An unusual cause of tricuspid and pulmonary valve stenosis and regurgitation

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Abstract

Carcinoid heard disease is a frequent sequela to metastatic carcinoid tumour. This rare condition has a typical pathological presentation with characteristic macroscopic and microscopic findings. We present here a case detailing the classical findings of carcinoid heart disease in a tricuspid valve.

Keywords carcinoid heart disease; carcinoid syndrome; cardiac valve pathology; endocardial plaque

Case report

A 58-year-old man with a history of a gastrointestinal neuroendocrine tumour and hepatic metastasis presented to his clinical team with increasing abdominal pain and peripheral oedema. A variety of investigations were performed including an echocardiogram. On the echocardiogram, there was tricuspid and pulmonary stenosis and regurgitation and the clinical suspicion of carcinoid heart disease was raised. The patient proceeded to have a tricuspid and pulmonary valve replacement and the excised native valvular tissue was sent for histopathological analysis.

Macroscopically the valve tissue was fragmented and disrupted and measured 50 × 30 × 15 mm on aggregate. The tissue was grey and firm. No vegetations were seen.

Microscopically the spongiosa and fibrosa of the tricuspid valve are thickened by a plaque consisting of smooth muscle cells, collagen, and extracellular matrix material. In addition, there is loss of elastic staining. Figures 1 and 2 show the histology of a normal tricuspid valve. Figures 3 to 6 show the pathological changes in the tricuspid valve in carcinoid heart disease.

Discussion

Carcinoid heart disease (CHD) is most often seen in patients with carcinoid tumours/neuroendocrine tumours that have metastasized to the liver, though rarely it can occur with localized disease.[1] These tumours are rare affecting 1.2–2.1 per 100,000 people and although CHD maybe an uncommon presentation of carcinoid syndrome it does occur in up to two thirds of patients

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Figure 1 A low power (x20 H&E) view of a normal tricuspid valve. There are three or four layers, the ventricularis, fibrosa, spongiosa and atrialis. The atrialis is situated on the atrial aspect and the ventricularis, the ventricular aspect. The ventricularis layer can be absent.[6] The fibrosa is the thickest layer and the spongiosa contains elastic fibres set in an extracellular matrix.

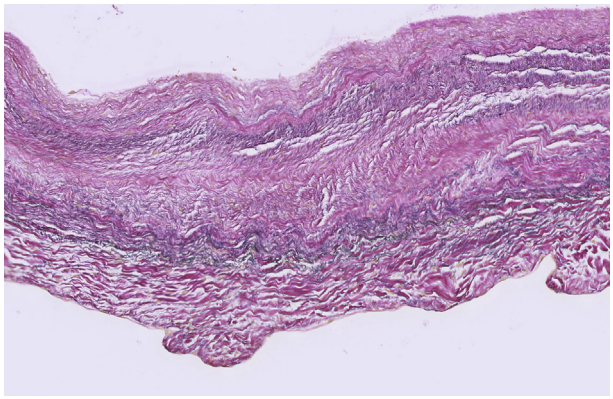

Figure 2 Normal tricuspid valve (x50 Elastic Van Gieson stain). Note the elastic fibres of the spongiosa stained dark blue with this elastic stain.

Figure 3 A low power view of the tricuspid valve in carcinoid heart disease (H&E ×20). Note that the spongiosa and fibrosa are thickened by a plaque consisting of smooth muscle cells, collagen, and extracellular matrix material.

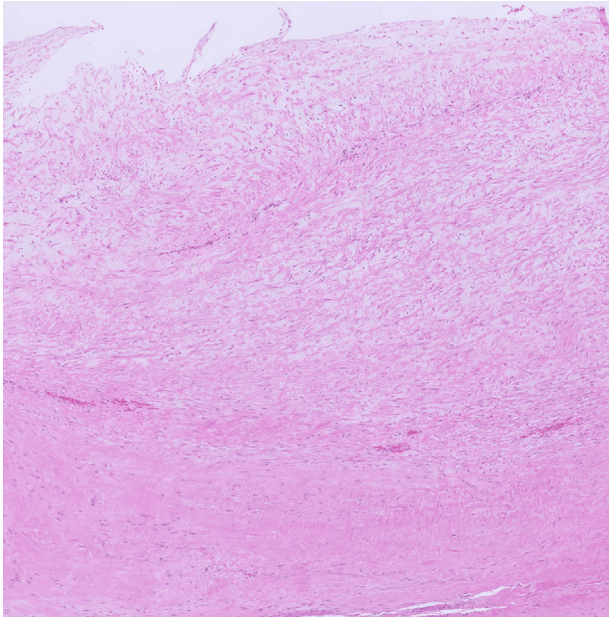

Figure 4 A higher power view of the plaque on the tricuspid valve in carcinoid heart disease (H&E ×50). There is an increase in collagen and extracellular matrix as well as smooth muscle cells.

and is a significant cause of morbidity and mortality.[1,2] Carcinoid heart lesions typically involve the right side of the heart and arise as consequence of vasoactive factors such as serotonin, prostaglandins, histamine, and tachykinins being secreted into the hepatic vein by the liver metastases. It is thought that serotonin stimulates fibroblast growth, leading to the excessive collagen deposition. Left sided heart disease affects less than 10% of patients with CHD as the pulmonary circulation acts as a filter using pulmonary monoamine oxidase to degrade the high circulating levels of serotonin.[1,3] The high serotonin levels in the serum and the presence of its metabolite 5-hydroxyindole acetic acid (5-

