.2 ng/mL), troponin I of 55.4 pg/mL (normal, <34.2 pg/mL) and N-terminal pro-brain natriuretic peptide (NT-proBNP) of 1162 pg/mL (normal, <125 pg/mL). Of note, his CK level 1 year prior to this visit had also been elevated (402 U/L). Further investigation of electrophoresis of CK isoenzyme revealed a macro-CK type 1 (figure 1). Coronary angiography showed no significant stenoses in the coronary vessels. Blood and urinary immunoelectrophoresis analyses and a serum nephelometric assay of the light chain were all negative. However, ^{99m}Tc-pyrophosphate (PYP) scintigraphy demonstrated diffuse intense ^{99m}Tc-PYP uptake in the heart. A myocardial biopsy specimen demonstrated amyloid deposits with Congo red staining (figure 2A). In addition, an immunoenzymatic staining was positive with a horseradish peroxidase labelled antitranssthyretin antibody (figure 2B). Therefore, we confirmed

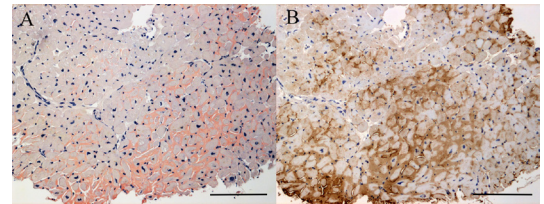


Figure 2 (A) A myocardial biopsy specimen showing amyloid deposits with Congo red staining. (B) An immunohistochemistry specimen showing positive staining with a horseradish peroxidase labelled antitranssthyretin antibody. Scale bar = 100 µm.

Learning points

- ▶ Macro-creatine kinase (CK) type 1 is an enzyme-antibody complex formed by one of the CK isoenzymes and immunoglobulins.
- ▶ This is the first reported case of a coexisting transthyretin amyloidosis and macro-CK type 1.

a diagnosis of amyloid transthyretin (ATTR) amyloidosis.

Previous studies have reported a staging system for ATTR amyloidosis using an NT-proBNP, high sensitivity troponin or estimated glomerular filtration rate.¹ Although the association with cardiac amyloidosis and troponin has been established, the relationship between ATTR amyloidosis and CK remains unknown.^{2,3} The typical CK isoenzymes include CK-BB, CK-MB and CK-MM, whereas macro-CK type 1 is an atypical CK enzyme with a higher molecular mass. Macro-CK type 1 is an enzyme-antibody complex formed by one of the CK isoenzymes and immunoglobulins. As its molecular weight is slightly different from these isoenzymes, macro-CK type 1 migrates between CK-MM and CK-MB on electrophoresis of CK isoenzymes.⁴ Although there is no well-established association of a particular disease with macro-CK type 1, it has been reportedly associated with a variety of diseases such as hypothyroidism, malignancies, autoimmune diseases, myositis, irritable bowel syndrome and bronchopulmonary chronic illness.⁵

To the best of our knowledge, this is the first reported case of a coexisting ATTR amyloidosis and macro-CK type 1. The deposition of transthyretin might potentially explain the formation of an immune complex, but further investigations will be needed to see whether macro-CK type 1 is associated with ATTR amyloidosis.

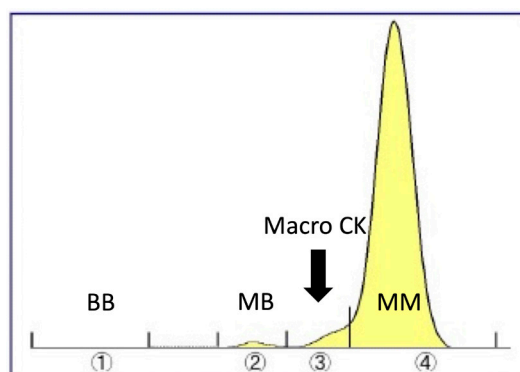


Figure 1 Electrophoresis of creatine kinase (CK) isoenzyme revealing a macro-CK type 1 (arrow).



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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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