Clinical Research

Morphological observations of tumors in cardiac conduction system

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Tumors of the cardiac conduction system (CCS) have rarely been reported. The CCS from 198 cardiac-related deaths (Group 1), and 838 deaths from non-cardiovascular diseases or trauma (Group 2), were studied. Sampling was done of the sinoatrial node (SAN) and atrio-ventricular node (AVN) along their long axis of each node as a single block and the His bundle (HB) perpendicular to its long axis in 2-4 blocks. Five-micron serial sections were made; tissue slices were taken intermittently, every 20th from the SAN, every 10th from the AVN, and every 30th from the HB and bundle branches (BB), by continuous slices three times. Tumors in the CCS were found in 12 cases (1.155 %), where 10 (0.965%) were primary tumors, and 2 (0.193%) were metastatic tumors. The primary tumors included 4 fibromata compressing the HB (0.386 %), 4 hemangiomata (0.386%), 1 AVN tumor (0.097 %), and 1 rhabdomyoma (0.097 %). In 8 of the 10 cases, the tumors were located in the AVN or HB. The metastatic tumors originated from lymphocytic leukemia and malignant lymphoma (histiocytic type) in lung, and were all found in the SAN. Of the 12 cases, 2 were from the group 1. Tumors in the CCS are the smallest tumors in different parts of the body, which can cause sudden death. (J Geriatr Cardiol 2007;4:164-167.)

Key Words cardiac neoplasms; sudden cardiac death; cardiac conduction system

Introduction

The cardiac conduction system (CCS) is a rare location for tumors, usually discovered only at time of autopsy. In a report of 4860 autopsies from China, 15 cardiac tumors were identified, and only two were in the CCS (AV node tumor). CCS tumors have been reported only sporadically in the literature.2,3

Materials and methods

The hearts from sudden death patients were collected from autopsies in the Guangzhou Institute of Criminal Sciences (from January, 1989 to December, 1995) and the Department of Forensic Medicine of University of Turku (from March to May, 1995, and from May to July, 1996). One hundred and ninety-eight sudden deaths could not be attributed to lethal extra-cardiac disease (Group 1), and all had negative drug screens. Eighty and thirty eight cases died of non-cardiovascular disease (Group 2). There were 803 male and 233 female patients, aged 2 months to 98 years.

The CCS of two groups were sectioned using the method established by the authors.4 Sampling was done of the sinoatrial node (SAN) and atrio-ventricular node (AVN) along their long axis, with each node as a single block and the his bundle (HB) perpendicular to its long axis in 2-4 blocks. The total number of tissue blocks for each case was about 4-6. The tissue blocks were dehydrated and then embedded in wax. Five-micron serial sections were made by continuous slices thrice [tissue slices were taken intermittently, every 20th from the SAN, every 10th from the AVN, and every 30th from the HB and bundle branches(BB)]. In all, about 20-30 slices were taken from each case. In two cases the CCS were sectioned completely, and 60-80 sections per case were examined. All sections were stained with hematoxylin and eosin, and some also with Masson’s trichrome and elastic fiber staining. Sections were examined under light microscope.

Results

3.1. The varieties and locations of the tumors

The 12 cases of CCS tumor were listed in the Table 1. The CCS tumors all arose from tissues in the ventricular septum (fibroma compressing His bundle, hemangiomata) or from residual embryonic cells (rhabdomyoma and the AV node tumor). The tumors mainly affected the atrio-ventricular conduction system, especially the HB. The distribution of tumors in these 12 cases was 8 in the HB (benign 7, metastatic 1), 3 in the SAN (benign 1, metastatic 2), 1 in the AVN, and none in the bundle branches.

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3.2. Morphology of the tumors

3.2.1. Fibroma compressing His bundle

The fibroma compressing HB is different from fibroma in the heart; it is very small, can only be observed by microscope, is located in the ventricular septum, and is found compressing the bundle of His. The tumors are round or ovoid in shape. They emerge from the lower margin of the pars membranacea or from the top of the interventricular septum (Fig. 1), compressing the bifurcating portion of the HB. The basal portions of the tumors are usually not sharply demarcated from the surrounding tissues. The largest areas of the cross sections of the tumors are 1.2mm×1.1mm, 1.0mm×1.0mm, 1.0mm×0.9mm, and 1.0mm×0.7mm, respectively. The tumors are composed of collagen fibers and elastic fibers; myocytes were not observed. In the compressed portion of the His-bundle, the bundle cells are shrunken and sometimes even show fibrosis.

3.2.2. Hemangioma

As observed under microscope, the hemangioma was composed of irregularly distributed dilated capillaries or multiple sinusoidal clefts of various shapes and sizes. In one case there was also hyperplastic fibrous tissue in addition to the vascular neo-growth, as well as the surrounding CCS tissues which were atrophic (Fig. 2).

3.2.3. AV node tumor

The boy died of a traffic accident; however, a tumor located in the region of the AVN was found under autopsy, measuring 1.6mm×4.0mm×2.9mm, without a capsule, and growing invasively. The tumor cells were similar to stratified squamous epithelium and formed solid cords or nests (Fig. 3), some with cystic or glandular structures containing PAS positive substance, foamy phagocytes, and calcified granules in the cavities. The interstitial tissue showed marked hyalinization.

3.2.4. Rhabdomyoma of the ventricular septum

One case was characterized by multiple rhabdomyomata. The tumors were small and not encapsulated. One of the tumors was situated at the left side of the top of the interventricular septum where the HB showed “saddle-like” deformation due to compression by the overlying rhabdomyoma. Some of the cells in the HB also showed rhabdomyomatous change. The tumor cells were large and vacuolar, and some of them were spider-like; the spider cells were seen with eccentric nuclei granular cytoplasm and thin cytoplasmic extensions projecting toward the cell membrane.

