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Popeye's sign, heart disease, and amyloidosis

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A 69-year-old man presented to our cardiology clinic troubled by breathlessness on exertion. He had a history of hypertension, atrial fibrillation, and bilateral carpal tunnel syndrome. Physical examination showed jugular venous distension, bilateral ankle oedema, and a bunching of the right biceps when he flexed his arm—so called Popeye's sign—indicating rupture of the proximal biceps tendon (figure and video); a rupture was confirmed by an ultrasound scan. Serum N-terminal-pro-B-type natriuretic peptide was 7088 pg/mL (normal range for patients aged 0–74 years is less than 125 pg/mL). A 12-lead electrocardiogram showed low voltage in the limb leads, as well as a pseudo-infarct pattern in the precordial ones (appendix). A transthoracic echocardiogram showed left ventricular hypertrophy with a maximum wall thickness of 20 mm and a left ventricular ejection fraction (LVEF) of 40%. Cardiac MRI showed signs of myocardial infiltration. ^{99m}Technetium-3,3-diphosphono-1,2-propanodicarboxylic acid (^{99m}Tc-DPD) scintigraphy showed grade 3 myocardial uptake (figure). Serum and urine immunoelectrophoresis and free light chain assays ruled out a monoclonal component. Genetic sequencing analysis of the transthyretin gene found no mutations. Tying all the findings together, a diagnosis of heart failure secondary to wild-type transthyretin amyloid (ATTRwt) cardiomyopathy was made. The patient was treated with a combination of diuretics—namely, furosemide 80 mg twice a day, hydrochlorothiazide 12·5 mg once a day, and spironolactone 100 mg once a day—but he did not respond well. He remained symptomatic with advanced functional impairment and persistent signs of systemic venous congestion.

ATTRwt, previously known as senile systemic amyloidosis, is a disease that typically affects the heart and tendons of elderly patients. A history of bilateral carpal tunnel syndrome or, less frequently, spontaneous tendon rupture in a patient with heart failure and preserved or mildly depressed LVEF should raise clinical suspicion of the condition. A definitive diagnosis of ATTRwt cardiomyopathy can be confirmed non-invasively with a positive finding on ^{99m}Tc-DPD scintigraphy, together with the absence of a monoclonal component in serum and urine samples, and a normal genetic sequencing analysis of the transthyretin gene. Current therapy for patients with ATTRwt cardiomyopathy is limited, with diuretics for relief of cardiac congestion being the mainstay of treatment. However, a recent randomised, placebo-controlled trial, published in September 2018, showed a significant reduction in the risk of death and hospitalisation from cardiovascular causes in patients with ATTRwt cardiomyopathy treated with

tafamidis, a transthyretin stabilising agent. Tafamidis is expected to be available for clinical use in the near future.

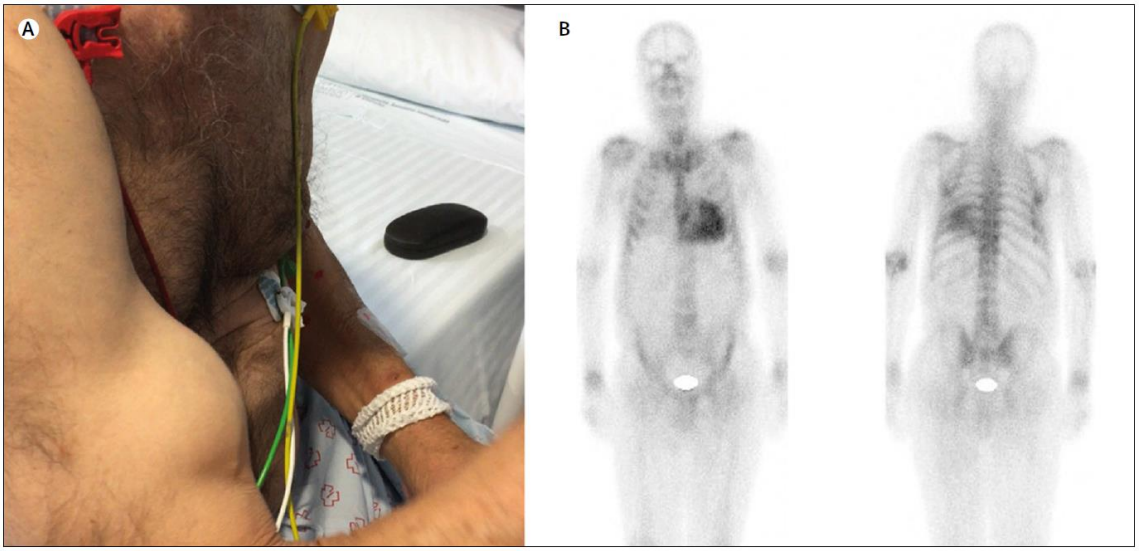

Figure: **Popeye's sign in wild-type transthyretin amyloidosis**
(A) Popeye´s sign indicating rupture of the proximal biceps tendon. (B) ^{99m}Technetium-3,3-diphosphono-1,2-propanodicarboxylic acid scintigraphy images from both front and back show grade 3 myocardial uptake.

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