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Situs inversus totalis with Aberrant Left Subclavian Artery: A Case Report

Situs inversus totalis con Arteria Subclavia Izquierda Aberrante: Informe de un Caso

Dong Jun Kim[1]; Yujin Kim[1]; Hyewon Hu[2]; Min Suk Chung[3] & Ji-Hyun Lee[4]

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SUMMARY: *Situs inversus totalis* is a rare congenital condition characterized by the reversed positioning of internal organs. It can occur in various forms, including complete or partial reversal, and is often discovered accidentally through medical imaging or postmortem examination. In some cases, it may also be accompanied by vascular anomalies. This report describes a rare instance of *Situs inversus totalis* in an 83-year-old female cadaver (cause of death: multiple organ failure) during a dissection conducted by a medical student. The cadaver showed mirrored positioning of the thoraco-abdominal organs and blood vessels, along with variations in the vessels. Notable additional anomalies included the presence of an aberrant right subclavian artery and a bicarotid trunk, the absence of a brachiocephalic trunk and a recurrent laryngeal nerve. The rare anatomical anomaly of *Situs inversus totalis*, which involves the mirror-image transposition of the organs, is discussed with the additional anomalies highlighted. Thus, this report is expected to enhance the understanding of the correlation between *Situs inversus totalis* and associated anomalies and to provide useful information for accurate diagnosis and relevant surgical procedures.

KEY WORDS: *Situs inversus totalis*; Abnormalities; Subclavian artery; Recurrent laryngeal nerve.

INTRODUCTION

Situs inversus totalis is a congenital anomaly that results in the reversal of the normal positioning of the internal organs. It occurs in approximately 0.01 % of the population and can manifest in different forms, including *Situs inversus totalis* with levocardia, dextrocardia, *Situs inversus totalis* incompletus, and *Situs inversus totalis* (SIT) (Sun *et al*., 2013).

SIT, in which all internal organs are reversed, affects all thoracic and abdominal structures. Consequently, the heart is situated on the right side of the thorax, with its apex oriented towards the right instead of the left. The stomach and spleen are located on the right side of the abdomen, whereas the liver and gallbladder are on the left side. Additionally, the positional relationships between the blood vessels, nerves, lymphatic vessels, and intestines are reversed. Nevertheless, functional problems are rare because of the unchanged connections between organs. The life expectancy of patients with *Situs inversus totalis* is normal, and in 90–95 % of cases, the heart is anatomically normal (Marta *et al*., 2003). *Situs inversus totalis* does not typically affect the health of a patient. However, in some cases, Kartagener's syndrome, a type of primary ciliary dyskinesia, may result in respiratory difficulties. Although uncommon, heart or lung problems may also manifest in individuals with this condition (Mishra *et al*., 2012).

Situs inversus totalis is often diagnosed incidentally through medical imaging such as chest radiography, electrocardiography, or ultrasound scans. In other cases, it may be reported after an autopsy or dissection of a cadaver. It is frequently accompanied by vascular anomalies of the heart or abdomen (Kamitani *et al*., 2005). These anomalies may explain clinical symptoms, such as dysphagia or dyspnea, which cannot be attributed to other medical causes. Furthermore, inadequate precautions during surgical

[1] Ajou University School of Medicine, Suwon, Republic of Korea.
[2] Division in Anatomy and Developmental Biology, Department of Oral Biology, Human Identification Research Institute, BK21 FOUR Project, Yonsei University College of Dentistry, Seoul, Republic of Korea.
[3] Department of Anatomy, Ajou University School of Medicine, Suwon, Republic of Korea.
[4] Department of Anatomy and Acupoint, College of Korean Medicine, Gachon University, Seongnam, Republic of Korea.

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procedures, particularly in cases involving cardiovascular anomalies or atypical anatomical structures, can increase the surgical risks. Therefore, a comprehensive understanding of the condition is crucial (Koo *et al*., 2019).

In this report, we present a case of SIT featuring the absence of a brachiocephalic trunk, an aberrant left subclavian artery (ALSA, also known as arteria lusoria), a bicarotid trunk, and a left non-recurrent laryngeal nerve (NRLN). This report discusses the anatomical aspects of vascular anomalies and SIT, aiming to enhance the understanding of the correlations between them. These findings will improve our understanding of this rare condition and provide valuable information for diagnostic techniques and improving the relevant surgical procedures and treatment approaches.

