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SHORT COMMUNICATION

Cystic tumour of the atrioventricular node: three cases of sudden death

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Abstract Cystic tumour of the atrioventricular nodal region is a rare primary cardiac tumour that can cause sudden death. Antemortem diagnosis and successful excision of this type of tumour are extremely rare. Three cases of sudden death are reported: A 25- and 40-year-old with a history of heart block and a 60-year-old with no medical history. There have been more than 120 cases of sudden death attributed to primary cardiac tumours in the literature. Although over 100 of these lesions were histologically benign, their intracardiac locations precipitated conductive and haemodynamic abnormalities that resulted in sudden death. The most common intracardiac lesion causing sudden death, cystic tumour of the atrioventricular node, however, may not be discovered unless the atrioventricular node is microscopically examined.

Keywords Atrioventricular node · Cystic tumour · Sudden death

Introduction

Cystic tumour of the atrioventricular (AV) node is a benign, congenital, cystic mass located at the base of the atrial septum in the region of the AV node [1]. It is a rare primary cardiac tumour that can cause heart blockage and is the smallest tumour capable of causing sudden death [2]. They have been termed both 'lymphangioma' and 'mesothelioma of the atrioventricular node'. Approximately 70 reported cases of these tumours have been described in the literature to date, but most are post-mortem findings. Antemortem diagnosis and successful excision of this type of tumour are extremely rare [3]. The precise incidence of this tumour cannot be determined given the infrequency of detailed examination of the cardiac conduction system at autopsy and the lack of macroscopic clues to its presence [4]. We report three cases of a cystic tumour of the atrioventricular nodal region in which the tumour was detected at autopsy.

Case 1

A 25-year-old woman who had a history of congenital heart block from the age of 11 years had a pacemaker fitted 6 months prior to her death. One evening when she was at home with her parents, her father described her being normal and in no distress. She was found dead in bed the following morning.

At autopsy, the conduction system looked macroscopically normal with no cystic changes seen with the naked eye. Microscopy of the right ventricle showed no evidence of fibrosis, or fatty infiltration to indicate that there was arrhythmogenic right ventricular cardiomyopathy and there was no histological evidence of a cardiomyopathy in the left ventricle. However, histology of the conduction system showed a microscopic cystic tumour of the atrioventricular node which infiltrated and destroyed the node, penetrating bundle and bundle of His (Fig. 1a) which explained her heart block. The tumour consisted of cystic spaces filled with

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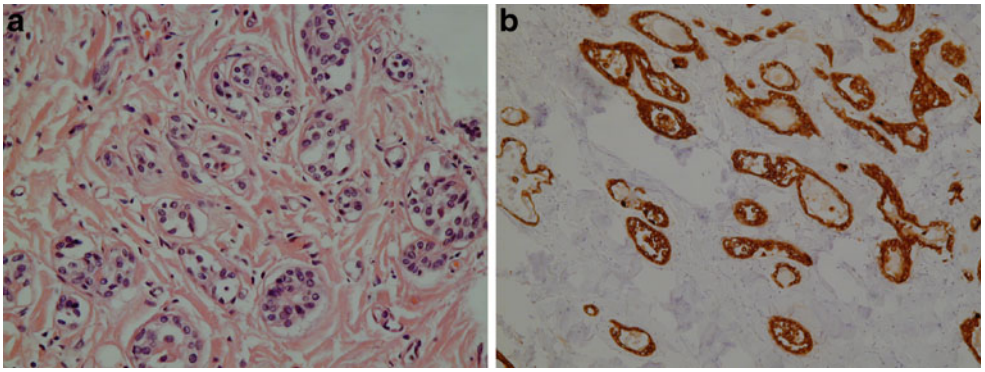

Fig. 1 **a** Section showing a cystic conduction tissue tumour consisting of spaces filled with mucin and lined by cuboidal, transitional and squamous cells in a 25-year-old female (haematoxylin and eosin stain, magnification ×200). **b** Immunohistochemistry showed the tumour to be positive for CEA

mucin and lined by cuboidal, transitional and squamous cells. Immunohistochemistry showed strong positivity for carcinogenic embryonic antigen (CEA; Fig. 1b). No other cause for her sudden death could be found at autopsy. There was no family history of sudden death or heart disease, and results from a toxicology and genetic screen were negative.

