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Double-Sided Superior Vena Cava: Developmental Considerations Associated with the Thymic Veins

Vena Cava Superior de Doble Cara: Consideraciones de Desarrollo Asociadas con las Venas Tímicas

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SUMMARY: The superior vena cava is usually located only on the right side, but persistence of the left superior vena cavais observed in about 0.3 to 0.5 % of adults. A routine dissection of the cadaver of a 91-year-old Japanese female, whose cause of death was sepsis due to cholecystitis, was performed at Nagasaki University and revealed a double-sided superior vena cava. On the right side, the superior vena cava opened to the right atrium, while on the left, it opened into the extended coronary sinus. Veins in the left head, neck and upper limb regions joined to form the persistent left superior vena cava, with eventual drainage into the expanded coronary vein. An anastomosing branch occurred between each superior vena cava, and two thymic veins opened to the anastomosing branch. The azygos vein in the azygos venous system opened into the right superior vena cava, whereas a hemi-azygos vein opened into the azygos vein. The accessory hemi-azygos vein also opened into the azygos vein and opened cranially into the left superior vena cava. The left supreme intercostal vein also opened into the left superior vena cava. Several studies have reported a persistent left superior vena cava and the various considerations for its occurrence. Here, we propose a new hypothesis for the embryonic development of the persistent left superior vena cava with the thymic vein. This hypothesis essentially states that the left brachiocephalic vein fails to mature due to inadequate venous return from the thymic vein during the embryonic period, and the left superior vena cava then remains to maintain venous return from the left head, neck and upper limb. We also discuss the clinical significance of the persistent left superior vena cava.

KEY WORDS: Persistent left superior vena cava; Thymic vein; Azygos venous system; Anatomical variation.

INTRODUCTION

The superior vena cava (SVC) is usually present only on the right side postnatally (Standring, 2016). Generally, the right SVC is formed by a joining of the right and left brachiocephalic veins, which drain the venous return from the head, neck and bilateral upper limbs to the right atrium (Moore *et al*., 2013). However, several reports and reviews have appeared regarding persistenceof the left superior vena cava (PLSVC) (Sakamoto *et al*., 1993; Uemura *et al*., 2009; Notsu *et al*., 2020). These reports have indicated an incidence of the PLSVC of about 0.3 to 0.5 %, with an increase to about 3 % in patients with congenital heart disease (Perles *et al*., 2013). In recent years, advances in imaging techniques have resulted in more case reports of the PLSVC in patients from a variety of clinical departments, including cardiology, radiology and anaesthesiology (Park *et al*., 2017; Savu *et al*., 2020; Chen *et al*., 2021). These discoveries draw attention to the necessity of providing more detailed anatomical information about the PLSVC.

The present study involved a detailed gross anatomical investigation of the double-sided SVC, heart, and the azygos venous system in a Japanese female cadaver. We report details of the PLSVC and introduce a new consideration regarding the relationship between the PLSVC and thymic vein during the embryonic process. We also describe the clinical implications of the PLSVC.

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CASE REPORT

During routine dissection of the cadaver of a 91-year-old formalin-preserved Japanese female whose cause of death was sepsis due to cholecystitis, a double-sided SVC was detected.

We performed a further dissection of the bilateral SVCs, the veins entering into the SVCs, the heart and the azygos venous system in this cadaver. We measured the structure lengths and external diameters (EDs) with a Mitutoyo vernier calliper (Mitutoyo, Kanagawa, Japan) with an accuracy of 0.1 mm.

We obtained comprehensive informed consent for the dissection and analysis from the individual while living and postmortem from the family. Ethical committee approval was not required because this study involved treatment of only one case report.

One SVC was identified on each side (Figs. 1A, 1B, 2A, and 2B). The left subclavian vein (12.2 mm ED), the left internal jugular vein (3.5 mm ED) and the anterior jugular vein (6.9 mm ED, with the external jugular vein flowing into the anterior jugular vein) merged and entered the PLSVC (length 65.1 mm). The PLSVC opened into the coronary sinus (the ED of the ostium was 21.5 mm) (Fig. 3). Besides the PLSVC, the great cardiac vein, middle cardiac vein and small cardiac vein entered the coronary sinus (Fig. 3). The anterior cardiac vein entered into the right auricle. The internal diameter of the coronary sinus ostium leading to the right atrium was 22.7 mm. The right subclavian vein (11.7 mm ED) and the right internal jugular vein (12.1 mm ED) united to form the right SVC (length 62.7 mm). The right SVC opened into the right atrium (the ED of the opening was 22.7 mm).