CASE REPORT

The present study reports a case of SIT identified during the dissection of a Korean female cadaver in a gross anatomy practice course for medical students. The cadaver was 83 years old and the cause of death was multiple organ failure. No surgical history or serious pathological conditions were noted during the examination.

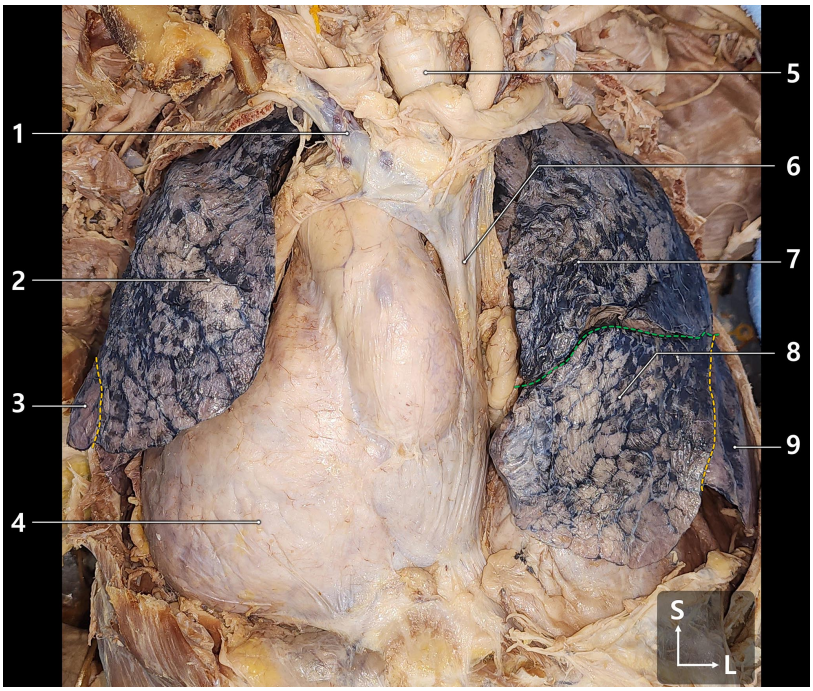

Fig. 1 A view of the thoracic organs with *Situs inversus totalis*. The mirrored positions of the heart (covered by the pericardium) and lungs, as well as reversed large blood vessels are observed. 1; right brachiocephalic vein, 2; superior lobe of right lung, 3; inferior lobe of right lung, 4; heart (pericardium), 5; trachea, 6; superior vena cava, 7; superior lobe of left lung, 8; middle lobe of left lung, 9; inferior lobe of left lung; S; superior, L; left, The orange and green dotted lines represent the oblique and horizontal fissures of the lungs, respectively.

Abbreviations. ALSA: aberrant left subclavian artery NRLN: non-recurrent laryngeal nerve SIT: *Situs inversus totalis*

Anomalies of the Chest Organs. After removing the anterior thoracic wall, a reversed heart enclosed in the pericardium was observed. The heart was skewed towards the right, with its apex also oriented in the same direction. The superior vena cava entered the upper left side of the heart, resulting in the right brachiocephalic vein being longer than the left (Fig. 1). After removing the pericardium, it was observed that the left atrium and ventricle were situated anteriorly within the heart. The pulmonary trunk originated from the left ventricle, and the aorta originated from the right ventricle of the heart. The ascending aorta ran towards the right side of the body. The left coronary artery arose from the ascending aorta and ran downward and backward, whereas the right coronary artery originated from the ascending aorta and was divided into the anterior interventricular and circumflex branches (Fig. 1).

The lungs were also in a mirrored position. The left lung was divided into three lobes by the horizontal and oblique fissures, and the right lung was divided into two lobes by the oblique fissure (Fig. 1). The positional relationship between the large vessels and bronchi in the lung hilum was also mirrored. The right pulmonary artery located above the bronchus, and the left pulmonary artery situated anteriorly and inferiorly to the bronchus (Fig. 2).

