

SEVERE CARCINOID CARDIAC DISEASE IN A YOUNG PATIENT WITH NEUROENDOCRINE TUMOR OF UNKNOWN ORIGIN

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INTRODUCTION AND AIM

Progress in the treatment (both surgical and medical) of patients with neuroendocrine tumors (NET) led in the last decade to the improvement of symptoms but also of the survival of these patients. Carcinoid cardiac disease is a rare cause of intrinsic right heart valve disease with significant impact on morbidity and mortality. It occurs in up to 50% of patients with carcinoid syndrome and in 10-20% of them it is the first symptom of the disease.

The aim of this paper is to present the case of a young male patient with NET of unknown origin and severe carcinoid heart disease.

PATIENT

We present the case of a young male patient (38yrs old at diagnosis) complaining of abdominal pain in the last 5 yrs before diagnosis. Abdominal ultrasound (US) revealed, at the beginning of symptoms, small liver lesions interpreted as being haemangiomas (2010). After 4 years, in the summer of 2014, the patient noticed flushing of the face that progressively worsened in frequency (up to 15 episodes/day) accompanied, after 6 months, by diarrhoea (4-5 times/day) and night sweats, distension of the abdomen, bilateral ankle swelling and progressive limitation in effort.

In July 2015 due to abdominal pain he performed an US that identified multiple tumors in both lobes of the liver. CT scan of the abdomen revealed liver metastases spread to both lobes of the liver, the largest in the right lobe - 76/80/52mm, and in the left liver lobe - 17mm.

Biochemical screening for NET was positive: 5-HIAA > 60mg/24h (N: 2-9), serotonin (Ser) 1212 microg/L (N: 80-400), NSE 26,7 ng/mL (N: 0 - 12), Chromogranin A (Cg A) 1130 microg/L (N: 27-94). Gastrin, VIP, Glucagon, Calcitonin, AFP, CEA were all normal

RESULTS

Cardiac findings

In the summer of 2015 due to the discovery of important ascites, and murmurs of tricuspid and pulmonary regurgitation echocardiography was performed and revealed important tricuspid (Fig 1B) and pulmonary regurgitations (Fig 1C) and severe right heart failure.

Very high level of pro-BNP (8Xupper normal limit) were also detected.

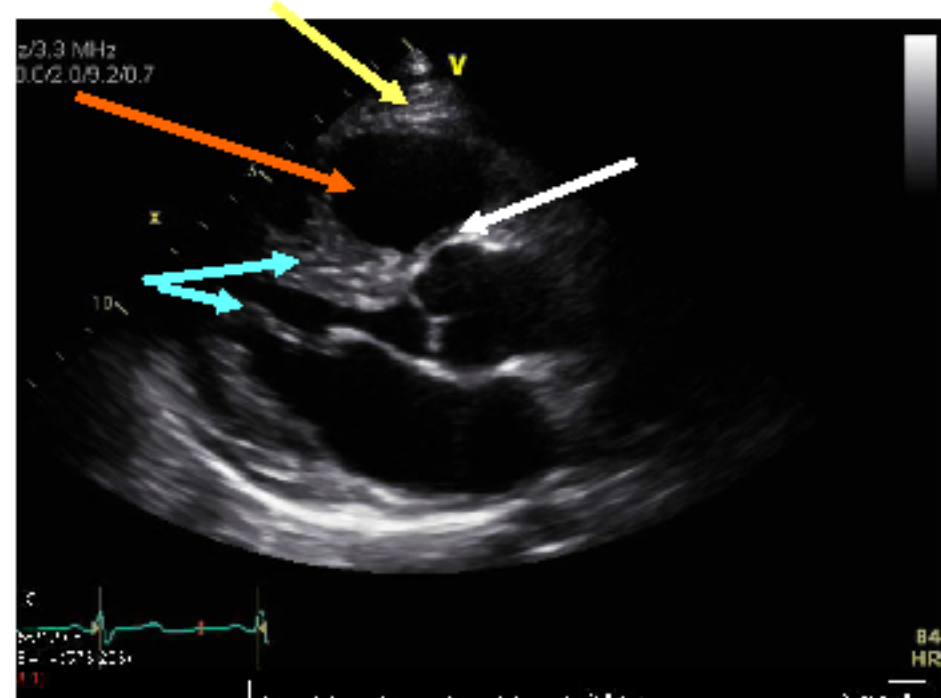


Fig 1A Echocardiography revealing severe dilatation of the right ventricle, thickening of mitral valve with less severe insufficiency of the mitral valve (cyan arrow)

