



# Stumbling across transthyretin amyloid cardiomyopathy during diagnostic work-up for stomach cancer

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A 91-year-old socially active and independently ambulatory man was diagnosed with stomach cancer, pathologically confirmed as adenocarcinoma on biopsy. During cancer staging work up, <sup>99m</sup>Tc-hydroxymethylene diphosphonate bone scintigraphy showed prominent radio-tracer uptake in the heart (Fig. 1A). Electrocardiogram showed sinus bradycardia and low voltage in frontal lead (Fig. 1B). Echocardiography showed hypertrophy in the left ventricle (LV) with highly reflective myocardium and impaired relaxation type of diastolic dysfunction (average E/e' ratio, 15.3) with enlarged left atrium (Supplementary Videos 1 and 2). Speckle tracking imaging showed an 'apical sparing' pattern on the bull's eye plot of global longitudinal strain (Fig. 1C). Cardiac magnetic resonance imaging revealed septal LV hypertrophy, late gadolinium enhancement base-apex gradient, pericardial effusion, and pleural effusion (Fig. 1D). <sup>99m</sup>Tc-3,3-diphosphono-1,2-propanodicarboxylic acid scan (Fig. 1E) and single-photon emission computed tomography (Fig. 1F) showed intense myocardial uptake suggestive of transthyretin (TTR) amyloid cardiomyopathy (ATTR-CM). Endomyocardial biopsy showed pericellular interstitial deposition of amorphous and pale pink material (Fig. 1G), positive birefringence on Congo red staining (Fig. 1H) and positive TTR immunohistochemical

staining (Fig. 1I). AL amyloid cardiomyopathy was ruled out based on serum free light chain quantification and serum, urine immunofixation electrophoresis. Genetic testing for TTR showed no mutation. On multidisciplinary discussion with the patient and family members, we decided to perform stomach cancer surgery because his functional capacity has been well preserved. After curative gastrectomy (Supplementary Fig. 1), the patient has been doing well for more than a year with tafamidis treatment for ATTR-CM. As ATTR-CM is more and more accidentally found in bone scintigraphy during cancer work up, further investigation for optimal treatment strategy in these patients are required.

## Conflict of interest

No potential conflict of interest relevant to this article was reported.

