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Forensic significance of conduction system abnormalities as a precise cause of accidental death

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Abstract We examined the pathology findings of the cardiac conduction system in 42 human autopsies who were considered to have died an accidental death. Abnormalities in serial sections of the conduction system were found in seven and of these three had an accessory pathway in the conduction system. In one of these there was mild Ebstein's anomaly (ME), two had fibromuscular dysplasia of the atrioventricular node artery with mitral valve prolapse, and two others had abnormal routes showing fragmentation of the bundle of His with ME. A full investigation of the cardiac conduction system can therefore be useful for determining the precise cause in cases of accidental death.

Keywords Forensic pathology · Accidental death · Conduction system · Accessory pathway · Syncope

Introduction

It is occasionally difficult to ascertain the precise mode of death when there has been an accident and various possibilities, such as disease, suicide and homicide need to be carefully considered. Moreover, sudden syncope or collapse may also be the cause of an accident, and a sudden arrhythmogenic event may play a considerable role.

As pathological changes of the heart that were caused by trauma [1] and poisoning [2], conduction system abnormalities are also known to be relatively rare but one of the important causes of sudden death [3, 4], and many pathologists have focussed on the cardiac conduction system to explore the pathogenesis of sudden death in various pathological conditions [5, 6, 7, 8, 9, 10, 11, 12]. It is well accepted that patients with cardiac conduction system abnormalities occasionally experience syncope or collapse as the episode before death. We therefore investigated abnormalities of the cardiac conduction system in cases of accidental death by examining the heart, including serial sectioning of the conduction system.

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Materials and methods

In 119 cases of serial full autopsies performed in our department between April 1999 and April 2001, 93 were cases of unnatural death and we considered that 42 of these 93 cases may have been accidental death. Of these 42 cases, there were 9 cases of falling, 16 of drowning, 10 were involved in a traffic accident (6 passengers, 2 drivers, 2 motorcycle riders), 4 had died in a fire and 3 had been poisoned.

At autopsy, we carefully examined the entire organs both macroscopically and microscopically. The heart was excised and dissected free from the great vessels. After removing the blood in the heart, the weight, including epicardial coronary arteries and epicardial fat, was measured to the nearest gram. The right and left ventricles were cut at 1-cm intervals parallel to the levels of the papillary muscle from the apex. The hearts were then opened according to the direction of blood flow, and any abnormalities of the myocardium, endocardium or valves were noted. These were then fixed in 10% buffered formaldehyde. Sections at the level of the papillary muscle and the apex were examined in detail histologically. The major epicardial coronary arteries, left main, left anterior descending, left circumflex, and right coronary artery (RCA) were cut transversely at 5-mm intervals and decalcified as required. After we had determined that there were no pathological findings leading to syncope in any organs other than the heart, having also determined that there was no significant coronary artery disease both macroscopically and microscopically, a block of the right atrium including the sulcus terminalis was obtained in order to study the sinoatrial (SA) node [13]. From this block, 4–6 sections were obtained. Another block was excised from the anterior margin of the coronary sinus to the medial papillary muscle of the right ventricle, including at least 1 cm of the atrium and 1.5 cm of the ventricle on either side of the tricuspid valve [14]. The block was cut along planes perpendicular to the sulcus, from posterior to anterior to obtain 7–10 blocks. These blocks were processed and embedded in paraffin and an average of 6–40 microscope, 3-μm tissue sections (30-μm intervals) were obtained from each block. Histological sections were stained with hematoxylin and eosin, Masson's trichrome and Elastica-von Gieson stains.

