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Original Article

Manifestations of bodily isomerism

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ABSTRACT

We report the findings present in 49 postmortem specimens from patients with so-called heterotaxy, concentrating on those found in the extracardiac systems of organs. Also known as bodily isomerism, we suggest that it is important to segregate the syndromes into their isomeric subtypes to be able to make inferences regarding likely extracardiac and intracardiac findings to allow for proper surveillance. We demonstrate that this is best done on the basis of the atrial appendages, which were isomeric in all the hearts obtained from the specimens available for our inspection. The abdominal organs do not demonstrate isomerism, and they show variable features when compared to the isomeric atrial appendages.

1. Introduction

Occurring in approximately 1 in 10,000 live births, so-called heterotaxy is known to be characterized by mirror imagery of the bronchi in the same individual, in other words bronchial isomerism [1–6]. It was also demonstrated some time ago that, when assessed on the basis of the extent of the pectinate muscles relative to the atrioventricular junctions, there is also evidence of isomerism of the atrial appendages [7]. Not all authorities, however, accept the notion that isomerism also exists within the heart [8]. Moreover, although the abdominal organs are not located within their expected position in the setting of heterotaxy, there is minimal evidence of abdominal isomerism. The presence of the overall abnormal anatomical findings, nonetheless, has significant functional implications, not least because splenic function is known to be disturbed even in the setting of multiple spleens [9]. Intestinal malrotation is also known to be an associated problem [10–19].

An appreciation of the relationships between the findings in the thoracoabdominal organs and the intracardiac findings can allow for proper surveillance and, when possible, for early intervention. Proper understanding, however, requires segregation of isomerism, or heterotaxy, into its subtypes. So as to assess the relationships between cardiac and noncardiac findings, therefore, we have examined archived postmortem specimens diagnosed on the basis of appendage morphology but shown subsequently to be obtained from patients known to have so-called heterotaxy. This has permitted us to combine the information provided by examination of the specimens with that obtained from the original postmortem reports. In this way, we have been able to characterize the cardiac findings in the subsets of right as opposed to left isomerism and to determine the associations and differences between these findings with those in the remaining systems of organs. We discuss here how best to describe the findings in the various systems of organs so as most efficiently to convey the functional implications of the pertinent cardiac anatomic data.

2. Methods

Using the sequential segmental approach, we analyzed the hearts, and thoracoabdominal organs when available, obtained from patients known to have so-called heterotaxy. The autopsy material is held in the Farouk S. Idriss Cardiac Registry at the Ann & Robert H. Lurie Children's Hospital in Chicago, IL. Specimens had been archived from the 1940s and continue to be added in the present day. Bronchial morphology was assessed on the basis of the length of the bronchi, also using the pattern of branching of the bronchial tree relative to the pulmonary arteries. Short and eparterial bronchi were considered to be morphologically right, while long and hyparterial bronchi were considered to be morphologically left [3–6]. We also assessed the lobation of the lungs, taking trilobed lungs to be morphologically right and bilobed

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lungs to be morphologically left. Within the heart, we used the extent of the pectinate muscles relative to the atrioventricular junctions to distinguish between morphologically right and left atrial appendages, as described previously by Uemura and associates [7]. This approach follows the principle established by Van Praagh and his colleagues and dubbed the morphological method [20], namely, that structures within the heart should be defined on the basis of their most constant components and not according to other features that themselves might have variable. We then assessed the connections of the systemic and pulmonary veins, the atrial septum, the atrioventricular junctions, the ventricular mass, the ventriculoarterial junctions, and the arrangement of the intrapericardial arterial trunks.

We also took note of additional extracardiac findings, utilizing the reports from the original postmortem examination when the archived organs other than the heart were not available. The spleen was identified as being absent, multiple, or single. When multiple spleens were present, we ascertained whether they were left or right sided. With regard to the stomach, liver, pancreas, and gallbladder, each organ was again described as being either right, left, or midline. We took particular note of evidence for intestinal malrotation, specifically the presence of a short mesentery. The presence or absence of renal anomalies, abnormalities of the reproductive system anomalies, and cerebral anomalies were also noted. These were coded as either being present or absent, with specific details obtained when available. Clinical data contained in the original reports were also used to determine the presence or absence of bacteremia or fungemia documented by cultures immediately prior to death or done at the time of postmortem examination. We performed chi-square analysis for variables of interest, including bacteremia or fungemia, fatty liver, hepatic fibrosis, intestinal malrotation, and brain anomalies. Chi-square analysis was also performed to compare categorical variables, using SPSS Version 20.0 (Chicago, IL). Frequencies are reported as percentages or fractions.

3. Results

We had access to a total of 49 specimens obtained from patients shown subsequently to have so-called heterotaxy. The initial diagnosis of cardiac isomerism had been made by assessing the extent of the pectinate muscles within the atrial appendages relative to the right and left atrioventricular junctions (Fig. 1). In this way, we were able to show that 12 specimens (24%) showed evidence within the heart of left isomerism (Fig. 1), with 37 (76%) showing evidence of right isomerism (Fig. 2 and Table 1).

