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Case Report

Intraoperative frozen pathological diagnosis of cystic tumor of the atrioventricular node: a case report and review of the literature

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Abstract: Cystic tumor of the atrioventricular node is an extremely rare primary tumor of the heart. Here we report a case of a 41-year-old female who presented with dizzy and palpitations. Electrocardiography revealed third-degree atrioventricular block. Echocardiography and Chest computed tomography showed a mass attached to the interatrial septum. Intraoperative frozen pathological examination revealed that the mass was the cystic tumor of the atrioventricular node. The diagnosis was proved by histopathology and immunohistochemistry. This is the first case that was diagnosed dependent on frozen pathological examination and treated successfully with surgery.

Keywords: Cystic tumor, atrioventricular node, frozen pathological examination, histopathology, immunohistochemistry

Introduction

Cystic tumor of the atrioventricular node is a benign cardiac tumor located at the base of the atrial septum in the region of the atrioventricular node [1]. Although the tumor is classified as benign, it can cause various degrees of heart blockage and is the smallest tumor capable of causing unexpected death. It is very difficult to identify the tumor without invasive studies, especially to distinguish from myxomas. Therefore, most cases are diagnosed incidentally at autopsy and antemortem surgical excision is extremely rare.

Clinical presentation

Our patient was a 41-year-old female who presented with dizzy and palpitations. Electrocardiography revealed third-degree atri-oventricular block. Echocardiography and chest computed tomography showed a mass attached to the interatrial septum. During the surgery, surgeons found the mass size to be 15×15×10 mm located at the interatrial septum. The upper boundary was at the level of the oval hole and the lower boundary was at the level of the posterior tricuspid valve. The anterior boundary was the root of the cuspis medialis and the posterior boundary was the wall of the coronary sinus. The mass of which section was a cystic structure containing a small amount of yellow colloid liquid. Surgeons partially excised the mass which was sent to the Department of Pathology for intra-operative consultation.

Materials and methods

Intraoperative frozen and histopathologic examinations

The fresh tissues were sliced using a cryostat microtome and stained with hematoxylin and eosin (HE). The residual tissues were fixed in 10% formalin and embedded in paraffin according to standard procedures. Tissue sections were stained with hematoxylin and eosin (HE).

Immunohistochemical staining

Immunohistochemical staining was performed on paraffin-embedded sections by standard techniques using cytokeratin (pan) (clone AE1/AE3; MXB; Ready to use), epithelial membrane antigen (EMA; clone E29; MXB; Ready to use), cytokeratin 5/6 (clone D5/16B4; MXB; Ready to

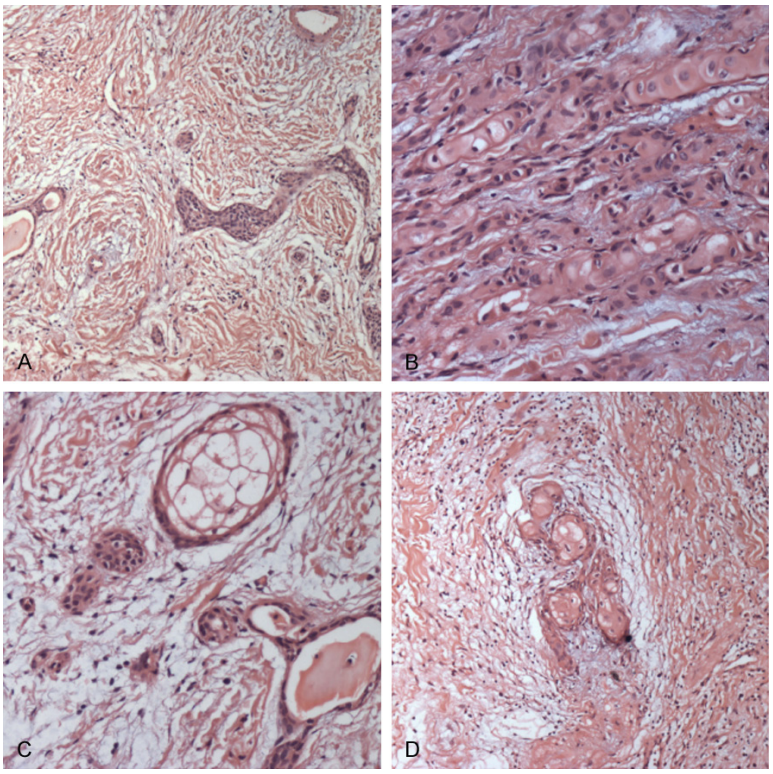

Figure 1. Pathologic findings (hematoxylin and eosin staining). A. Various sizes of cystic structures and solid nests (×40). B. Squamoid cells with eosinophilic cytoplasm and sebaceous cells with clear cytoplasm (×100). C. Neither cytological atypia nor appreciable mitotic figures (×200). D. Fibrosis and chronic inflammatory cells (×40).