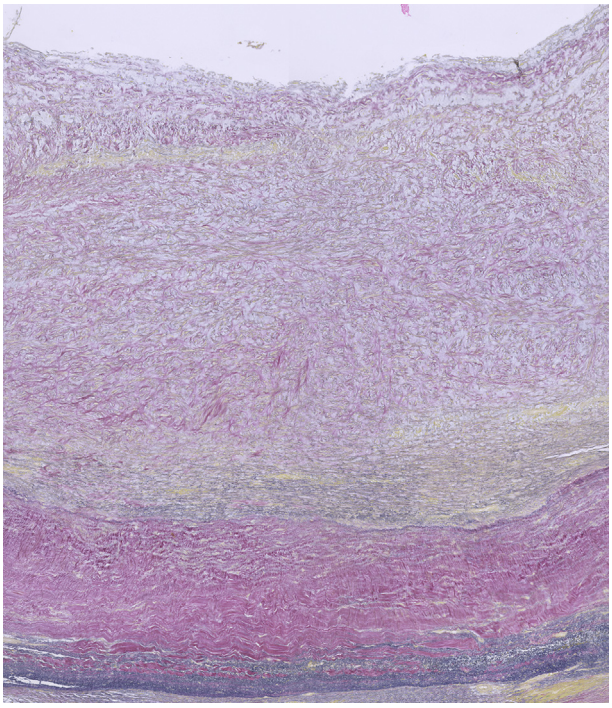

Figure 5 A medium power view of the plaque on the tricuspid valve (x50 Elastic Van Gieson stain). The plaque is situated at the top of the image. Note there are no elastic fibres seen in this area compared to those seen in Figure 2.

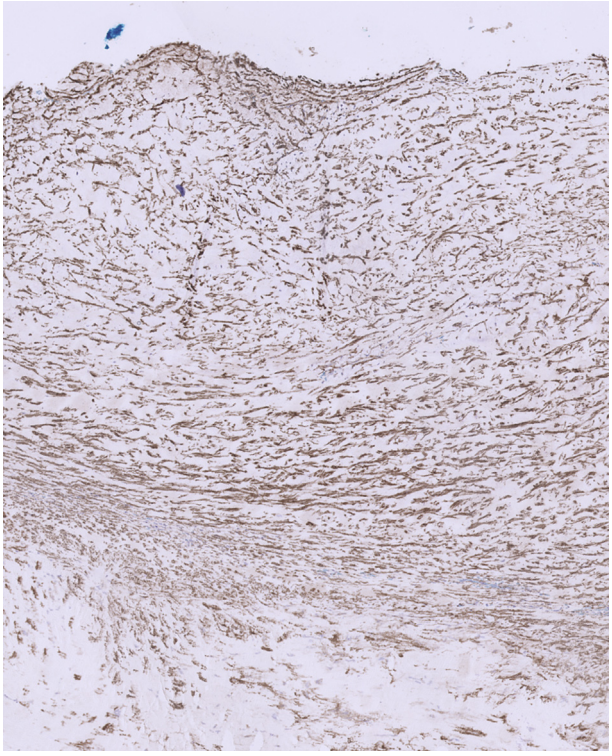

Figure 6 A medium power view of the plaque seen in carcinoid heart disease (x50 Smooth Muscle Actin stain). Note the increase in smooth muscle cells stained with antibodies to SMA in the plaque.

HIAA) in the urine can be used as biomarkers of disease. All patients with midgut neuroendocrine tumours should be screened for CHD using appropriate investigations such as measuring N-terminal pro-brain natriuretic peptide (NT-proBNP) and echocardiography. NT-proBNP is released by the atria and ventricles in response to the volume and pressure overload.[4]

Macroscopically, the disease is characterized by gross fibrous endocardial thickening forming plaque like lesions on the atrioventricular valves often with mild fusion of the commissures. In addition, there can be thickening and focal fusion of chordae tendineae. This usually leads to retraction and fixation of the tricuspid and pulmonary valve leaflets.[2,5]

Microscopically, the plaques consist of extracellular matrix rich in proteoglycans, collagen, and smooth muscle cells. There is typically a loss of elastic fibres. The increase in collagen within the valve cusps reduces the ability of the cusps to move. Stenosis of the tricuspid valve causes back pressure on the right atrium leading to dilatation and hypertrophy and consequently venous congestion with resultant peripheral oedema as seen in this patient.

Conclusion

The diagnosis of CHD will usually have been made prior to receiving valvular tissue in the pathology department. However, if this is not the case, the presence of these specific macroscopic and microscopic findings should warrant urgent investigation for an underlying neuroendocrine tumour. ◆

Practice points

- CHD is common in those with metastatic carcinoid tumour and carries significant morbidity and mortality.
- All patients with midgut neuroendocrine tumours should be screened for CHD.
- This is a predominantly right sided cardiac disease with fibrous plaques forming on the tricuspid and pulmonary valves that can lead to valve stenosis and regurgitation.
- Microscopically increased collagen, extracellular matrix and smooth muscle cells can be seen within the plaques along with a loss of elastic fibres.

Multiple choice questions

Question 1

Which of the following is false?

A) The liver degrades high circulating serotonin levels therefore sparing the left side of the heart
B) Fibrous plaques form on the endocardial surfaces of the atrioventricular valves
C) All patients with midgut neuroendocrine tumours should be screened for CHD
D) CHD typically leads to features of right sided heart failure

Correct answer: A) The lung degrades high circulating serotonin levels therefore sparing the left side of the heart

Question 2

Which of the following is not a biomarker of CHD?

A) Serum serotonin
B) Serum dopamine
C) Urinary 5-hydroxyindole acetic acid (5-HIAA)
D) Serum N-terminal pro-brain natriuretic peptide (NT-proBNP)

Correct answer: B)

Question 3

Which of the following is not a histological features of carcinoid heart disease?

A) Increased collagen
B) Increased smooth muscle cells
C) Increased extracellular matrix
D) Increased elastic fibres

Correct answer: D)

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