Case 2

A 60-year-old female had her heart examined in view of a history of sudden death. There was no significant medical or family history, and scene investigation was unremarkable. At autopsy, the heart initially looked macroscopically normal. However, a small 5-mm cystic lesion in the region of the atrioventricular node was found on dissecting out the conduction system (Fig. 2a). Microscopic examination confirmed a cystic tumour of the atrioventricular node in which cystic spaces were filled with mucin and were lined by cuboidal, transitional and squamous cells. The cysts and cells infiltrated the A–V node itself (Fig. 2b). Immunohistochemistry showed strong positivity for CEA, B72.3 antigen and CK5/6 (Fig. 2c). Toxicology and genetic screen were negative.

Case 3

A 40-year-old lady experienced chest pain and collapsed suddenly while shopping. At A&E, she was in ventricular fibrillation, resuscitation was unsuccessful and the patient was confirmed dead. She was asymptomatic until 2005 when she was diagnosed with complete heart block following childbirth. A dual chamber pacemaker was inserted. An echocardiogram later on that year showed mild to moderate mitral regurgitation and mild impaired left ventricular function. In 2006, she presented with breathlessness—atrial lead of pacemaker was found to be displaced and it was re-implanted. Her pacemaker was found to be functioning, and she reported to be feeling well when seen in clinic early 2009.

At autopsy, the heart was macroscopically normal including the atrioventricular nodal conduction system. However, microscopic examination of the AV nodal region showed a tumour consisting of a single layer of cuboidal cells building up to multiple layers of round cells with eosinophilic cytoplasm and round nuclei forming squamous as well as glandular areas. This was infiltrating and destroying completely the conduction tissue. The tumour was strongly positive for EMA, CK 5/6 and MNF-116 and negative for TTF-1 and CD56. The tumour epithelium (in

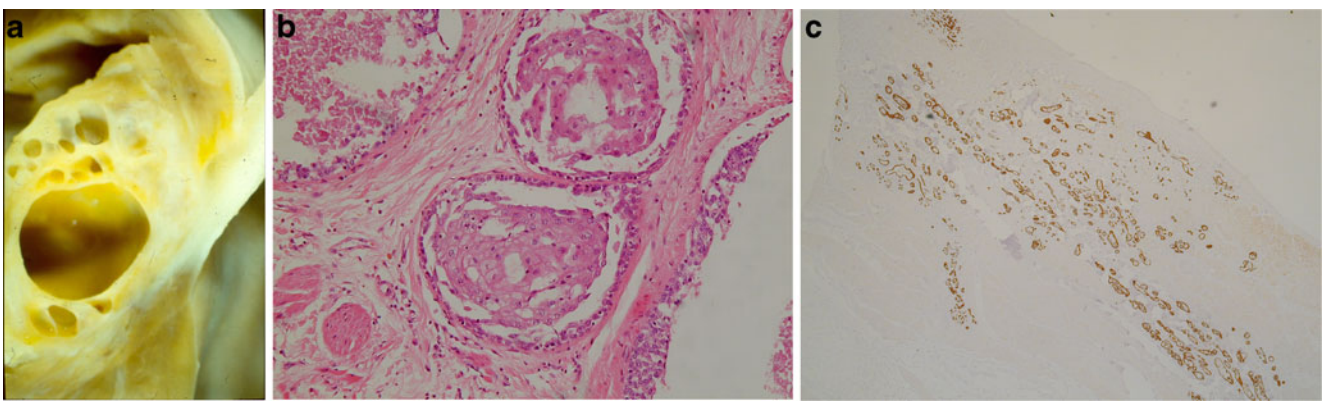

Fig. 2 **a** A small 5-mm cystic lesion located in the triangle of Koch in the region of the A–V node in a 60-year-old female. **b** Section showing cystic lesion with spaces filled with mucin and lined by cuboidal, transitional and squamous cells (Haematoxylin and eosin stain, magnification ×400). **c** The tumour stained positively for CK5/6

all three cases) contained epithelial mucin and CEA. There was no evidence of malignancy, and the findings seemed consistent with an AV nodal tumour. Results from a toxicology and genetic screen were negative.