A single anastomosing branch (length, 40.0 mm; ED of left side, 3.8 mm; ED of right side, 4.8 mm; ED at the centre, 3.0 mm) was present between the bilateral SVCs (Figs. 2A and 2B). The height of the anastomosing

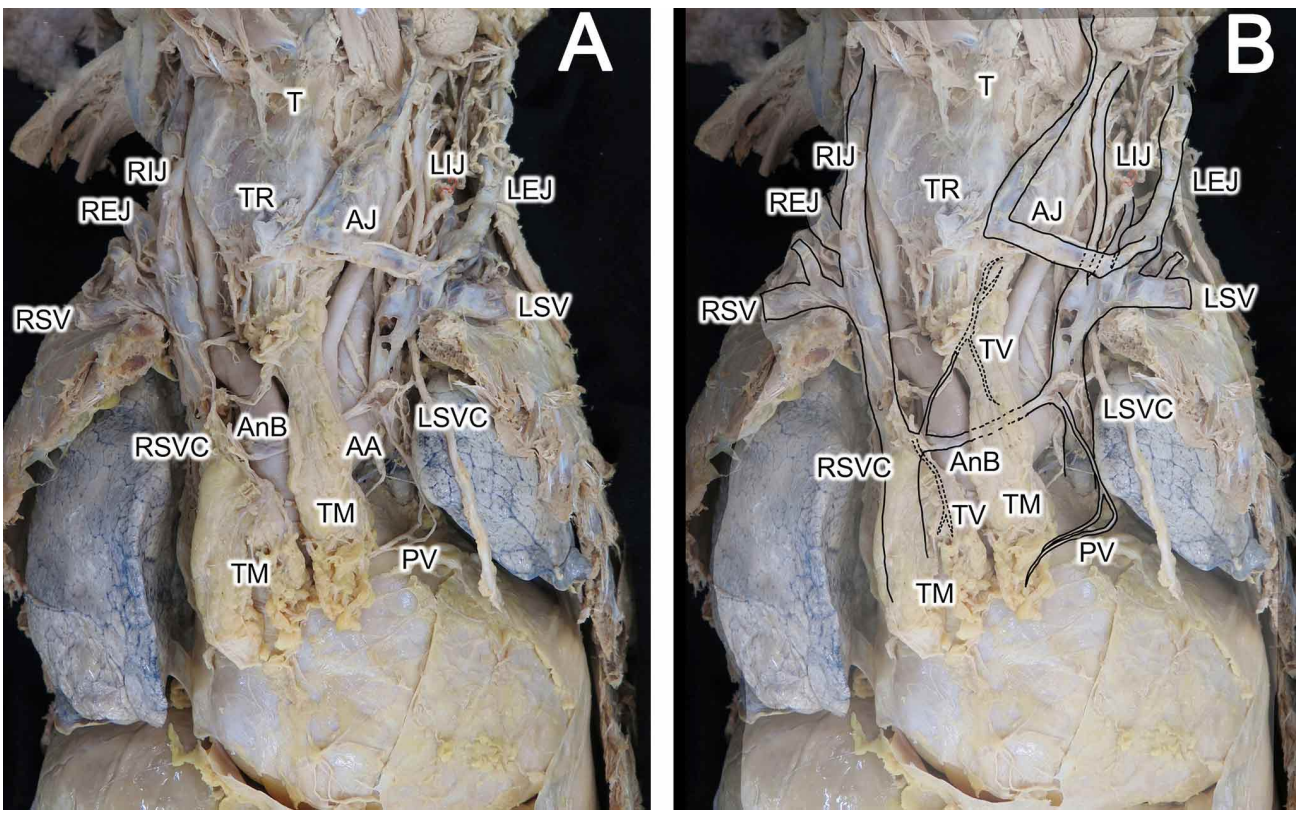

Fig. 1. Photograph (A) and that with schematic illustration (B) showing the anterior view of the mediastinum. Abbreviations: AA, aortic arch; AJ, anterior jugular vein; AnB, anastomosing branch; LEJ, left external jugular vein; LIJ, left internal jugular vein; LSV, left subclavian vein; LSVC, left superior vena cava; PV, pericardial vein; REJ, right external jugular vein; RIJ, right internal jugular vein; RSV, right subclavian vein; RSVC, right superior vena cava; T, trachea; TM, thymus; TR, thyroid; TV, thymic vein.