Table 1 Summary in the seven autopsies of accidental death with conduction system abnormalities (*HW* heart weight, *NV* nodo-ventricular connection, *FV* fasciculo-ventricular connection, *MVP* mitral valve prolapse, *AVNA* atrioventricular node artery, *EF* endocardial friction lesion, *ME* mild Ebstein's anomaly, *ASD* atrial septal defect, *CO* carbon monoxide, *CO-Hb* carboxyhaemoglobin)

Case	Age (years)	Sex	HW (g)	Type of accident	Cause of death	Macroscopical abnormality	Conduction system abnormality	Other findings
Case 1	21	M	269	Fell from a motor vehicle	Brain injury	None	Accessory pathway (NV)	None
Case 2	17	F	263	Fell into river while cycling	Drowning	None	Accessory pathway (FV)	None
Case 3	19	M	386	Fell down	Brain injury	MVP	Stenosis of AVNA, deposition of proteoglycan after drinking alcohol	None
Case 4	48	M	333	Found dead in the sea	Drowning	MVP with EF	Stenosis of AVNA	Blood alcohol 1.78 mg/ml
Case 5	51	M	302	Found dead in the sea	Drowning	ME	Intramembranous bundle of His with fragmentation	None
Case 6	73	F	304	Found dead in the sea	Drowning	ME, ASD	Intramembranous bundle of His with fragmentation	None
Case 7	48	F	283	Found dead at the scene of fire	CO poisoning	ME	Accessory pathway (NV)	Blood alcohol 2.50 mg/ml, blood CO-Hb; 69%

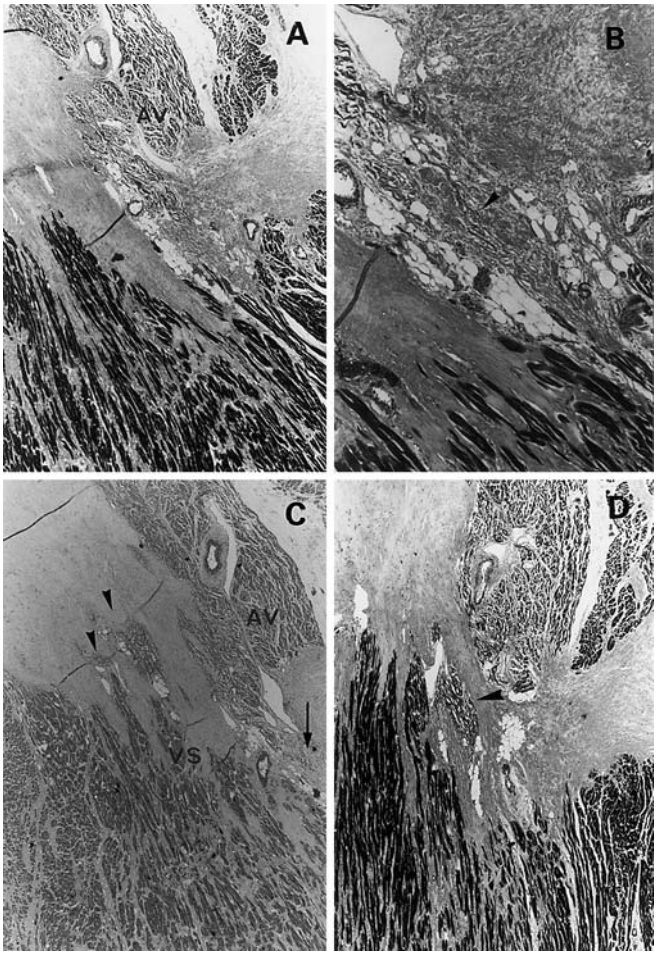

Fig. 1A–D Microscopical appearance of case 1. **A** Specimen containing AV node (AV) (Masson's trichrome ×3), **B** high-power view of **A**, nodal fibres (*arrowhead*) extend to the ventricular septum through a gap in the central fibrous body (*VS* ventricular septum) (Masson's trichrome ×25), **C** serial section. In addition to the nodal fibres reaching to the ventricular septum (*arrow*), dispersed conduction fibres in the central fibrous body (*arrowhead*) were also found beneath the septal fibres (H&E ×10). **D** Serial section, nodal fibres (*arrowhead*) completely reach the ventricular septum (Masson's trichrome ×25)

Results

In 7 of the 42 cases, we observed abnormal findings only in the conduction system that were considered to have arrhythmogenic potential (Table 1). There were no obvious foci of ischemic lesions or contraction band necrosis [15] in all seven cases which are described in more detail.