Discussion

Sudden unexpected death accounts for 200,000–400,000 deaths each year in the USA. Although the vast majority of these fatalities are related to atherosclerotic heart disease, a small percentage (approximately 0.0025%) stem from primary cardiac neoplasms. A review by Cina et al. found 120 cases of sudden death attributed to primary cardiac tumours in the literature [4]. Although 103 of these lesions were histologically benign (86%), their intracardiac locations precipitated conductive and haemodynamic abnormalities that resulted in sudden death. The most common intracardiac lesion causing sudden death, AV nodal tumour also called endodermal heterotopia of the AV node, however, may not be discovered unless the AV node is microscopically examined. More recent reports of sudden death caused by primary cardiac tumours include a case of primary intimal sarcoma of the left coronary artery [5] and a case of pulmonary embolism from right atrial myxoma [6].

AV nodal tumour is a cystic lesion arising it is believed from sequestered endodermal elements of the primitive foregut during cardiac organogenesis [1]. It is a very uncommon primary cardiac tumour, and its constant location in the AV nodal region separates it from other cardiac cysts and tumours. The nomenclature has been diverse according to different histogenetic theories proposed since its first description in 1911. It was known erroneously as cystic mesothelioma of the AV node [2] but is not of mesothelial origin because of strong carcinoembryonic antigen positivity and occasional positivity with B72.3, glycoproteins found in endodermally derived tissue and not in mesothelial tissue [1]. Most authors have abandoned the term ‘mesothelioma of the AV node’ and prefer the term ‘cystic tumour of the AV node’. Patients with these tumours can develop complete heart block or sudden death. Indeed, it has been called the smallest tumour to cause sudden death [3]. It is not usually discovered until autopsy with a careful dissection of the conduction system and microscopic examination [4] as our cases illustrate. The female to male ratio is approximately 3 to 1, which was reflected in our cases. Because of a female predominance, it has been suggested that the diagnosis of AV nodal tumour be considered in teenage girls with complete heart block [7].

While its role in causing heart block is established [8], there is controversy about the role of this tumour in causing sudden death. The presentations have varied: the majority of patients have been predominantly female aged 15 to 40, dying suddenly; however, other patients have had documented heart block for many decades and a non-cardiac cause of death. Although high degree heart block is present in many patients, most episodes of sudden death probably are secondary to ventricular tachyarrhythmias as seen in one of our cases [9]. There are multiple case reports linking AV nodal tumour to sudden death and in the largest series published, an autopsy study of 17 cases, sudden death occurred in 14 which appears to highlight its role in sudden death when it infiltrates and destroys the AV node [10]. Another study indicated it as a cause of sudden death in four young people [11]. Yet, patients can present with heart block due to this tumour and die of other causes [12]. When the tumour is microscopic and not destroying the AV node, what is its role in sudden death where no other cause can be found? Several authors claim it as an incidental finding at autopsy not involving the conduction tissue and situated in the atrial septum [13] or in papillary muscle [14]. Therefore, caution should be exercised in such cases and other possibilities such as channelopathies considered. The Brugada syndrome, which is characterised by right bundle branch block and ST segment elevation in leads V1 to V3, may lead to ventricular fibrillation and sudden unexpected deaths [15].

Tumours of the AV node have been associated with several congenital abnormalities including complex congenital heart disease, thyroglossal duct cysts, cysts in the ovaries and breasts, ventricular septal defect and encephalocele, suggesting a genetic defect involving migration of embryologic tissues in patients with these tumours [1]. An AV nodal tumour has also been reported in association with Emery–Dreifuss muscular dystrophy, an X-linked recessive disease [16].

It is interesting to note that with heart block caused by this type of tumour in two of our cases, pacemaker implantation did not prevent death which appears to confirm that these patients are at risk of lethal arrhythmias unconnected to the heart block. Familial occurrence is reported with these tumours [17] which may be important in further screening of family members.

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