Mesothelioma in the Atrioventricular Node
Case Report

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Summary

A patient with complete atrioventricular block and an implanted permanent pacemaker died of colon cancer at the age of 64 years. At autopsy, a cardiac tumor in the region of the atrioventricular node (mesothelioma of the atrioventricular node) was found. The origin of this type of tumor is controversial. Histochemical findings suggested that the tumor in this case was of endodermal origin. (Jpn Heart J 35: 255–261, 1994)

Key words: Atrioventricular node Mesothelioma Complete AV block

Complete atrioventricular (AV) block may be due to several causes, such as congenital diseases, coronary artery disease, sclero-calcific degeneration, myocarditis, fatty infiltration, bleeding, abscess, tuberculosis and syphilis. Moreover, primary and secondary tumors should also be considered in cases of heart block.

Primary cardiac tumors are uncommon and mesotheliomas of the AV node are rare. More than 50 cases have been reported in the literature, and only two from Japan.1,2) Mesotheliomas of the pericardial surface are a separate entity; the origin of conduction system tumors is controversial. Recently, some authors have proposed that this tumor is of endodermal origin.3–5) We herein report an autopsy case and describe a histochemical approach to investigation of the tumor origin.

Case Report

A 64-year-old man received chemotherapy for sigmoid colon cancer and
died at Juntendo University Hospital on February 2, 1991. An AV block and hypertension were recognized at the age of 30. In 1982, at the age of 56 years, the patient was admitted to Juntendo University Hospital for management of complete atrioventricular block. Clinical examination revealed a pulse rate of 40 beats per minute (bpm) and a blood pressure of 160/70 mmHg. A grade of 3/6 systolic ejection murmur was heard at Erb’s area. An electrocardiogram (ECG) showed complete AV block and a heart rate of 40 to 50 bpm (Figure 1). The escape QRS width was 0.08 sec. An electrophysiologic study demonstrated an A-H block (Figure 2). Sinus node function and His-Purkinje conduction were normal.

Though the patient had no symptoms and the ECG was unchanged, cardiomegaly slowly progressed. A permanent pacemaker was implanted in 1984, and the patient had an uneventful course during the next 6 years. In 1990, examinations of the gastrointestinal tract (barium enema, sigmoidscopy, and CT scan) disclosed a malignant tumor of the sigmoid colon with distant metastasis, and chemotherapy was given. The patient eventually died of septicemia as a complication of colon cancer in 1991.

**Laboratory findings:** The erythrocyte sedimentation rate was 71 mm/hour and the white blood cell count was 9600/mm³. Serum chemistry studies were
Figure 2. His-bundle electrogram. P waves are not followed by H potentials, and H potentials precede each QRS complex by an H-V interval of 50 msec. These findings demonstrate A-H block with junctional escape rhythm.

within the normal limits except for the following values: alkaline phosphatase of 27.6 K-A U; y-glutamyltransferase of 115 IU/l; leucine aminopeptidase of 512 mg/dl; carcinoembryonic antigen (CEA) of 77 ng/ml and carbohydrate antigen 19-9 (CA 19-9) of 11773 U/ml. A CT scan of the chest showed multiple lung metastases. Cytologic examination of ascites fluid revealed adenocarcinoma (Class V).

A chest radiograph showed mild cardiomegaly and pleural effusion. The ECG had a persistent complete AV block and a pacing rhythm rate of 70 bpm. Echocardiography demonstrated normal ventricular systolic function and mild dilatation of both the right and left ventricles.

Pathologic findings: The heart weighed 460 g. The left ventricle had mild hypertrophy and dilatation. The right ventricle was mildly dilated.

The conduction system was studied by Lev's serial cut method. These sections were stained by the hematoxylin and eosin, azan, and pentachrome methods, and then examined microscopically. A tumor was found in the region of the AV node and the architecture of the AV node was almost completely replaced by the tumor.

The tumor consisted of cysts of various sizes in a dense fibrous tissue stroma (Figure 3). Large nests included a central lumen containing amorphous
Figure 3. Pathologic findings. A: The tumor is located at the approach portion and AV node (Hematoxylin and eosin ×5). IAS=interatrial septum; AVN art.=AV node artery; CFB=central fibrous body. B: The tumor consisted of cysts of various sizes. The cysts were lined uniformly by polygonal cells, and were frequently multilayered (Hematoxylin and eosin ×25).