Case descriptions

Case 1

A 21-year-old male student who fell while riding a motorcycle. The deceased was 172 cm in height and weighed 57.0 kg. The skull was severely fractured. The heart weighed 269 g and showed no macroscopically abnormal findings and microscopically the sinus node was normal. The fibres of the atrioventricular (AV) node were extended to the base of the ventricular septum (VS) through the poorly formed central fibrous body (CFB), and formed a nodo-ventricular connection (so-called Mahaim fibres) (Fig. 1).

Case 2

A 17-year-old female who was found dead in a river with her bicycle. She had been on her way to a friend's home by bicycle along a road beside the river and had appeared healthy prior to the accident. The deceased was 148 cm in height and weighed 54.0 kg.

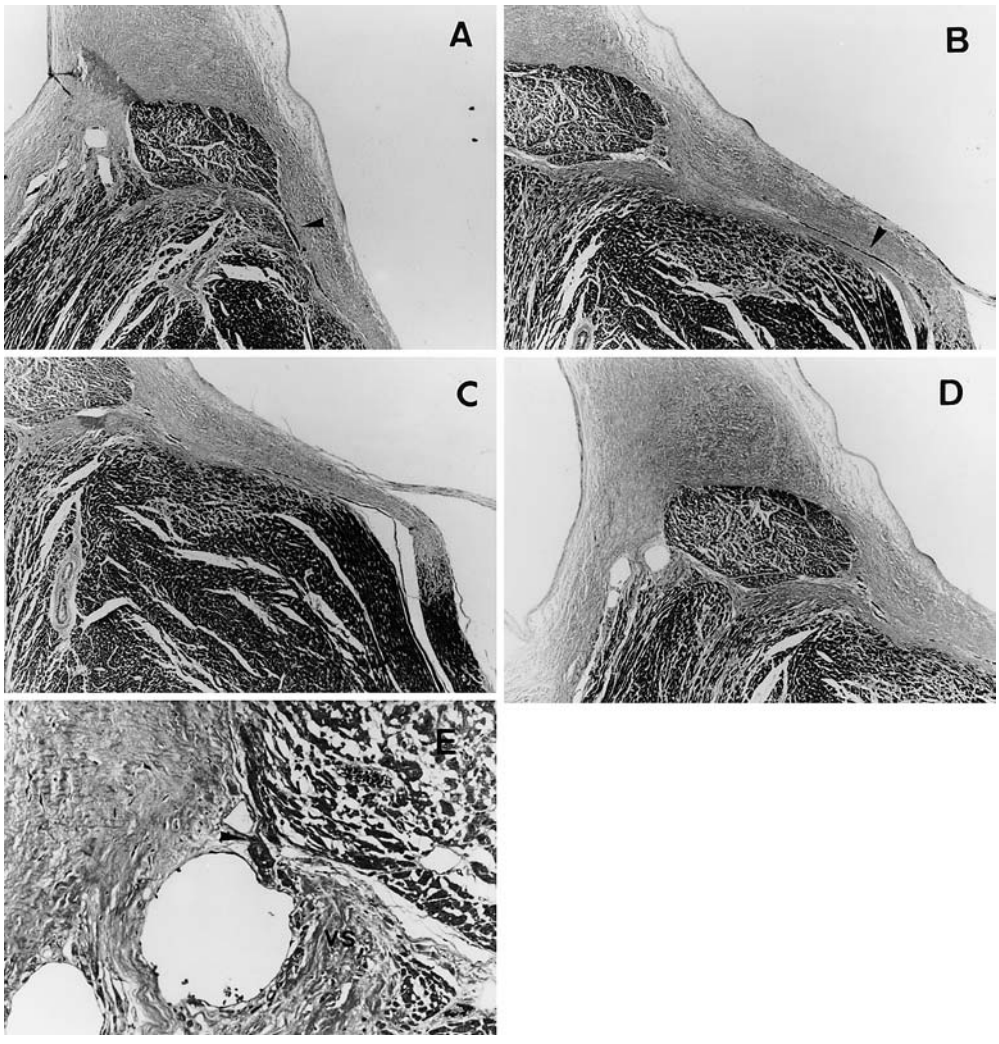

Fig. 2A–E Microscopical appearance of case 2. **A** Specimen containing the bundle of His of the ventricular summit. Conduction fibres (*arrowhead*) originate from the bundle of His (Masson's trichrome ×10). **B, C** serial sections. Conduction fibres (*arrowheads*) extend and reach the ventricular septum (Masson's trichrome ×10). **D** Another specimen containing the bundle of His (Masson's trichrome ×10), **E** serial section showing nodal fibres reaching the summit of the ventricular septum (*arrowhead*) (H&E ×50)

