CASE REPORT

Epithelial cyst of the cardiac papillary muscle: case report and review of the literature

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Background: Reports of endodermal heterotopia (previously known as inclusion cysts) in cardiac atria are rare and there is only a single previous case report of endodermal heterotopia in a cardiac papillary muscle.

Aim and methods: A cyst in a cardiac papillary muscle was identified during the autopsy of an 87-year-old man who had died from an unrelated myocardial infarction. The cyst was examined histologically and mucin staining and immunostaining were carried out.

Results: We report a unilocular cyst in a cardiac papillary muscle, which is lined by low cuboidal, pseudostratified and occasionally ciliated respiratory-type epithelium, surrounded by a layer of smooth muscle. The immunohistochemical features (MNFI16+, cytokeratin (CK)7+, CK8+, CK18+, CK19+, epithelial membrane antigen positive, scattered cells positive for neuroendocrine markers) suggest that this is an endodermal heterotopia. Immunostaining of positive thyroid transcription factor-1 provides evidence for bronchogenic differentiation.

Discussion: The differential diagnoses of cystic structures in cardiac papillary muscle and the origin and importance of endodermal heterotopias are discussed.

We report a unilocular cyst in a cardiac papillary muscle, with immunohistochemical features suggesting that it is an endodermal heterotopia. In particular, the epithelium immunostains for thyroid transcription factor (TTF)-1, providing evidence for bronchogenic differentiation. We discuss the differential diagnoses of cystic structures at this site, and the origin and importance of endodermal heterotopias. Intracardiac-endodermal heterotopias are rare, occurring most commonly in the atrio-ventricular node, where they can lead to disturbances in conduction and, sometimes, sudden death.¹ There are occasional case reports of endodermal heterotopia (inclusion cysts²) in the atria. However, we were able to find only a single case report (in the German literature)³ of endodermal heterotopia in a papillary muscle. Rare cystic structures discovered in the ventricles are generally blood-filled cysts and these become extremely rare beyond infancy.^{4–7}

CASE REPORT

Clinical history

An 87-year-old man was reported by his neighbours to have fallen at home. They were unable to gain access to his home, and police and paramedics arrived to find him cyanosed, but pain free. He then went into cardiac arrest and, despite cardiopulmonary resuscitation, was dead on arrival at hospital. This case is reported with the permission of HM Coroner and the deceased man's relatives.

Macroscopic findings

The cause of death was a recent posterolateral left ventricular myocardial infarction.

Other major autopsy findings included coronary artery and large vessel atheroma, thrombi in periprostatic veins, thromboemboli in peripheral branches of the right lower lobe pulmonary artery, oedematous lungs with bilateral pleural effusions, kyphosis and a reducible right inguinal hernia-containing small intestine, with no evidence of vascular compromise. An area of apparent cystic, myxoid degeneration in the papillary muscle of the posterior cusp of the mitral valve was sampled for histology. No further noticeable abnormalities and no tumours were found at any site.

Microscopic findings

The cystic area in the papillary muscle of the posterior cusp of the mitral valve was a 13-mm unilocular cyst lined by low cuboidal and pseudostratified, occasionally ciliated, respiratory-type epithelium, with scattered alcianophilic goblet cells, surrounded by a single, thin layer of mature smooth muscle, separating the cyst from the adjacent unremarkable myocardium (fig 1). Immunohistochemistry showed strong positive cytoplasmic staining for the cytokeratins MNFI16, 7, 8, 18 and 19, and epithelial membrane antigen. Anti-TTF-1 immunostained most of the epithelial cell nuclei.

Occasional cells immunostained for chromogranin A and synaptophysin, suggesting that scattered neuroendocrine cells were present. No immunostaining for carcinoembryonic antigen, CA125, cytokeratin 20 or the mesothelial marker, calretinin, was found.

DISCUSSION

Here we describe a macroscopically myxoid or cystic focus in a papillary muscle, which shows morphological and immunohistochemical features of a benign epithelial inclusion of probable endodermal origin.

Only one previous report of a cyst with endodermal derivation in a papillary muscle exists,³ although there are many reports of congenital endodermal heterotopia of the atrioventricular node¹ and atria.^{8–10} Cysts of the papillary muscle are usually blood-filled channels with an endothelial lining, and are rarely seen beyond infancy.^{5 6 11 12} Complications of such cysts include subaortic stenosis and ventricular outflow obstruction with large cysts^{7 6 11} and thromboembolic phenomena.¹² Although at a similar site, the small cyst in this case, which did not protrude from the papillary muscle, would probably not have had any important functional implications. The previously reported papillary muscle endodermal cyst was associated with endocarditis, although the authors suggest that this finding may have been coincidental.³

In adults, intramyocardial cysts are rare and may be lined by mesothelium or epithelium, the latter being known as endodermal heterotopia.³ Both types of cysts may be associated with syndromic and non-syndromic cardiac abnormalities.³