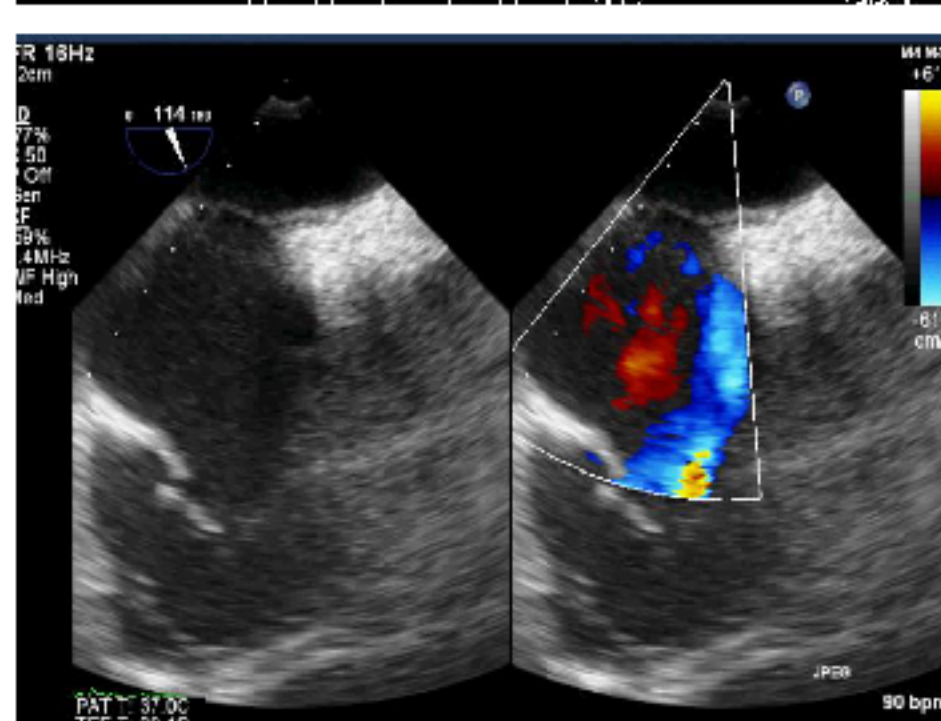


Fig 1B Transesophageal cardiac US : tricuspid valve regurgitation spurt of severe grade

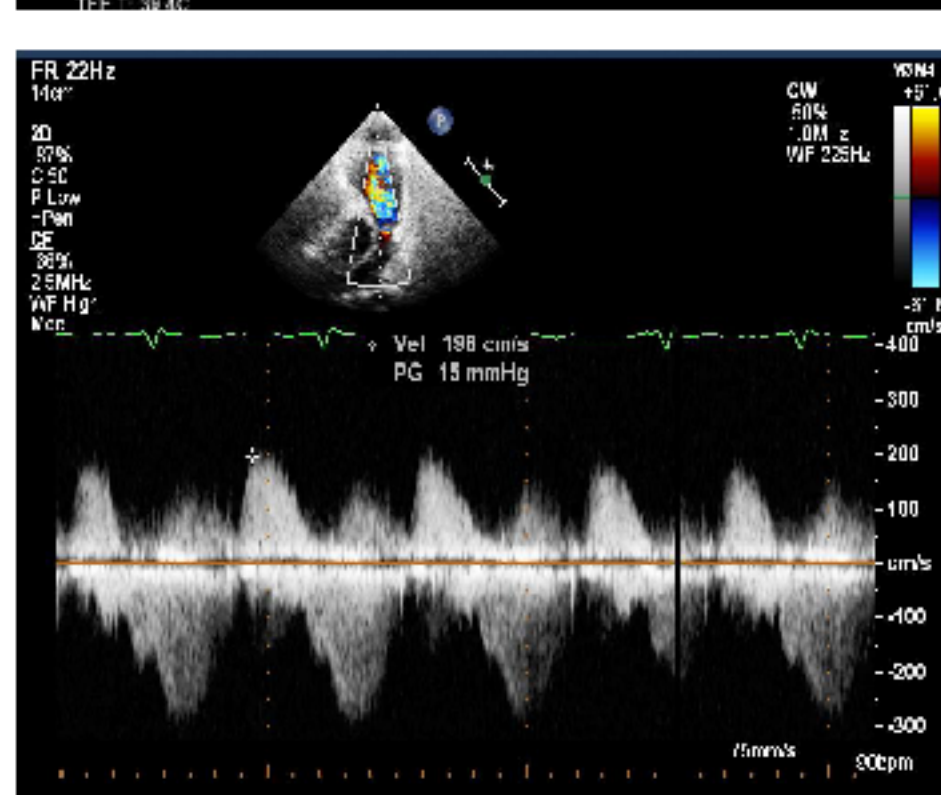


Fig 1C Pulmonary valve regurgitation

Cardiotonic medication (digoxine, spironolactone) was started in parallel to somatostatin analogues (SSAs) with improvement in the capacity of effort and temporary reduction of ascites.

November 2015 after intense treatment with SSAs valve prosthesis with bioprosthetic valves for pulmonary and tricuspid valves was successfully performed with complete remission of cardiac symptoms.