No obvious findings suggesting that external force had contributed to her falling into the river were found at autopsy or by the police investigations. The heart weighed 263 g, and there were no macroscopical abnormalities. The sinus node was normal. Part of the slices of the AV junction showed two points of fasciculo-ventricular connections (so-called lower Mahaim fibres) (Fig. 2).

Case 3

A 19-year-old male student who was found in a state of cardiorespiratory arrest on the platform of a railway station. He had suffered severe brain injury, recovered following resuscitation, but the electrocardiogram continuously revealed atrial fibrillation and he died 5 days later. He had been on his way home after drinking alcohol but unfortunately, the blood alcohol level was not measured in the hospital. The deceased was 182 cm in height and weighed 73.0 kg. The autopsy findings revealed that the brain injury had probably occurred when he fell down onto the platform. The heart weighed 386 g and showed mitral valve prolapse (MVP) characterised by billowing of the posterior leaflet and chordal disarray [16]. Microscopically, myxomatous degeneration of the leaflet and chorda were evident. Localised replacement fibrosis in the superior VS and interstitial fibrosis of the AV bundle with severe stenosis of the AV node artery due to medial hypertrophy were seen. Deposition of proteoglycan was also seen in the wall of the AV node artery and conduction system (Fig. 3).

Case 4

A 48-year-old male who had drowned in the sea and had a blood alcohol level of 1.78 mg/ml. The deceased was 166 cm in height and weighed 56.0 kg. The heart weighed 333 g, and showed MVP with myxomatous degeneration. A nodular endocardial mass compatible with a friction lesion was formed at the subendocardium of the left ventricle where the posterior leaflet was macroscopically seen to be attached. Microscopically, this lesion was a fibrotic tissue-like scar without any cellular proliferation. In addition, stenosis by fibroendothelial proliferation of the intima of AV node artery with destruction of the internal elastic lamina was seen (Fig. 4). Localised replacement fibrosis was also seen at the base of the VS.

Case 5

A 51-year-old male who was found dead in the sea after he had been fishing. He had a history of syncope having occurred twice, but no cardiac abnormalities had been indicated by routine electrocardiogram examination. The deceased was 167 cm in height and weighed 50.0 kg. External examination revealed some laceration wounds which had occurred when he had fallen into the sea. Alcohol and toxicological examinations were negative.