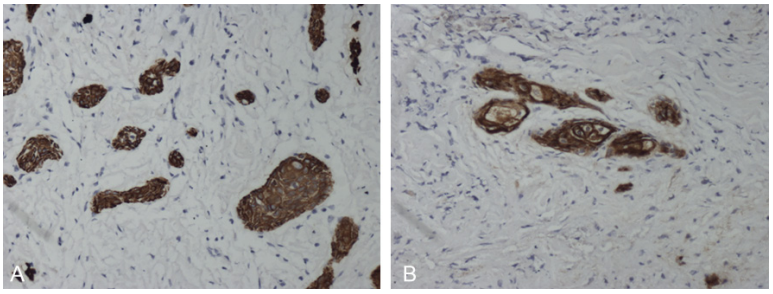

Figure 2. Immunohistochemical findings. A. Wide spectrum cytokeratins (×200). B. Epithelial membrane antigen (×200).

use), CEA (clone ZC23; MXB; Ready to use), calretinin (CR; clone SP13; MXB; Ready to use), Wilm's tumor (WT1; clone WT49; MXB; Ready to use), cytokeratin 20 (clone Ks20.8; MXB; Ready to use), actin (clone 1A4; MXB; Ready to use), thyroglobulin (Tg; clone TGB04+TGB05; MXB; Ready to use), chromogranin A (CgA; clone LK2H10+PHE5; MXB; Ready to use), synaptophysin (Syn; clone SP11; MXB; Ready to use), Ki-67 (clone MIB-1; MXB; Ready to use).

Results

Pathologic findings

Intraoperative frozen pathological and histopathological examinations showed that the cystic tumor contained various sizes of cystic structures and solid nests (**Figure 1A**). The cysts were lined by two or more layers of cuboidal or transitional cells and filled with amorphous hyaline eosinophilic material. The solid nests showed squamoid cells with eosinophilic cytoplasm and sebaceous cells with clear cytoplasm (**Figure 1B**). In some areas, the cell nests could be seen extending into the cardiac muscle fibers. However, neither cytological atypia nor appreciable mitotic figures were seen (**Figure 1C**). Some areas displayed a moderate degree of fibrosis and chronic inflammatory cells (**Figure 1D**).

Immunohistochemistry

The cells expressed wide spectrum cytokeratins (**Figure 2A**), epithelial membrane antigen (EMA) (**Figure 2B**), cytokeratins 5/6, carcinoembryonic antigen (CEA). The cells were negative for calretinin, Wilm's tumor, cytokeratins 20, smooth muscle actin, thyroglobulin, chromogranin, synaptophysin. The proliferation index of Ki-67 was very low (1%). Therefore, the case was diagnosed as cystic tumor of atrioventricular node. The stains confirmed that the tumor cells were of endodermal origin rather than mesothelial origin.

Discussion

Cystic tumor of the atrioventricular node (CTAVN) is an extremely rare primary tumor of the heart. It is a biologically-benign, congenital

Table 1. Summary of cases of successful resection of the tumor

Time	Gender	Age	Clinical symptoms	Size (mm)	Excised
1992	Female	21	Palpitation, dyspnea First-degree AV block	0.5	Completely
2000	Female	59	Palpitations, various Degrees of AV block	30	Partially
2003	Female	66	Dyspnea, palpitation Various degrees of AV block	30	Cartially
2005	Female	45	Palpitation, dyspnea First-degree AV block	30	Completely
2008	Female	19	Pillow orthopnea chest pain First-degree AV block	no distinct mass	Cardiac transplant
2009	Female	41	Palpitation, dyspnea Third-degree AV block	30	Completely
2009	Female	42	Syncope First degree AV block	30	Completely
2011	Female	33	Dyspnea, dizziness, palpitation, numbness	26×27	Completely
2011	Female	24	Dyspnea, dizziness, palpitation, numbness	25×20	Completely
2013	Female	43	Dyspnea, fatigue First-degree AV block	25×17	Complety
2014	Female	57	No overt symptoms First-degree AV block	40	Partially

neoplasm which is the smallest and most common cardiac neoplasm responsible for sudden death [2-5]. Because of its constant location in the atrioventricular node region separates it from other cardiac cysts and tumors [6].