Additional variations were observed in the vessels. The most notable arterial variation of this cadaver was the presence of a short bicarotid trunk and an ALSA. The bicarotid trunk is a condition where the common carotid arteries of both sides originate from a single common origin on the aortic arch, instead of originating separately (Fig. 2 A, C). Thereby the ALSA originated directly from the posterior aspect of the aortic arch without the brachiocephalic artery. Then the ALSA crossed the midsagittal plane, passing posteriorly to the esophagus and trachea, and extended towards the left upper limb (Fig. 2 B, D). The veins were also mirrored, with the azygos vein draining into the superior vena cava on the left side of the heart through the azygos arch.

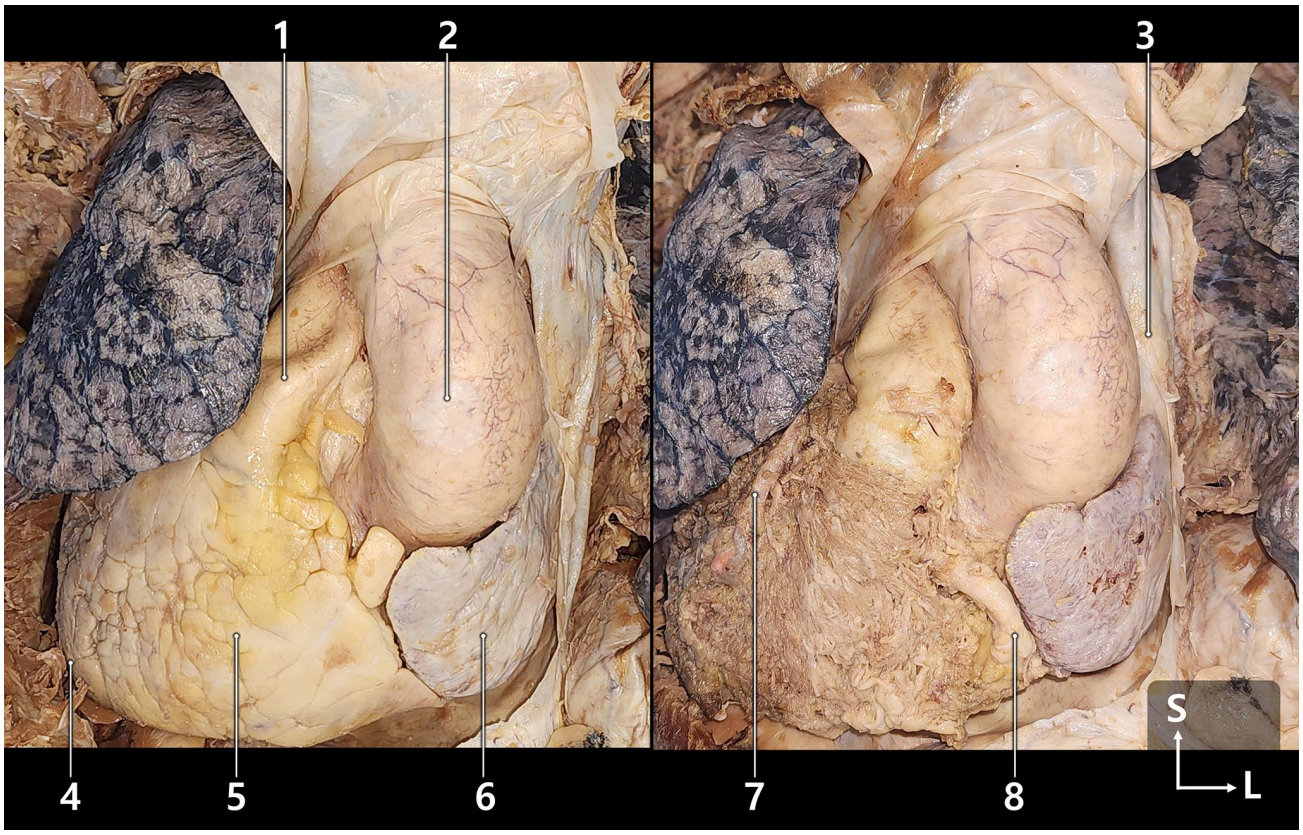

Fig. 2. The view of the heart showing the apex directed to the right, and the left atrium and left ventricle covered by the epicardium (which was originally the right atrium and right ventricle), can be observed (left). After removing the epicardium and fat tissue, the reversed coronary arteries can be seen (right).1; pulmonary trunk, 2; ascending aorta, 3; superior vena cava, 4; apex of heart, 5; left ventricle, 6; left atrium, 7; anterior interventricular branch, 8; left coronary artery, S; superior, L; left.