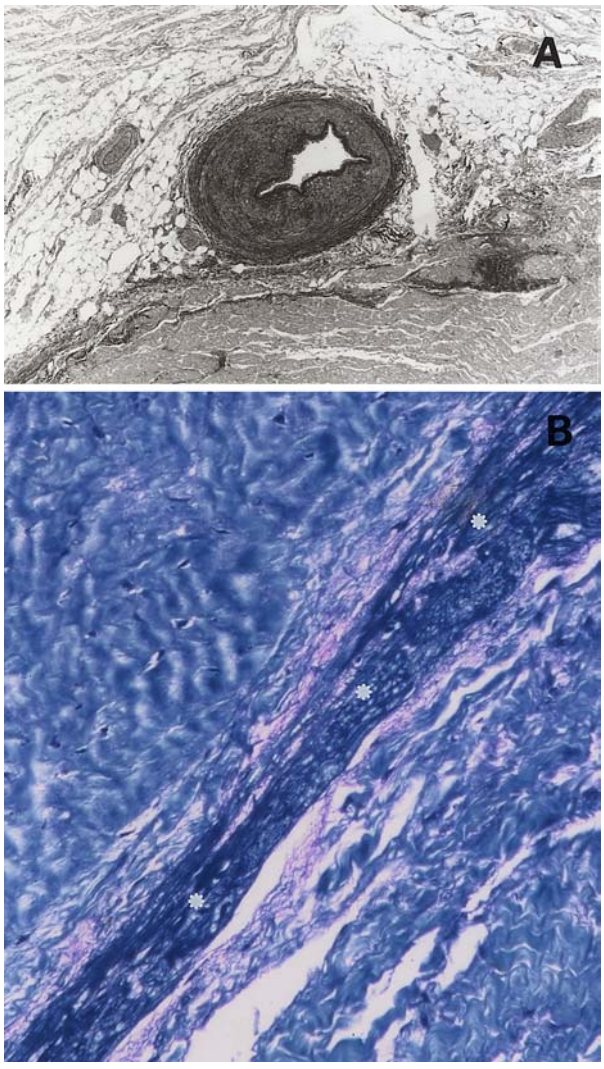

Fig. 3A–B Microscopical appearance of case 3. **A** Severe stenosis of the AV node artery (elastica-von-Gieson ×10), **B** deposition of proteoglycan in the parenchyma of the bundle of the left branch (*asterisks*) (toluidine blue ×100)

Case 6

A 73-year-old female who was found dead in the sea near the seashore and had appeared healthy prior to the accident. She was considered to have fallen into the sea whilst walking along the seashore. The deceased was 149 cm in height and weighed 36.0 kg. Alcohol and toxicological examinations were negative.

The heart weights in cases 5 and 6 were 302 and 304 g, respectively. The heart of case 6 showed an atrial septal defect (secundum type), but the other pathological features of the two hearts were very similar. There was a downward displacement of the septal tricuspid leaflet from the valvular ring, which was considered to be mild Ebstein's anomaly (ME). In the conduction system, the SA node was normal in both cases. The right-sided AV junction in both cases did not close completely, and a wide gap was formed near the AV node. Each case demonstrated fibrosis in the AV node (Fig. 5). In both cases, the proximal bundles of His were lying at the right-sided pars membranosa and were fragmented (Fig. 6). In case 6 in particular, the CFB was markedly hypoplastic, and the bundle of His was not surrounded by CFB. The fibres abnormally reached the left-sided ventricular summit, and were compressed by the right-sided ventricular myocardium.

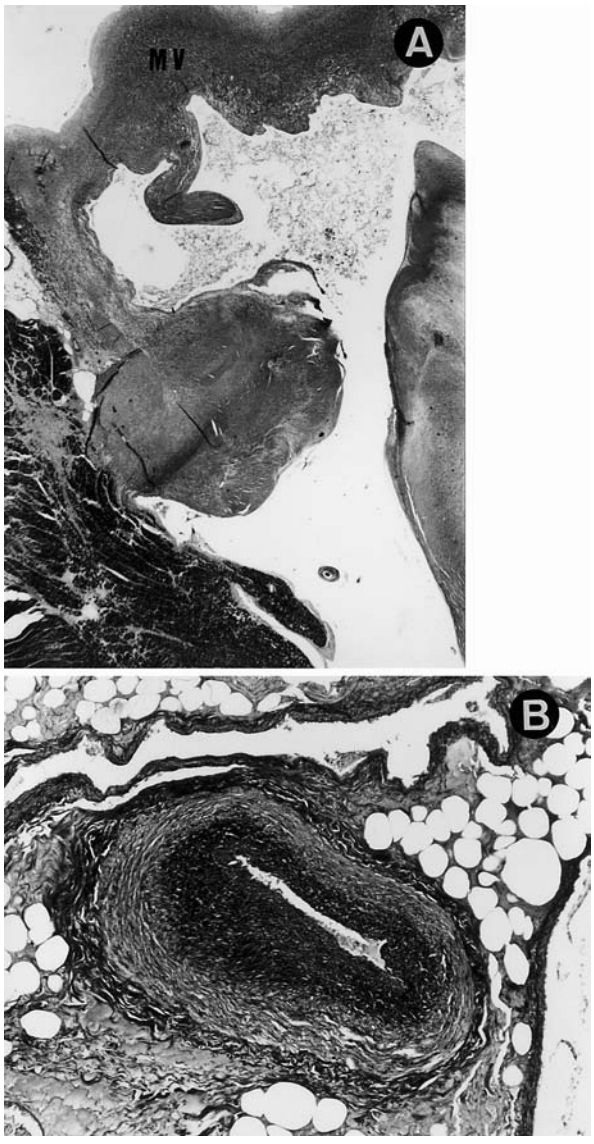

Fig. 4A–B Pathological findings of case 4. **A** Microscopical appearance of friction lesion (*MV* leaflet of the mitral valve), a nodular fibrous mass is formed at the subendocardium of the left ventricle (Masson's trichrome ×4), **B** stenosis of the AV node artery (elastica-von-Gieson ×50)