3.2.5. Metastatic tumors of the SAN

A case of lymphocytic leukemia and a case of malignant lymphoma (histiocytic type) showed infiltration of anaplastic lymphocytes or histiocytes in the SAN and the perinodal nerves and ganglion (Fig. 4).

Table 1: The 12 Cases of CCS Tumor

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Position</th>
<th>Number of cases</th>
<th>Group</th>
<th>Age (yrs)</th>
<th>Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary tumor (benign)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Fibroma compressing His bundle</td>
<td>ventricular septum</td>
<td>4</td>
<td>1</td>
<td>31, 50</td>
<td>2 males,</td>
</tr>
<tr>
<td>2. Rhabdomyoma</td>
<td>(in the area of HB)</td>
<td>1</td>
<td>1</td>
<td>65, 77</td>
<td>2 females</td>
</tr>
<tr>
<td>3. Hemangioma</td>
<td>SAN, HB</td>
<td>4</td>
<td>4</td>
<td>20, 21, 25, 69</td>
<td>all male</td>
</tr>
<tr>
<td>4. AV node tumor</td>
<td>AV node area</td>
<td>1</td>
<td>1</td>
<td>7</td>
<td>male</td>
</tr>
<tr>
<td>Metastatic tumor</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Lymphocytic leukemia</td>
<td>SAN, HB</td>
<td>1</td>
<td>1</td>
<td>62</td>
<td>female</td>
</tr>
<tr>
<td>2. Malignant lymphoma (histiocytic type)</td>
<td>SAN and perinodal ganglion in lung</td>
<td>1</td>
<td>1</td>
<td>64</td>
<td>male</td>
</tr>
</tbody>
</table>

Cause of death

There have been reports concerning incidence of the tumors of the heart, but the incidence of the tumors in the CCS has so far not been reported. Among the 12 cases, 2 were in the sudden death group without lethal diseases in extra-cardiac tissues. The 2 tumors included a rhabdomyoma of the ventricular septum, and a fibroma compressing the HB. In these two cases it was thought that they might have died of the effects of tumors in the CCS. The other cases were in the non-cardiac disease or trauma group where 7 died from traffic accidents and 3 from other diseases.
4.1. The incidence of tumors in the CCS
Among the 1036 routine CCS examinations, there were 12 cases of tumors in the CCS, representing an incidence of 1.155% (10 were benign, 0.965%; and 2 malignant, 0.193%). This incidence was higher than the reported incidence of tumors in the heart (0.00017% and 0.28%). The reasons for this might be:
1. The reported incidence of tumors in the heart was obtained by naked eye examinations of the hearts, while in our study, all of the cases were examined by serial microscopic sections of the CCS.
2. There were 198 cases of sudden death without extra-cardiac lethal pathological changes. It might be that they had a closer relationship with tumors of the CCS.
3. Tumors of the CCS might not have been included in the reported cases used for calculating the incidence of the tumors in the hearts. If we only calculate the rate of 2 cases among 198 cases without extra-cardiac cause of death, then the resulting incidence would be 1.01%.

4.2. The distribution of tumors in the CCS
Among the 10 primary tumors of the CCS in our group, 8 were situated in the bifurcation of HB; the other two cases were in the SAN, and one in the AVN respectively, with none in the BB. The larger number in the bifurcation of the HB may be related to more fibromata and rhabdomyomata in that position. The metastatic tumors were prone to occur in the SAN and rarely occurred distal to the AVN. This is in agreement with previous reports that metastatic tumors are mainly observed in the right heart. The predisposition of metastatic tumors in the SAN is related to the route of metastasis, i.e. the tumor thrombus proceeded to retrograde in the lymphatic vessels or through the vena cava, and reached the pericardium or myocardium of the right heart. The SAN is adjacent to that position.

4.3. Tumors in the CCS may serve as the basis for electric instability of the heart.
The CCS is the specialized tissue for pacing and regulation of the cardiac rhythm. Any one of the above-mentioned tumors, even microscopic in size, may produce following results.

1. Compression which is mainly caused by benign tumors. In our cases, there were fibroma compressing His bundle, and rhabdomyomata and hemangiomata of the interatrial or ventricular septum. Although the sizes differed, all of them caused compression of the AV-bundle or the SAN; hence there was pressure atrophy, malnutrition, neuropathy, and malfunctioning of the conduction tissue. In severe cases, there was fibrosis or disconnection of cells, which might cause blockage of conduction.

2. Destruction of the CCS by tumor infiltration where malignant tumors grew invasively, destroying the CCS tissue, separating them into pieces, and thus forming a pathological basis for arrhythmia and cardiac blockage.

3. Cardiac neuropathy where in 1983, James coined the name cardiac neuropathy for the inflammatory or degenerative changes in the nerves and/or gangliaons in the heart in some sudden deaths. In our cases, there was invasion of gangliaons at the periphery of the SAN by lymphadenoma cells. The affected sympathetic and parasympathetic nervous tissue may influence the rhythm of the conduction and repolarization of the heart cells, thus leading to sudden death.

According to our material, although the incidence of tumor in the CCS among sudden cardiac death cases is only 1.01%, the evidence suggests that small benign tumors located in the cardiac conduction system be lethal. This seems to be only true with tumors in the CCS. So, in cases of sudden cardiac death, we suggest that the CCS be examined more carefully.

References