Abbreviation: TTF, thyroid transcription factor

Figure 1 The low-power haematoxylin and eosin (H & E)-stained section shows a unilocular cyst with a maximum diameter of 13 mm. Higher magnification shows the low cuboidal and pseudostratified benign epithelial lining and the surrounding single layer of smooth muscle abutting the normal myocardium. Alcian blue periodic acid Schiff diastase (ABPASD) staining shows mucin in goblet cells. Immunostaining for cytokeratins (CK) 7, 8, 18 and 19 is positive (immunoperoxidase technique) and there is scattered positivity for the neuroendocrine marker synaptophysin (SYN) and uniform nuclear positivity for thyroid transcription factor (TTF)-1. Original magnification: $\times 10$.

The immunohistochemical features of this cyst are similar to those in a series of atrioventricular node cysts described by Fine and Raju.¹³ A range of epithelial differentiation has been described in congenital endodermal heterotopia, including attenuated, cuboidal, ciliated, squamous and transitional epithelium, sometimes with goblet cells and neuroendocrine cells^{1-9,14} and, in one case, thyroid parenchyma.¹⁵

Endodermal remnants may be classified further in many ways. Classification by anatomical site may allow the prediction of clinical effects and complications. In 1962, Willis¹⁰ proposed a subdivision into cysts arising in the superficial myocardium—for example, in the atrial wall—and those arising deeper in the myocardium—for example, in the atrioventricular node in the interventricular septum. However, not all heterotopias fit exactly into this classification.⁹ Schindler *et al*³ suggest a classification into enteric versus bronchial cysts. Cysts containing any ciliated epithelium are classified as bronchial cysts. In Rosai and Ackerman's¹⁶ *Surgical pathology*, there is a more detailed classification, dependent on both the type of epithelial lining and the number of smooth muscle layers in the wall, which should mirror the morphology of the corresponding organ. Enteric cysts are then subdivided into oesophageal, gastroenteric and pancreatic types. Bronchogenic cysts are described as being surrounded by only a single layer of smooth muscle. In this case, the presence of TTF-1-positive ciliated epithelium and a single smooth muscle layer favour a diagnosis of bronchogenic cyst. To our knowledge, this is the first report of positive immunostaining for TTF-1 in a bronchogenic cyst at any site.

In this case, the myxoid appearance described macroscopically was most probably the result of mucin in the cyst. However, there are three previous reports of cases in which scanty epithelial elements were associated with atrial myxomas, raising the possibility that endodermal remnants may, in some cases, be associated with the development of an atrial myxoma.¹⁷⁻¹⁹ An alternative explanation for this is that endodermal remnants are more common than has been realised and that the reported associations of endodermal remnants and atrial myxoma are merely fortuitous. No immunostaining for epithelial markers has been described in atrial myxomas lacking glandular elements.¹³

In early development, the simple tubular heart is located immediately adjacent to the buccopharyngeal membrane and the developing foregut structures,²⁰ explaining why entrapment of endodermal components may occur. The endodermal (foregut) components normally differentiate into pharynx, thyroid gland, respiratory tract, oesophagus and upper gastrointestinal tract,²⁰ and entrapped intracardiac endodermal remnants may therefore pursue a similar differentiation pathway. In agreement with this hypothesis, all cases reported have shown attenuated, cuboidal, ciliated, squamous and transitional differentiation, sometimes with goblet cells and neuroendocrine cells^{1-9,14} and, in one case, thyroid parenchyma.¹⁵

Two alternative, less likely hypotheses for the development of congenital intracardiac endodermal heterotopias exist. The association of endodermal remnants with atrial myxomas may suggest intracardiac entrapment of primitive

multipotential cells that give rise to multigermline layer heterotopias with a mesodermal element (atrial myxoma) and an endodermal element.¹⁹ A teratoma may also give rise to glandular structures: a case of a malignant interatrial septal teratoma has been described in a 2-year-old.²¹

Although the myocardium is an unusual site for metastatic carcinoma, myxoid or mucoid foci with histological glandular differentiation can raise the suspicion of carcinoma.¹⁻¹⁹ Some mucinous carcinomas, including those of pancreatic, gastrointestinal and ovarian origin, can have bland histological appearances.²²⁻²³ We describe here a detailed analysis of the immunostaining profile of a bronchogenic cyst, which may be useful in distinguishing well-differentiated metastatic carcinoma from congenital heterotopia, particularly in a specimen in which the epithelium is poorly preserved. In this case, there was no suspicion of malignancy, and the cyst lining showed no features of dysplasia.

In summary, we have undertaken a morphological and histological analysis of a bronchogenic cyst of the papillary muscle, in addition to reviewing its likely embryological origin. This is, to our knowledge, only the second description of a papillary muscle endodermal cyst. This is also the first description of TTF-1 expression in a bronchogenic cyst.

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