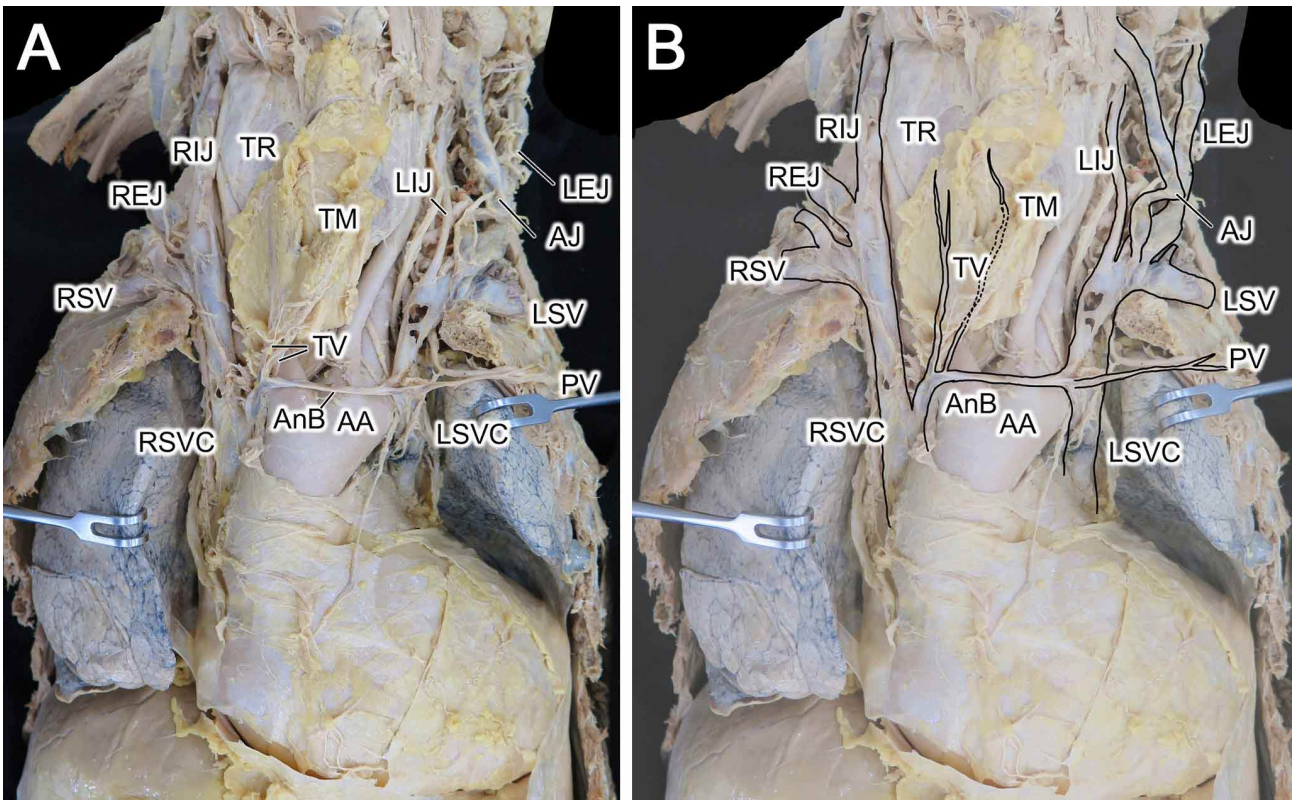

Fig. 2. Photograph (A) and that with schematic illustration (B) showing the anterior view of the mediastinum. The thymus was flipped cephalad. Abbreviations: AA, aortic arch; AJ, anterior jugular vein; AnB, anastomosing branch; LEJ, left external jugular vein; LIJ, left internal jugular vein; LSV, left subclavian vein; LSVC, left superior vena cava; PV, pericardial vein; REJ, right external jugular vein; RIJ, right internal jugular vein; RSV, right subclavian vein; RSVC, right superior vena cava; sub, subcostal vein; TM, thymus; TR, thyroid; TV, thymic vein.

branch was higher on the left than on the right side. The right thymic vein (1.3 mm ED) and the left thymic vein (1.4 mm ED) flowed into the right end of the anastomosing branch at 11.2 mm and 11.4 mm, respectively (Figs. 2A and 2B). The PLSVC opened to the coronary sinus (the ED of the ostium was 21.5 mm). No shunt was evident in the atrial or ventricular septa.