Additionally, the right vagus nerve was present, and the right recurrent laryngeal nerve encircled the aortic arch (Suppl. Fig. 2). However, the left recurrent laryngeal nerve did not encircle the subclavian artery, resulting in a left NRLN. The NRLN originates from the left vagus nerve, slightly below the level of the inferior margin of the thyroid gland (Fig. 2 B, D). The shape of the thoracic duct was also mirrored. These associated variations of the heart, the great vessels, and the vagus nerves are schematically illustrated in Suppl. Fig. 3.

Anomaly of the Abdominal Organs. All the abdominal organs were reversed (Fig. 4). The liver was located on the left side, and the stomach on the right side. The pylorus of the stomach was on the left side, leading to the first part of the duodenum. The jejunum was located on the right side, whereas the ileum was located on the left side and connected to the cecum. The ascending colon was on the left side, whereas the descending and sigmoid colons were on the right side. The splenic flexure on the right side was situated superior to the hepatic flexure. The shape of the abdominal vessels, including the celiac trunk, superior mesenteric artery, and inferior mesenteric artery, was also mirrored. The jejunal and ileal arteries were reversed, showing the development of the vasa recta from the right jejunal artery and the arterial arcade from the left ileal artery. Additionally, the left colic artery was observed to originate from the superior mesenteric artery. (Fig. 5, left). The spleen was located on the right side Fig. 5, right). The locations of kidneys were also mirrored. The left kidney was located beneath the liver, spanning from approximately the level of T12 to L3, and was slightly more caudal compared to the right kidney. (Fig. 6).

DISCUSSION

SIT is a rare anatomical anomaly characterized by the reversal of organ position in a mirror image. Estimates of the prevalence of SIT in the global population range from 1 in 8,000 to 1 in 25,000, depending on the literature evaluated (Casey, 1998). The individuals with SIT are more likely to have vascular anomalies, especially those affecting the thoracic and abdominal organs. Although there are no commonly