Case 7

A 47-year-old female who was found dead at the scene of a fire. The deceased was 155 cm in height and weighed 38.0 kg. There were moderate burns all over the body and the blood CO-Hb concentration was 67%. Other toxicological examinations were negative. The heart weighed 283 g and also showed ME. The SA node was normal, there was no abnormal course of the bundle of His, as seen in cases 5 and 6, however the fibres of the AV node extended below and formed an nodo-ventricular accessory pathway at the right-sided VS, due to incomplete fusion of the annulus.

Discussion

Following accidental death in Japan, autopsies tend to be performed only for a limited number of victims where the

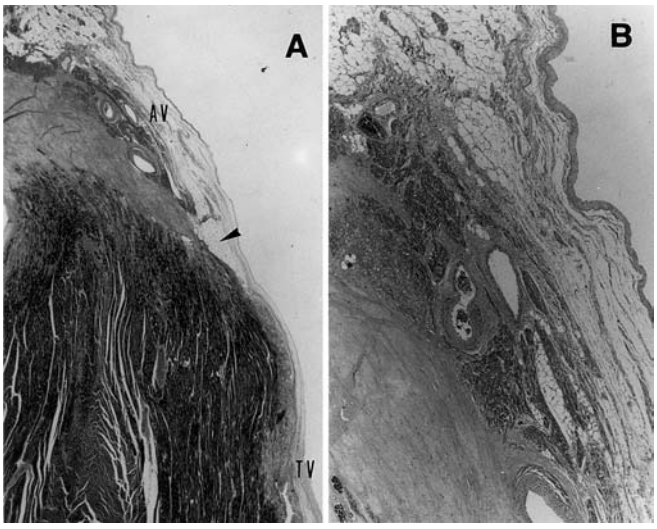

Fig. 5A–B Microscopical appearance of the AV node of case 5. **A** Downward displacement of the tricuspid valve, and a gap formation at the atrioventricular annules (*arrowhead*) (*AV* AV node, *TV* tricuspid valve) (Masson's trichrome ×4), **B** high-power view of AV node where fibrofatty infiltration is evident in the AV node (Masson's trichrome ×10)

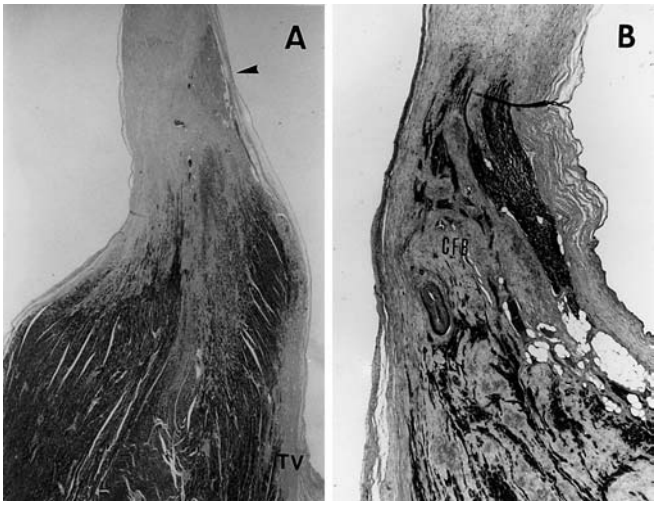

Fig. 6A–B Microscopical appearance of the bundle of His in cases 5 and 6. **A** Low-power view of case 5. The bundle of His (*arrowhead*) travels along the right side in the membranous septum. Downward displacement of tricuspid valve (*TV*) from the normal position was evident (Masson's trichrome ×4). **B** Case 6. The bundle of His (*arrowhead*) travels along the right side in the membranous septum, the central fibrous body (*CFB*) is markedly hypoplastic, and only part of the fragmented bundle travels in the CFB (Masson's trichrome ×10)

manner of death cannot be established by post-mortem police investigations. However, the precise reason for many of the accidents in the cases investigated by us had not been fully explored before this study. Retrospectively, the precise cause of the accident was not accurately identified in any of these seven cases reported here.