As shown in Figures 4A and 4B, the right first to eleventh intercostal veins, the right subcostal vein, and the left ninth intercostal vein directly entered the azygos vein (AV), which then opened into the right SVC (11.0 mm ED). The left tenth intercostal vein, eleventh intercostal vein, and left subcostal vein opened into the hemi-azygos vein (HAV). The HAV opened into the AV in front of the ninth vertebral body. The left second to eighth intercostal veins joined to form the accessory hemi-azygos vein (AHAV), which then opened into the AV in front of the eighth vertebral body. The cephalad AHAV opened to the left SVC (3.2 mm ED). The left supreme intercostal vein opened into the left SVC.

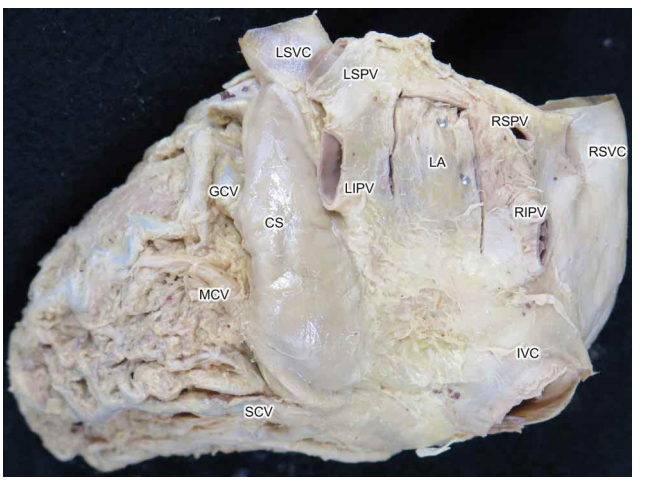

Fig. 3. Photograph showing the posterior view of the heart.Abbreviations: CS, coronary sinus; GCV, great cardiac vein; IVC, inferior vena cava; LA, left atrium; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; LSVC, left superior vena cava, MCV, middle cardiac vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein; RSVC, right superior vena cava; SCV, small cardiac vein.