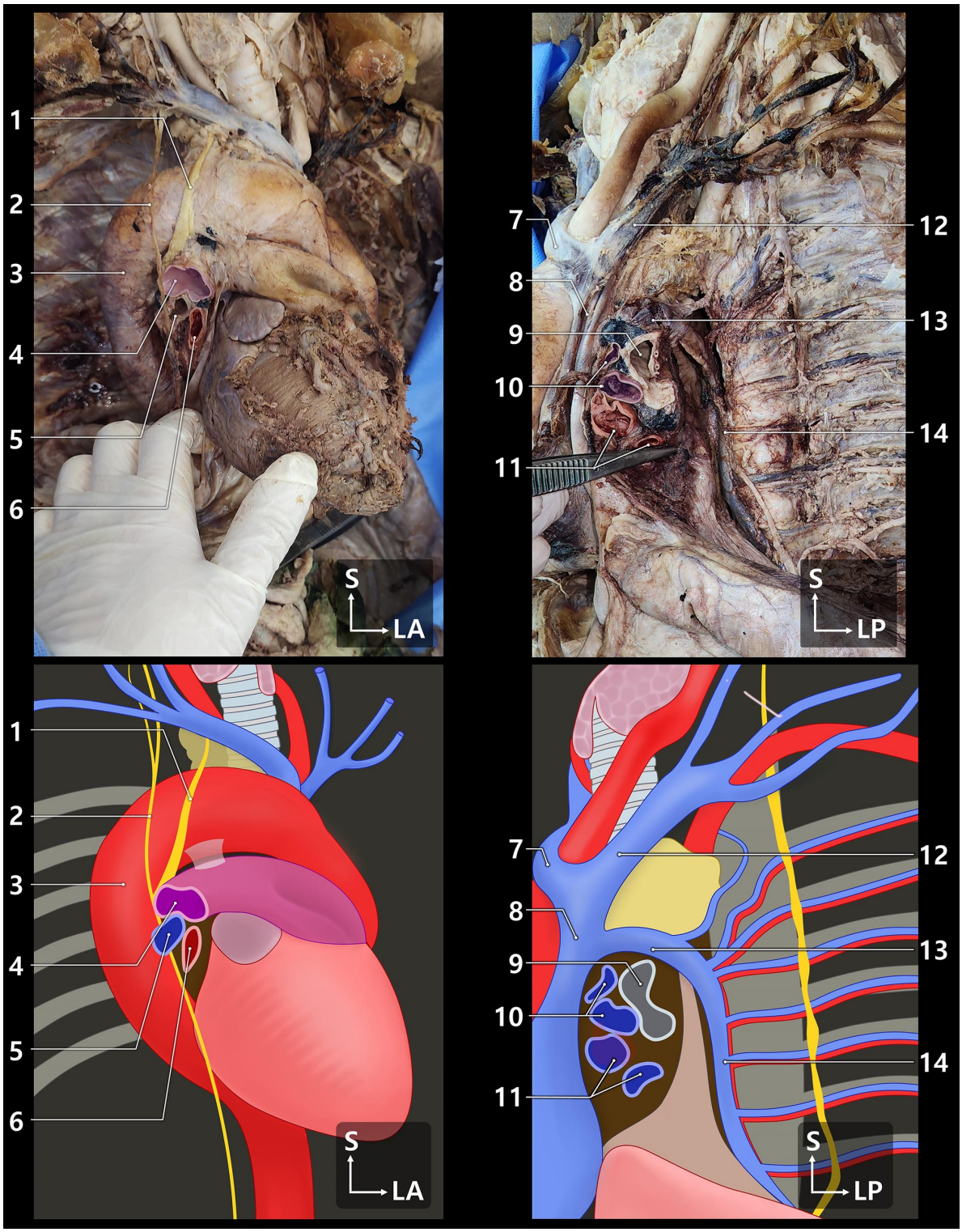

Fig. 3. The mirrored positions of the vessels and bronchi in the lung hilum, complemented by schematic illustrations below. While right pulmonary artery is located above the bronchus (left), left pulmonary artery is below the bronchus (right). Azygos vein is observed on the left side of the heart (right). 1; right vagus nerve. 2; right phrenic nerve, 3; descending aorta, 4; right pulmonary artery, 5; right bronchus, 6; right superior pulmonary vein, 7; right brachiocephalic vein 8; superior vena cava, 9; left bronchus, 10; left pulmonary artery, 11; left pulmonary vein, 12; left brachiocephalic vein, 13; azygos arch, 14; azygos vein, S; superior, LA; left anterior, LP; left posterior.

observed variations, several anomalies such as double inferior vena cava or aberrant hepatic arteries have been reported in the literature (Taskent *et al*., 2019).

This report highlights the finding of an ALSA anomaly in a patient with SIT. Originally, the term "aberrant 'right' subclavian artery" refers to an uncommon vascular abnormality that the right subclavian artery arising directly from the aortic arch, without a brachiocephalic trunk. This specific anomaly occurs in 0.7 % of global population (Popieluszko *et al*., 2018). However, in this case, because SIT occurred simultaneously, we named the ALSA: aberrant "left" subclavian artery instead of the typical aberrant "right" subclavian artery. In addition, a bicarotid trunk and NRLN were also found in this case. According to Michal *et al*., the most common vascular anomaly coexisting with ALSA is the bicarotid trunk (19.2 %) (Polguj *et al*., 2014). The development of the thoracic and cervical regions is influenced by the aortic arch embryology. Hence,

