

Concomitant Cardiac Carcinoid and Amyloid in a Patient with a Caecal Neuro-Endocrine Tumour with Metastases

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Keywords

Dyspnoea, Tumours, Diarrhoea, Carcinoid syndrome.

Case

A seventy-two year old man presented with increasing dyspnoea, on a background of known coronary artery disease and four stents to his right coronary artery six months previously. His main complaint on admission was of bilateral leg swelling and abdominal discomfort and bloating. He also had some diarrhoea with some blood and increasing shortness of breath.

On examination his blood pressure was 90/60 and he had giant v-waves in his jugular venous system consistent with marked tricuspid valve regurgitation. He had bibasal pleural effusions, right greater than left and a palpable liver edge with some ascites. He had no pedal oedema. His ECG was of low voltage but was otherwise normal. He was anaemic.

Echocardiogram showed severe tricuspid regurgitation with failure of leaflet coaptation due to shortening of the chordae tendineae. He also had marked concentric left ventricular hypertrophy, 15mm, with speckling suggestive of cardiac amyloid.

CT scan showed a tumour in the caecum, which was causing sub-acute obstruction, a large (5cm) adrenal deposit, and substantial liver metastases. Biopsy confirmed the tumour to be neuroendocrine in nature with appearance consistent with carcinoid tumor. The same tissue sample was also found to have kappa light chain amyloid deposits.

Twenty-four hour urine for 5HIAA was elevated at 113 μmol . Urinalysis for Bence-Jones proteins and serum electrophoresis revealed a monoclonal IgG kappa band with a serum paraprotein

measurement of 7.9G/L. Incidentally, his TSH came back at 75mIU/L, T4 2.0pmol/L and he was commenced on thyroxine. His iron levels also came back low at 4.0umol/L.

Palliative right hemicolectomy was undertaken. Recovery from this was extremely slow. His albumin decreased to 14g/L likely due to a combination of liver dysfunction due to right heart failure and metastatic replacement, enteropathy, diarrhoea and poor intake. He developed anasarca. He continued to deteriorate and subsequently died several weeks later without post mortem examination.

Discussion

Although cardiac involvement in either carcinoid syndrome or amyloidosis is well-recognised [1-12], the association of pathological findings consistent with both serotonergic syndrome and cardiac amyloidosis have only been reported once previously [13]. At that time, only M-mode ultrasound was available. Echocardiogram in this case showed severe tricuspid regurgitation with failure of leaflet coaptation due to shortening of the chordae tendineae, which is almost pathognomonic of carcinoid syndrome. He also had the marked concentric left ventricular hypertrophy with speckling that is typical of cardiac amyloid deposition.

Biochemistry revealed only a modest rise in serotonin of 113 ng/mLs, which is not particularly high for carcinoid syndrome resulting in the typical clinical and echocardiographic features of cardiac serotonergic syndrome (more often seen to be in the thousands); this is likely due to respiratory monoamine oxidase activity reducing measured venous levels [14]. Though thyroid carcinoma has been associated with carcinoid and amyloid syndromes, as well as with multiple endocrine neoplasia [15-17], he had no clinical findings to suggest carcinoma and thyroid biopsy was not performed.

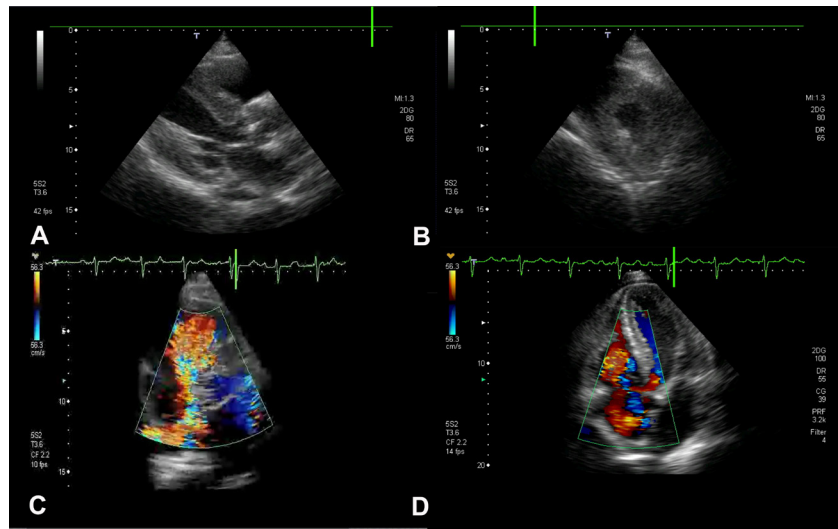


Figure 1: Echocardiographic views demonstrating findings of both amyloid deposition and serotonin syndrome. (A) Parasternal long axis view in diastole showing significant concentric left ventricular hypertrophy. (B) Parasternal short axis view in diastole showing significant concentric left ventricular hypertrophy. (C) Apical four-chamber view in systole showing significant tricuspid regurgitation. (D) Parasternal short axis view in systole showing significant tricuspid regurgitation.