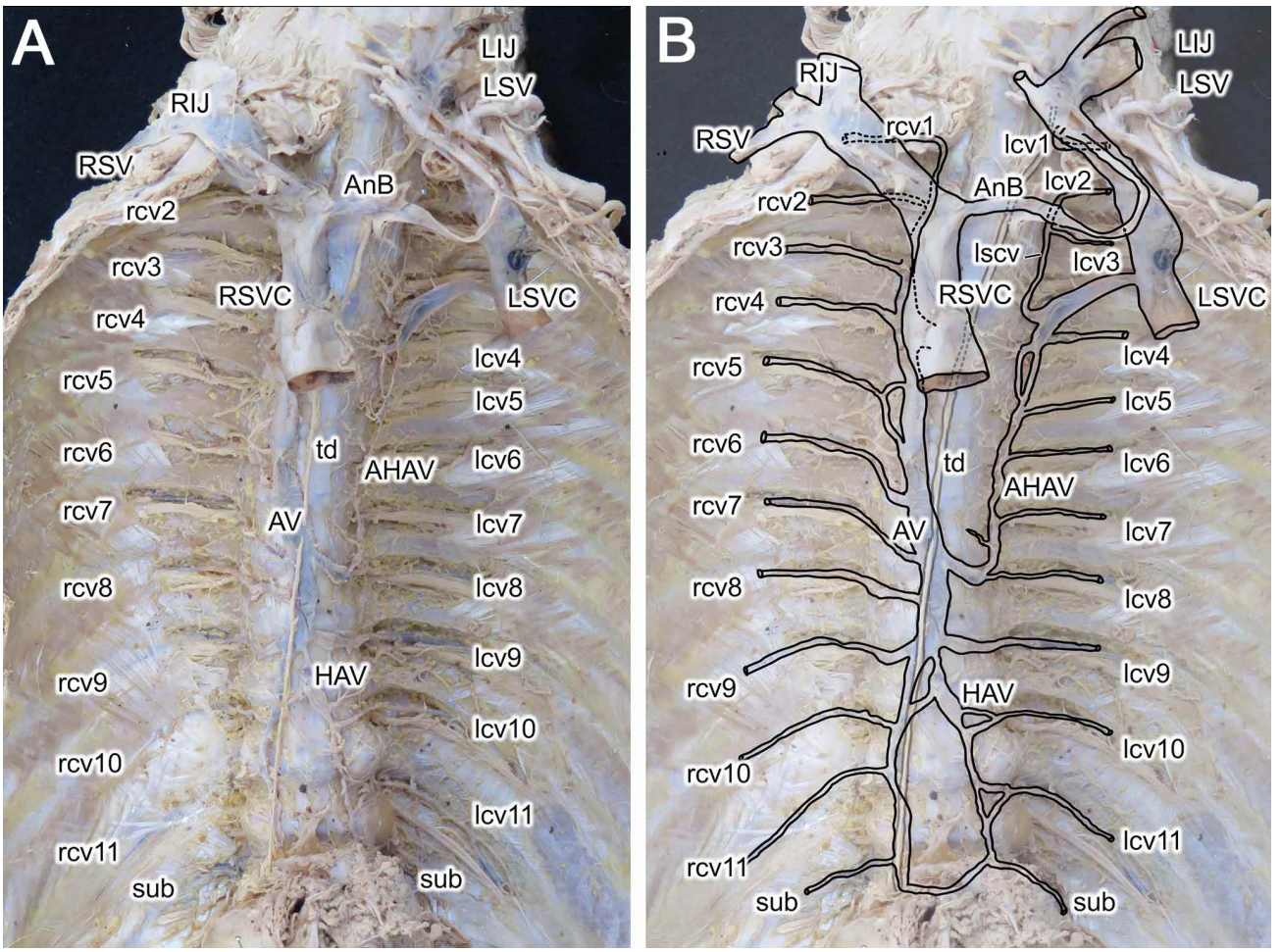

Fig. 4. Photograph (A) and that with schematic illustration (B) showing the azygos venous system. Abbreviations: AHAV, accessory hemi-azygos vein; AnB, anastomosing branch; AV, azygos vein; HAV, hemi-azygos vein; lcv, left intercostal vein;lscv, left superior intercostal vein; LSV, left subclavian vein; LSVC, left superior vena cava; rcv, right intercostal vein; RIJ, right internal jugular vein; RSV, right subclavian vein;sub, subcostal vein; td, thoracic duct.

DISCUSSION

The PLSVC is the most common thoracic venous anomaly, with an incidence of approximately 0.3–0.5 % in healthy adults. Several classifications have been suggested for the PLSVC (McCotter, 1916; Nandy & Blair Jr., 1965; Yamadori & Takashima, 1966; Takenoshita, 1986; Uemura *et al*., 2012). According to Uemura *et al*. (2012), based on the anastomosis between the left and right SVCs and the azygos venous system structure, our case would be classified as IIa-P type. This type was the most frequent (20.8 %) among the 53 PLSVC cases classified by Uemura *et al*. (2012).

Zhivadinovik *et al*. (2016) studied 100 cadavers and reported a coronary sinus ostium diameter of 8.1 ± 1.51 mm. This diameter in our case was 22.9 mm, which was significantly larger than usual. The reason for this is that the normal coronary sinus receives only venous return from the coronary veins, whereas, in our case, the coronary sinus received venous return from the left head, neck and upper limb via the PLSVC, in addition to the coronary veins.

In the azygos venous system of the present case, the left ninth intercostal vein entered directly into the AV, while the HAV collected the left tenth to 11th intercostal and subcostal vein and entered into the AV. By contrast, the AHAVcollected the left second to eighth intercostal veins, as well as communicating with the AV at the level of the eighth vertebra. The cephalad AHAV also entered the

PLSVC. The left supreme intercostal vein also opened into the PLSVC (Fig. 4A, 4B). These results indicated that the relatively leftward azygos venous system remained, as reflected in the symmetry of the venous system in the embryonic stage.

During the fourth week of embryonic development, the cardinal veins form a symmetrical venous system. The right and left anterior and posterior cardinal veins are responsible for venous return in the cephalic and caudal parts of the embryo, respectively. The anterior and posterior cardinal veins unite before entering the heart to form the common cardinal veins. These common cardinal veins then enter the right and left sinus horns. The right and left SVCs are formed by the ipsilateral common cardinal vein and the proximal part of the anterior cardinal vein.