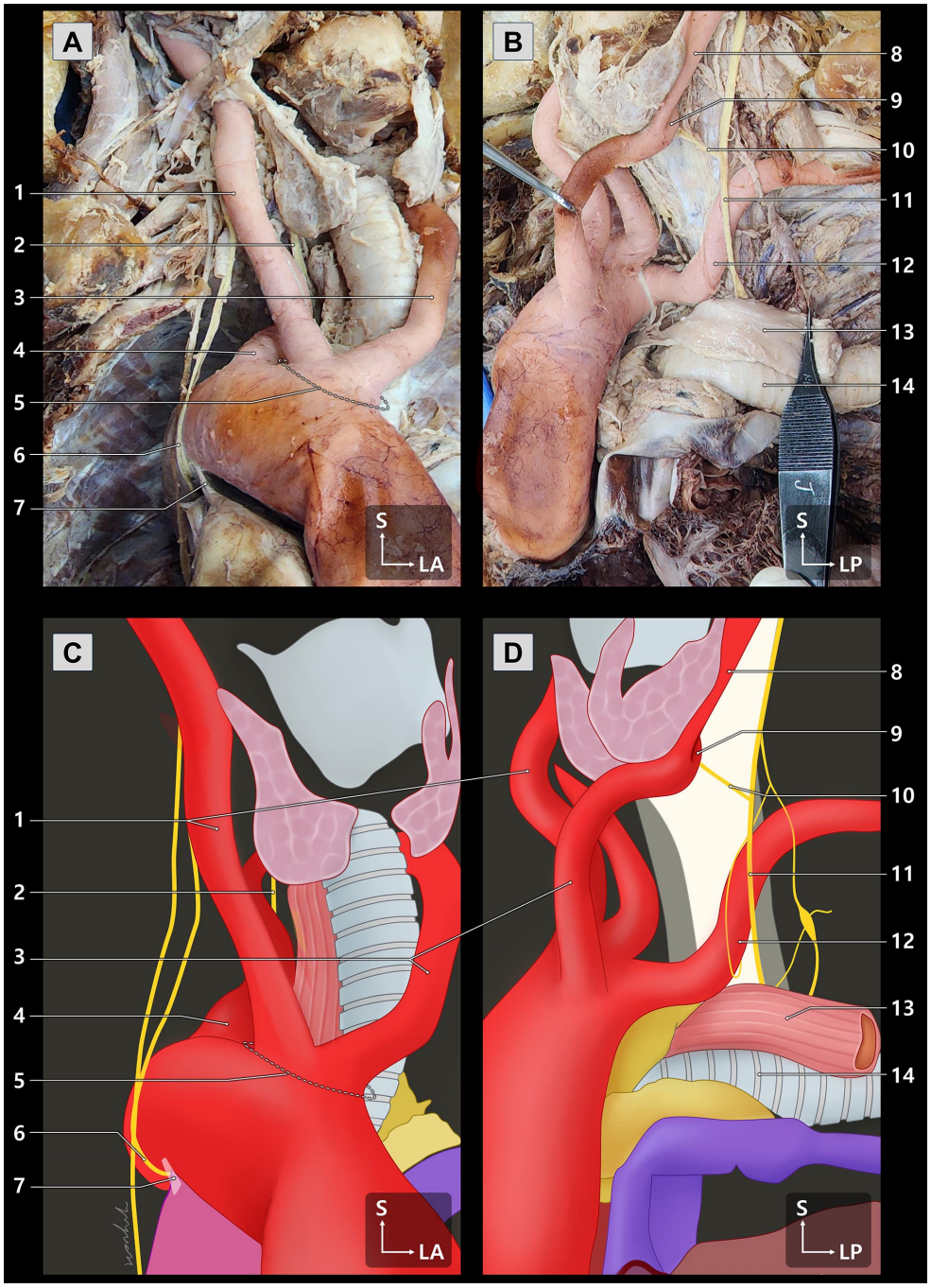

Fig. 4. The left (A) and right (B) view of the aortic arch and blood vessels in the thoracic cage, complemented by schematic illustrations below (C, D). The bicarotid trunk, aberrant left subclavian artery, and non-recurrent laryngeal nerve are distinctly observed in panels A and C. The aberrant left subclavian artery is obscured by other structures and is not visible. left non-recurrent laryngeal nerve observed in panels B and D. 1; right common carotid artery, 2; right recurrent laryngeal nerve, 3; left common carotid artery, 4; right subclavian artery, 5; bicarotid trunk, 6; right vagus nerve, 7; ligamentum arteriosum, 8; external carotid artery, 9; internal carotid artery, 10; left non-recurrent laryngeal nerve, 11; left vagus nerve, 12; aberrant left subclavian artery, 13; esophagus (reflexed), 14; trachea (reflexed), S; superior, LA; left anterior, LP; left posterior.