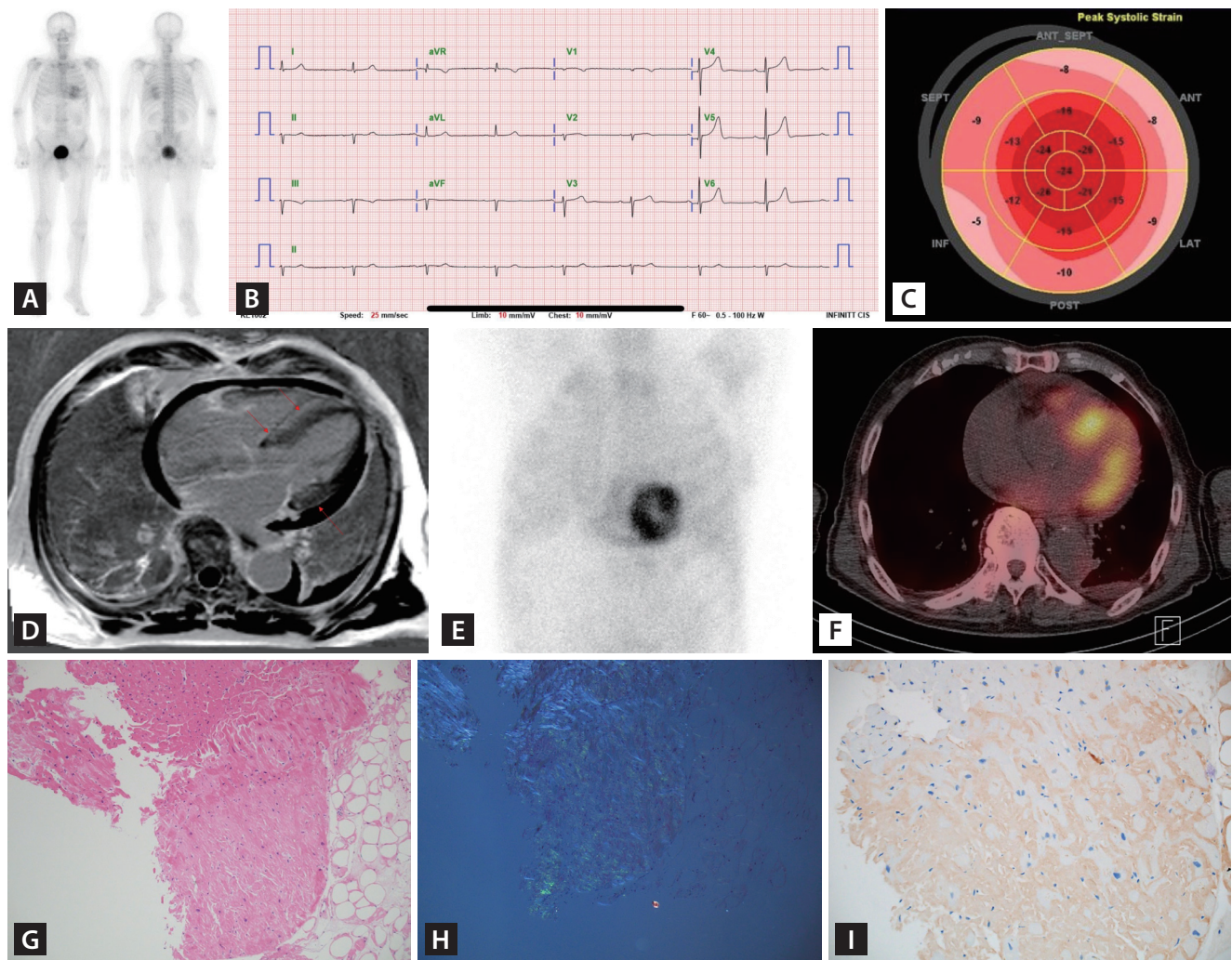
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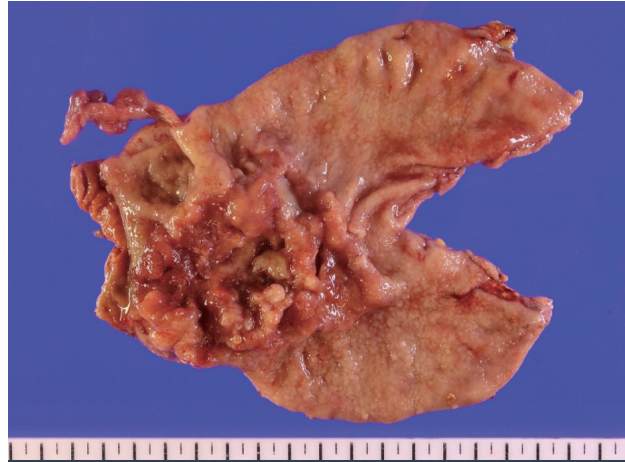
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**Figure 1.** (A)  $^{99m}\text{Tc}$ -hydroxymethylene diphosphonate bone scintigraphy showed prominent radiotracer uptake in the heart without any evidence of bone metastasis. (B) Electrocardiogram showed sinus bradycardia and low voltage in frontal lead. (C) Speckle tracking imaging showed an 'apical sparing' or a 'cherry-on-top' pattern on the bull's eye plot of global longitudinal strain. (D) Cardiac magnetic resonance imaging revealed late gadolinium enhancement (red arrows) with base-apex gradient, pericardial effusion, and pleural effusion. (E)  $^{99m}\text{Tc}$ -3,3-diphosphono-1,2-propanodicarboxylic acid oblique view and (F) single-photon emission computed tomography showed intense myocardial uptake suggestive of transthyretin amyloid cardiomyopathy. (G) Endomyocardial biopsy showed pericellular and nodular interstitial deposition of amorphous and pale pink material (H&E,  $\times 100$ ), (H) positive birefringence on Congo red staining ( $\times 100$ ) and (I) positive transthyretin immunohistochemical staining ( $\times 200$ ).

**Supplementary Video 1.** The parasternal long axis view of echocardiogram.

**Supplementary Video 2.** The apical four chamber view of echocardiogram.



**Supplementary Figure 1.** Surgical specimen of curative Billroth II subtotal gastrectomy.