CTAVN typically presents in adulthood at a mean age of 38 years ranging from newborns to 95 years, with a female-to-male ratio of 3:1 [7, 8]. The clinical presentation of CTAVN is not specific [9]. The symptoms include variable degrees of heart blockage and cardiac arrhythmias [10]. Some patients were clinically silent and may die suddenly with no signs or symptoms, then the tumor was diagnosed during autopsy. Therefore, the precise incidence of CTAVN is difficult to estimate.

Tran et al. suggested that cardiovascular magnetic resonance (CMR) and computed tomography (CT) have been useful in identifying tumors such as CTAVN occurring in the atrial septum and the AV nodal region [11]. Paniagua et al. reported a case which was detected preoperatively by echocardiography and magnetic resonance imaging (MRI) [12].

To our knowledge, only eleven cases were diagnosed antemortem and treated successfully with surgery (**Table 1**).

Balasundaram et al. reported the first case of successful resection of the tumor in 1992 [13]. According to the reported cases, all eleven patients were female (19-66 years). The clinical symptoms including palpitation, dyspnea, dizziness, various degrees of AV block, etc. However, Fukui et al. described a patient who had no overt symptoms. The tumor was detected during examinations prior to the operation of congenital extralobar pulmonary sequestration [14].

The literature reported tumor sizes varying from 0.5 mm to 40 mm. Lethal arrhythmia was dependent on tumor cell invasion into the AV conduction or His bundle, so the tumor size was not associated with lethal arrhythmia or sudden death [14, 15]. Sharma et al. reported a case of the CTAVN diagnosed in an explanted heart specimen. On gross examination, no distinct mass was in their case [16]. They routinely submit a minimum of two sections from the AV node region of all heart specimens. So they recommended that adherence to this protocol leads to detection of lesions when the AV node looked macroscopically normal with the naked eye. Patel et al. described a similar proposal [17].

Our patient was a 41-year-old female who experienced palpitation, dizziness, third-degree AV block, and the size of the tumor was 15×15×10 mm. During surgery, the surgeons sent a piece of the tumor to the pathologists and hoped that through analyzing the pathology characteristics of the tumor specimen they would be able to give them more explicit diagnosis and guide the treatment direction. Intraoperative frozen pathological examination revealed the tumor was CTAVN.

The differential diagnoses of cystic epithelioid tumors in the atrioventricular nodal region are very important for identification of metastatic carcinoma, bronchogenic cysts, myxomas, etc.. First of all, metastatic carcinoma must be ruled out. We communicated with the surgeon to determine that the patient did not have any history of cancer. The tumor cells appeared benign with no atypia or mitotic figures to suggest it was not a metastatic carcinoma. Bronchogenic cysts that have larger and single cysts with a muscular wall usually occur on the epicardial surface. Myxomas are generally located in the endocardium of the atrial septum near the fossa ovalis. The cells may be arranged singly, in cords, or in vasoformative ring structures and cytokeratin stain negative [18].

Immunohistochemical staining showed that the cells of the cyst expressed wide spectrum cytokeratins and epithelial membrane antigen, suggesting that they are of endodermal origin. The result supported the concept of a congenital endodermal tissue rest, capable of slow proliferation [19-21]. Its histogenesis was congruent with an alteration in cardiac neural crest cell development [22].

Postmortem studies shown that pacemaker implantation may not prevent sudden death because of lethal arrhythmias [23]. Thus, surgical intervention should always be indicated. It is also controversial whether the cyst should be completely excised from the atrial septum. Some believe that complete resection is essential because one complication with the tumor is sudden death, even if subsequent pacemaker implantation is required. While others report that the tumor was partially incised and left the cyst wall attached to the base of the IAS [24].

Our patient underwent partial resection and didn't need a pacemaker. The patient showed no recurrence 5 years after the operation. Our case provides a reference for future treatment of CTAVN. Since CTAVN can cause various degrees of heart blockage and unexpected death, awareness about the characteristics of tumor and antemortem diagnoses is very important.

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Disclosure of conflict of interest

None.

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