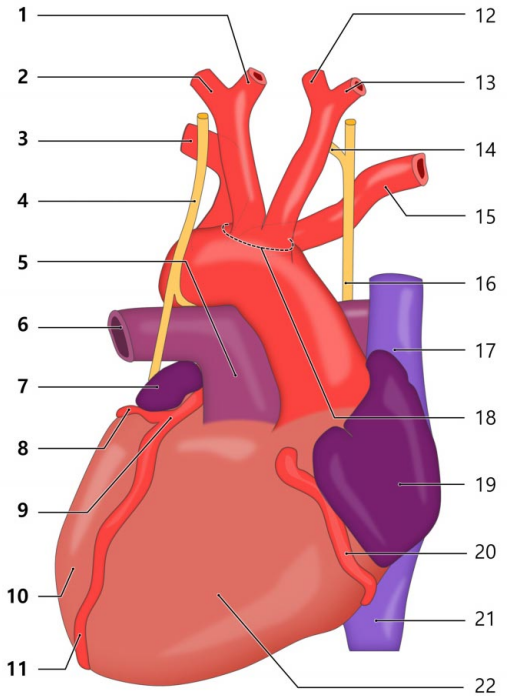

Fig. 5. Schematic illustration of *Situs inversus totalis* with associated variations. It highlights the dextrocardia, the inversion of the great vessels and coronary arteries, the bicarotid trunk originating from the aortic arch, and the non-recurrent left laryngeal nerve from the left vagus nerve. 1; right internal carotid artery, 2; right external carotid artery, 3; right subclavian artery, 4; right vagus nerve, 5; pulmonary trunk, 6; right pulmonary artery, 7; right atrium, 8; circumflex branch, 9; right coronary artery, 10; right ventricle, 11; anterior interventricular branch, 12; left internal carotid artery, 13; left external carotid artery, 14; left non recurrent laryngeal artery, 15; aberrant left subclavian artery, 16; left vagus nerve, 17; superior vena cava, 18; bicarotid trunk, 19; left atrium, 20; left coronary artery, 21; inferior vena cava, 22; left ventricle.

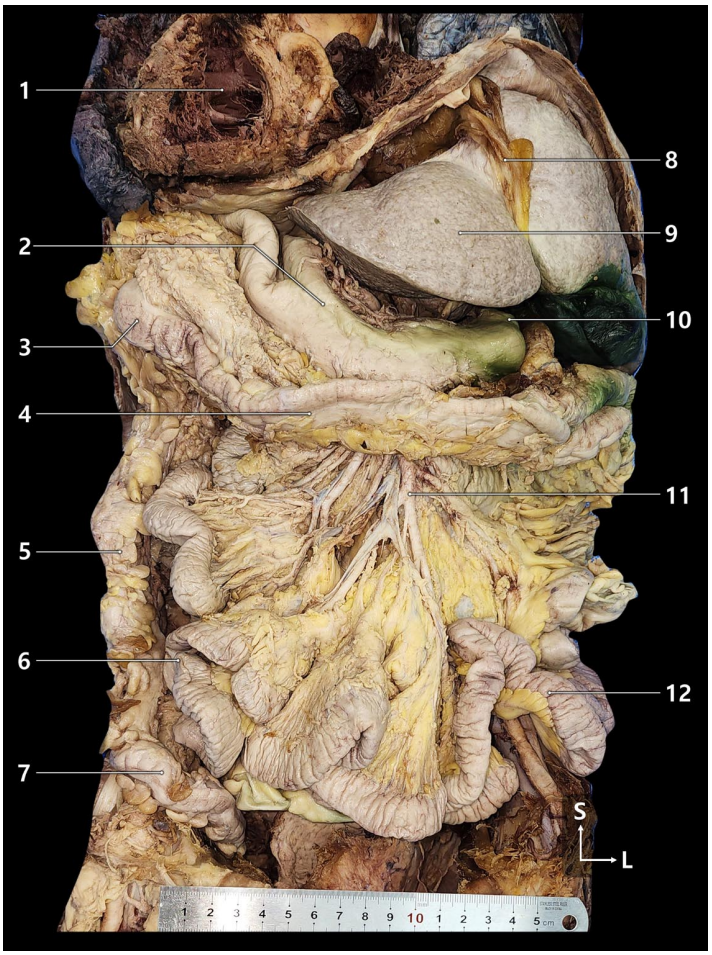

Fig. 6. The view of the abdominal organs with *Situs inversus totalis*. The mirrored positions of the liver, stomach, and large intestine can be observed. 1; heart (right ventricle), 2; stomach, 3; splenic flexure, 4; transverse colon, 5; descending colon, 6; ileum, 7; sigmoid colon, 8; falciform ligament, 9; right lobe of liver, 10; Duodenum, 11; superior mesenteric artery, 12; ileum, S; superior, L; left.