In 1975 Anderson et al. [17] suggested that there were two main anatomical types of Mahaim fibres: nodo-ventricular fibres which arise from the AV node as in case 1, and fasciculo-ventricular fibres, which arise from the bundle of His and bundle branches as in case 2. Some patients with Mahaim fibres have episodes of pre-excitation tachycardia with syncope, but do not usually have ventricular pre-excitation during sinus rhythm, and the resting electrocardiogram is usually normal [18]. Gallagher et al. [19] postulated that the mechanism of tachycardia is a macroreentry circuit using the nodo-ventricular fibres for the anterograde limb and the His-Purkinje system with a portion of the AV node for the retrograde limb. Referring to clinical investigations, many of the patients with this anomalous pathway had suffered some kind of arrhythmia, such as atrial fibrillation or flutter, or ventricular fibrillation [19], and in a few cases have been reported as the autopsy findings in cases of sudden death [20, 21]. Accordingly, arrhythmia with syncope might have occurred in our cases 1 and 2 and we should note these types of accessory pathway in cases of accidental death involving younger victims.

With regard to MVP, Morales et al. [22] found that dysplasia of the AV node artery, as in our cases 3 and 4, was more prevalent in MVP than in the normal control hearts. It has been reported that sudden death cases of MVP with small artery disease had occasionally experienced syncopal attack before death [23], and syncope due to arrhythmia is considered to be a risk factor of sudden death in MVP [24]. Accordingly, we consider that our cases 3 and 4 also had arrhythmogenic potential in the conduction system and we conclude that syncope due to arrhythmia may have occurred before the accidents.

A few authors reported that cases of ME have abnormal lesions in the conduction system [5, 6, 8, 21], but its significance or diagnostic criteria especially in the cases without obvious hemodynamic impairment is not clear. Our cases 5 and 6 showed abnormal location of the bundle of His that coursed in the membranous septum with fragmentation. Suarez-Mier et al. reported a case of sudden death where the bundle of His lay in the membranous septum [21] and Bharati and Lev have also reported that cases of sudden death with ME revealed fragmentation or looping of the bundle of His, as in our two cases [5, 6]. This alteration may increase automaticity, paroxysmal block and ventricular arrhythmia by producing a reentry circuit [5, 8]. We assume that the history of syncope in case 5 was caused by this lesion. Moreover, Rossi and Thiene reported three cases of ME with persistence of fatal accessory AV communications of high arrhythmogenic potentials [25]. They suggested that this accessory pathway probably underlay the pre-excitation and malignant tachycardia. This pathway is considered to be formed by a poor connection between CFB and the tricuspid ring because of a downward displacement of the septal leaflet [25]. Accordingly, we consider that arrhythmia with syncope might have occurred in our cases 5–7 and the significance of conduction system abnormalities with ME in forensic autopsies needs to be noted and discussed in further detail.

Of our seven cases, three suffered from an accident under the influence of alcohol. Concerning the correlation

between alchohol and unnatural death, some authors have suggested that alcoholics could possibly play a greater role than previously detected [26, 27]. Moreover, many authors have reported alcohol-induced ischemia [28], atriopathy [29], and clinical or preclinical functional disturbances in the heart [30, 31]. So we estimate that a person with conduction system abnormalities as in our cases may be more susceptible to arrhythmia after alcohol intake than normal individuals with no abnormalities.

The significance of conduction system abnormalities as a cause of the accidents remains unclear. However, in our investigations, some cases of accidental death had conduction system abnormalities that may have caused syncopal attacks. We therefore consider that a full investigation of the cardiac conduction system in accidental deaths may be significant for evaluating the arrhythmogenic potential in the heart in the same way as immunohistochemistry [32] and the TUNEL method [33].

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