3.1. Left isomerism

We summarize the cardiac findings in Table 1. Details of these findings, along with those obtained from specimens held in two additional archives, are also described in detail elsewhere. In brief, cardiac findings in the setting of isomeric left appendages included the presence of either separate or common atrioventricular junctions. Several of the hearts with a common atrioventricular junction had separate right and left atrioventricular valves, in other words ostium primum defects (Fig. 1). The majority of the hearts possessed a coronary sinus and showed interruption of the inferior caval vein with azygos continuation, along with symmetrical drainage of the pulmonary veins. Most had concordant ventriculoarterial connections with spiraling arterial trunks (Table 1). We failed to find an abnormal arrangement of the coronary arteries in any patient with left isomerism. Evidence of myocardial ischemia was noted in 14.3%, albeit with no evidence of coronary thrombosis in any patient. Endocardial or myocardial fibrosis was also observed in 14.3% (Table 2). In all the hearts with left isomerism, the bronchial morphology was also isomeric left (Fig. 3). In the majority, bronchial morphology was concordant with pulmonary lobation, although one patient had lungs bilaterally with solitary lobes. Neither thrombosis of the pulmonary arterial system nor evidence if tracheobronchitis was encountered (Table 2).

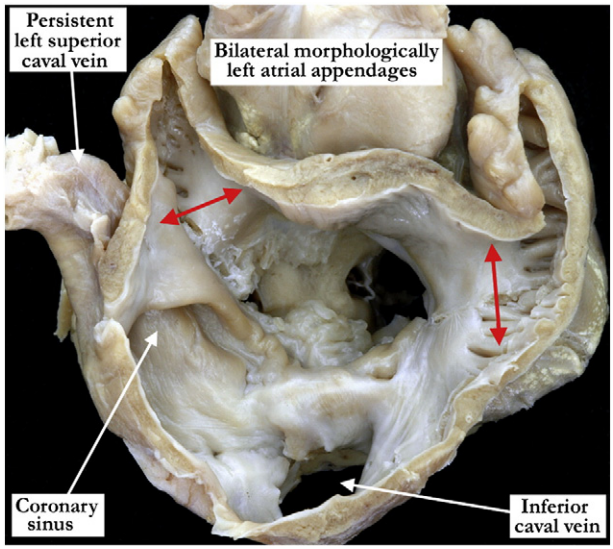

Fig. 1. A heart from a patient with left isomerism viewed from the base of the heart. Note the atrial appendages are morphologically left bilaterally. The appendages are finger-like with a narrow attachment to the venous component (double-headed red arrows). The pectinate muscles are confined to the appendages and do not extend around the atrioventricular junction with a smooth vestibule on both sides. No Eustachian valve is appreciated in this heart. A persistent left superior caval vein drains to the coronary sinus. There is also a common atrioventricular junction with tissue connecting the superior and inferior bridging leaflets across the crest of the ventricular septum, resulting in two orifices.

In nine tenths of the patients, multiple spleens were present (Fig. 4). These were left sided in x patients and right sided in the remainder. In one patient, however, the spleen was absent. No data regarding splenic function had been listed at the time of postmortem examination or reported in the clinical summaries (Table 2). The stomach was left sided in seven tenths of the cohort, with the liver positioned in the midline in two fifths, right sided in two fifths, and left sided in one fifth. The gallbladder was right sided in three fifths and left sided in the remainder. The pancreas was described as being left sided in three fifths and right sided in the remainder (Table 2). Another one sixth was found to have biliary atresia (Table 2). Intestinal malrotation was present in one third, although volvulus was neither present nor described as being present during life in any patient (Table 2). Abnormal thymic involution had been noted in one sixth, but no evidence was found for brain anomalies or anomalies of the reproductive or renal systems (Table 2).

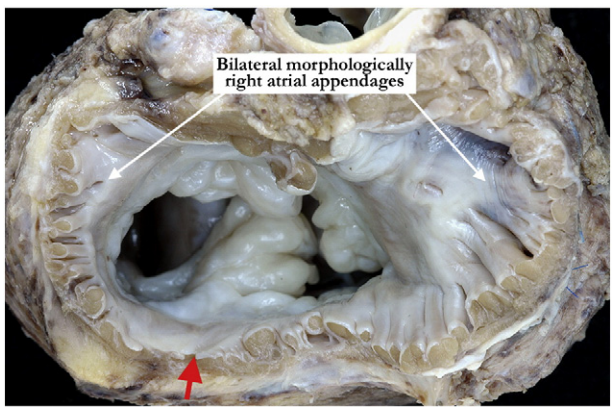

Fig. 2. This heart with isomerism of the right atrial appendages is viewed from the base of the heart. The atrial appendages are bilaterally morphologically right. Note the pectinate muscles extending around the atrioventricular junction to the crux of the heart (red arrow).