The thymus arises from the endoderm of the bilateral third pharyngeal pouches at the end of the fourth week of embryonic development. It descends towards the mediastinum from the seventh to the eighth week of the embryo (Hamilton *et al*., 1962). During the eighth week, the anastomosing branch of the left and right anterior cardinal veins arises from the blood flow of the thymic veins (Keibel & Mall, 1912; Cameron, 1915). This anastomosing branch usually develops into the left brachiocephalic vein, which collects blood flow from the left head, neck and upper limb. The LSVC then gradually disappears under normal developmental conditions. The terminal portion of the left posterior cardinal vein, which enters into the left brachiocephalic vein, remains as the left superior intercostal vein and receives venous return from the left second and third intercostal spaces (Hamilton *et al*.).

Di Marino *et al*. (1987) reported that, among the postnatal thymic veins, only the vein that flows into the left brachiocephalic vein is large, often reaching an external diameter of 3 mm.Two thymic veins were identified in this case, both less than 1.5 mm ED. They were located on the right side of the anastomotic branch, between the bilateral SVCs. These veins were considered to represent the middle of the process described by Keibel & Mall, in which the anastomotic branch grows after receiving the thymic vein and finally becomes the left brachiocephalic vein.

As indicated above, the LSVC is formed by the left common and the proximal part of the anterior cardinal veins and then disappears, as it should. The following reason was proposed to explain why the LSVC did not disappear: the anastomosing branch derived from the thymic vein did not develop into the brachiocephalic vein due to poor development of the thymus and thymic vein. This developmental failure of the anastomotic branch caused the LSVC to take over the venous return from the left head, neck, and upper limb; normally, this should have been channelled to the right. As a result, the LSVC had no opportunity to disappear and instead persisted.

The PLSVC is commonly incidentally diagnosed during central venous catheter insertion or pacemaker implantation on the left side (Park *et al*.). The presence of the PLSVC requires the clinician to take care when inserting central venous catheters, pacemakers, and Swan-Ganz catheters (Goyal *et al*., 2008). Definitive diagnosis of thePLSVC is achieved by coronary sinus dilation and confirmed by echocardiography, multi-slice computed tomography (CT) or magnetic resonance imaging (MRI). Multi-slice CT and MRI are particularly useful because they provide a thorough visualisation of the PLSVC. In cases requiring catheter placement via the PLSVC, these imaging data are needed to provide an accurate vascular image prior to the procedure.In intrathoracic surgery involving the lungs, oesophagus, mediastinum and heart, a clear recognition of the course of the left SVC and its associated azygos venous system would increase the safety of the operation.

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OGAMI-TAKAMURA, K. ; SAIKI, K.; ENDO, D.; MURAI, K.; NISHI, K. & TSURUMOTO, T. Vena cava superior de doble cara: consideraciones de desarrollo asociadas con las venas tímicas. *Int. J. Morphol., 40(1)*:24-29, 2022.

RESUMEN: Usualmente la vena cava superior se localiza solo en el lado derecho, sin embargo en aproximadamente 0,3 a 0,5 % de los adultos se observa la persistencia de la vena cava superior izquierda. En la Universidad de Nagasaki se realizó una disección de rutina del cadáver de una mujer japonesa de 91 años, cuya causa de muerte fue sepsis debido a una colecistitis. El cuerpo presentaba una vena cava superior doble. En el lado derecho, la vena cava superior llegaba al atrio derecho, mientras que en el lado izquierdo drenaba al seno coronario. Las venas de las regiones de la cabeza, el cuello y del miembro superior izquierdo formaban la vena cava superior izquierda persistente, con drenaje hacia la vena coronaria. Se observó una rama anastomótica entre cada vena cava superior y dos venas tímicas drenaban a la rama anastomótica. La vena ácigos drenaba a la vena cava superior derecha, mientras que una vena hemiácigos drenaba a la vena ácigos. La vena hemiácigos accesoria también drnaba en la vena ácigos y cranealmente lo hacia la vena cava superior izquierda. La vena intercostal suprema izquierda drenaba en la vena cava supe-

rior izquierda. Varios estudios han informado una vena cava superior izquierda persistente y las diversas consideraciones para su aparición. Aquí, proponemos una nueva hipótesis para el desarrollo embrionario de la vena cava superior izquierda persistente con la vena tímica, que esencialmente establece que la vena braquiocefálica izquierda no se dearrolla debido a un retorno venoso inadecuado de la vena tímica durante el período embrionario, y se mantiene la vena cava superior izquierda para el retorno venoso de la cabeza, el cuello y el miembro superior izquierdo. Además se informa de la importancia clínica de la persistencia de la vena cava superior izquierda.

PALABRAS CLAVE: Vena cava superior izquierda persistente; Vena tímica, sistema venoso ácigos; Variación anatómica.

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