CONCLUSIONS

Serotonin staining on the immunohistochemistry is suggestive for secondary determination from a small bowel NET.

A baseline echocardiogram should be performed in all patients diagnosed with NET and follow-up is mandatory, especially in patients with clinical features of right heart failure

In the summer of 2015 imaging studies were completed with abdominal MRI (Fig 2A) and Octreoscan (111-In-Octreotide Fig 2B) that revealed multiple somatostatin receptor-positive liver metastases. No primary tumour could be found.

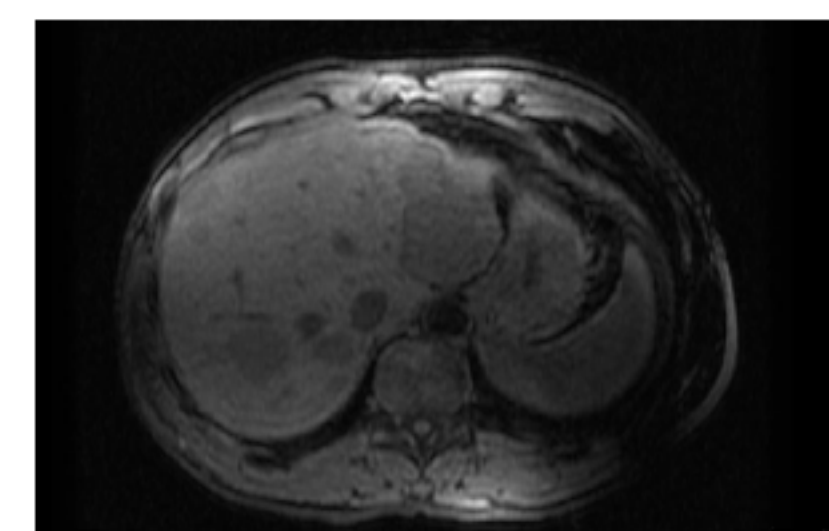


Fig 2A – Abdominal MRI

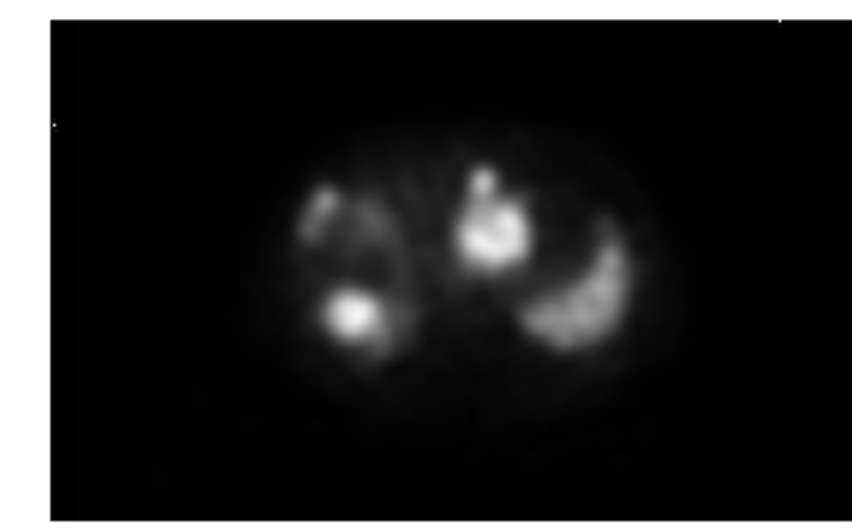


Fig. 2B - Octreoscan

Biopsy of liver metastasis diagnosed a Grade 2 NET (Ki67 4%): Microscopically - infiltrating epithelial tumour. Immunohistochemistry: Positive staining for CK 18, Syn, Cg A, Ser and focally for CD56. Negative for CK 7 and CK 20.

In August 2015 Somatostatin analogue treatment was started (Sandostatin LAR 30mg every 3 weeks) with significant improvement in symptoms (but still presence of flushing) but without improvement in NET markers .

Slight progression of liver metastasis was noticed on CT in April 2016 at the last follow-up when NET markers were still high: 5-HIAA 43.3mg/24h (N: 1-10), Ser 1518 microg/L (N: 70-270), NSE 27.5 ng/mL (N: 0 - 12), CgA 697.7microg/L (N: 20-125)

DISCUSSIONS

Extensive liver disease due to NET metastases is thought to play a permissive role for the development of cardiac carcinoid disease in NET patients by allowing large quantities of tumor products - mainly serotonin - to reach the right side of the patient's heart. Even so it seems that apparently reduction of serotonin levels in NET patients treated with SSAs did not influence the development of valve disease.

Surgical treatment for cardiac valve disease is the only definitive treatment for cardiac carcinoid valve disease thus significantly improving the survival of the patients. Due to the high perioperative mortality in these procedures it is important that these surgeries are performed in specialized centers with careful pretreatment of the subject .