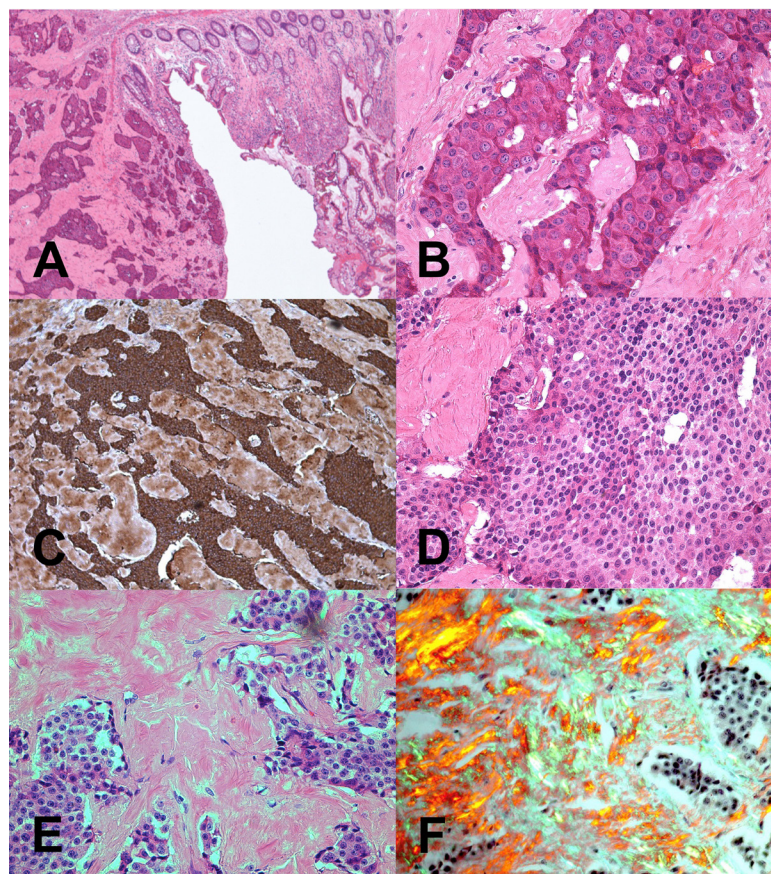


Figure 2: (A) Low power view of colonic mucosa (right) and one of two patterns of invasive carcinoid tumour islands (left). (B) High power view of one of two patterns of tumour showing broad cords of tumour cells separated by connective tissue. Prominent nuclei with small condensations of nuclear chromatin are present and the nucleus is surrounded by eosinophilic cytoplasm. No mitotic activity is seen and no amyloid was detected in this section of the tumour. (C) This shows positive Chromagranin A staining in the section of tumour shown in A and B. The dark brown stain represents the presence of secretory granules in neuroendocrine cells. (D) The second tumour pattern is illustrated here i.e. closely packed tumour cells of uniform size with a dense nucleus and limited cytoplasm. This pattern is also seen in carcinoid tumours. (E) Using light microscopy, the second tumour pattern stains positively with Congo red stain, showing deposition of pink material i.e. amyloid. (F) Under polarized light, Congo red stain shows light green birefringence, characteristic of amyloid. No mitotic activity is identified.

The colonic biopsy identified a chromogranin positive neuroendocrine tumor with closely packed tumor cells of uniform size constant with a carcinoid tumor. There was localised amyloid deposition in the same tumor, which was found to be composed of kappa light chain. Colorectal tissue is a common site of deposition in systemic amyloidosis [18] and while amyloidosis is a recognised (but unusual) feature of neuro-endocrine tumours [19,20], it is more commonly due to increased production of amyloid precursor protein or islet amyloid polypeptide [21,22].

Unfortunately, by the time this man presented he already had widely disseminated disease, as is usually the case with carcinoid syndrome, and this information was of little assistance in his management. Had a diagnosis been made earlier it is possible that tumour removal and plasmapheresis or somatostatin analog therapy [23-25] might have helped to retard the deposition of cardiac amyloid and tricuspid regurgitation but it is unlikely that cardiac surgery would have made any difference to his outcome [26,27]. Bone marrow biopsy was not performed.

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