Figure 4. Conduction system below the AV node. A: Bundle of His (His) is normal in appearance (pentachrome, ×5). B: Posterior fascicle of the left bundle branch (LBBp) is normal in appearance (pentachrome ×2.5). C: Anterior fascicle of the left bundle branch (LBBa) is normal in appearance (pentachrome ×2.5). D: The third portion of the right bundle branch (RBB) is normal in appearance (pentachrome ×5).
Figure 5. Scheme of the tumor location in the conduction system. The tumor is situated at the approach and AV node. IAS=interatrial septum; IVS=interventricular septum; RA=right atrium; RV=right ventricle; LA=left atrium; LV=left ventricle.

Figure 6. Histopathologic findings (×25). A: The tumor stained with anti-carcino-embryonal antigen (CEA). Abundant expression of CEA can be seen. B: The tumor stained with anti-CA 19-9. The cells of the cyst were especially immunoreactive. C: The tumor stained with anti-cytokeratin.

material whereas small nests appeared solid. The cysts were lined by uniform polygonal cells which frequently formed a multilayered wall. The cells in the nests were often squamoid. Both intracellular and extracellular regions were PAS-positive but intracellular staining was partially sensitive to prior diastase digestion, whereas extracellular staining was unaffected. Both intracellular and extracellular alcian blue staining were unaffected by prior hyaluronidase digestion.
The other conduction tissues, i.e., the sinoatrial node, His bundle, and left and right bundle branches, were normal (Figure 4). The tumor was situated at the approach to the AV node and at the AV node (Figure 5).

We also examined the cardiac tumor by staining with anti-CEA, anti-cytokeratin, and anti-CA19-9 antibodies for the detection of endodermal tissue. Our case was stained positively with all tested antibodies (Figure 6).

**DISCUSSION**

Tumors in the AV node may cause AV block or sudden death.\(^6\)-\(^9\) The cause of sudden death is likely ventricular tachycardia or fibrillation, as some reports indicate that permanent pacemaker implantation does not prevent sudden death.\(^8\),\(^10\),\(^11\) In the present case, AV block was detected at 30 years of age, pacemaker implantation was performed at the age of 58 years, and the patient died of an extracardiac event 6 years after pacemaker implantation. Thus, this tumor appeared to have been benign and slow-growing. It has been postulated that other factors are likely to trigger sudden cardiac death in patients with these lesions.\(^12\) Our patient did develop ventricular tachycardia when cancer chemotherapy was administered, and in association with septicemia.

In Japan, only two cases of cardiac mesothelioma have been reported. One patient had a Mobitz type 2 AV block and died of a subarachnoid hemorrhage at the age of 33 years. Another patient was a 32-year-old male with complete AV block and junctional escape rhythm. This patient died of multiple myeloma. In previous reports, the ages of the patients ranged from 8 months to 86 years and females were affected more frequently than males.\(^13\),\(^14\) All three cases reported in Japan, including ours, were males, and died of extracardiac events. Two of these three cases had malignant neoplasms. The relation between this tumor and other malignant tumors is not clear.

Although this tumor has been postulated to be the result of inadvertent incorporation of developing embryonic structures, it is unclear which tissue has been incorporated in the AV node, i.e., mesothelial tissue\(^15\)-\(^18\) or foregut endoderm.\(^10\),\(^19\)-\(^21\) Some investigators have suggested that tumors of the AV node are most frequently congenital rest of endodermal tissue.\(^3\),\(^6\) Our case showed findings that led us to a similar conclusion. On the other hand, Yamazaki et al\(^2\) reported a case that may have originated from abberant epithelial or mesothelial tissue as shown by immunohistochemical staining using anti-CEA, anti-keratin, anti-vimentin/tubulin, and anti-EMA antibodies. The mesothelioma of the AV node therefore appears to include tumors from multiple origins. This varied origin might account for the variability in prognosis, clinical course, and complications. Further study is needed to elucidate the origin of mesotheliomas of the
AV node.

REFERENCES