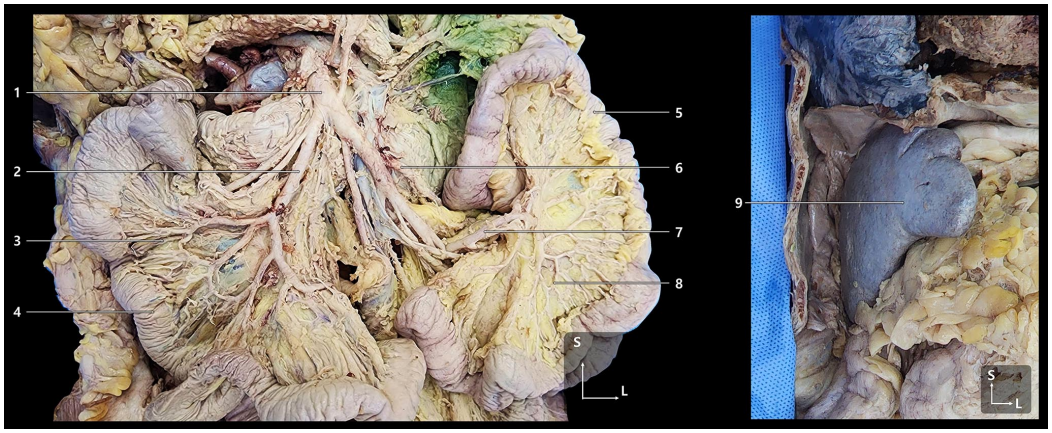

Fig. 7. The view of the small intestine shows the reversed position of the jejunal and ileal arteries, which are positioned at right and left, respectively. The left colic artery is also observed to originate from the superior mesenteric artery (left). Spleen, which is located on the right, can be observed (right). 1; superior mesenteric artery, 2; jejunal artery, 3; vasa recta, 4; jejunum, 5; ileum, 6; left colic artery, 7; ileal artery, 8; arterial arcade, 9; spleen, S; superior, L; left.

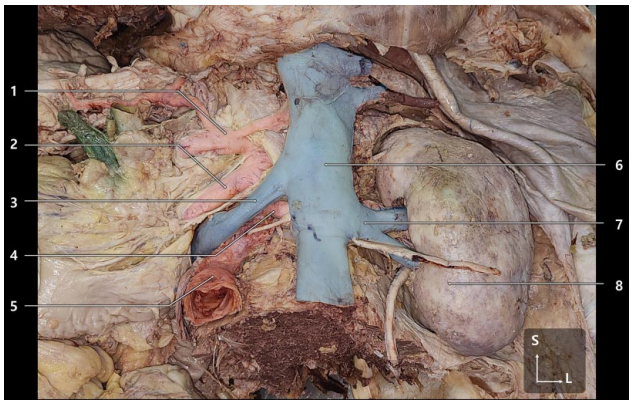

Fig. 8. Reversed blood vessels that supply the kidneys can be observed. The splenic artery can be seen on the right side according to the reversed position of the spleen. 1; splenic artery 2; right renal artery 3; right renal vein 4; left renal artery 5; abdominal aorta 6; inferior vena cava 7; left renal vein 8; left kidney, S; superior, L; left.

anomalies in the aortic arch can lead to neurological anomalies, such as the rare variant NRLN during embryonic development, and is found in 0.7 % of the general population (Popieluszko *et al*., 2018).

Embryologically, the normal brachiocephalic trunk arises from the right horn of the aortic sac and is divided into the right common carotid artery and right subclavian artery. Degeneration of the right fourth aortic arch and proximal portion of the right dorsal aorta may lead to the absence of the brachiocephalic trunk, resulting in ALSA (Natsis *et al*., 2017). The prevalence of NRLN correlates with an aberrant subclavian artery. On the right side, the normal inferior laryngeal nerve passes under the fourth aortic arch. If this portion is absent, the nerve migrates up directly from the vagus nerve, forming the NRLN (Popieluszko *et al*., 2018). In the case of SIT, no significant difference is known, except for the difference in the direction of embryological development.

From a clinical standpoint, ALSA commonly manifests as an asymptomatic condition. However, rare symptoms and clinical manifestations have been reported, including dysphagia, dyspnea, recurrent pulmonary infections, feeding difficulties, aneurysm formation, and acute ischemia of the right arm (Natsis *et al*., 2017). These symptoms occur due to compression of the trachea and esophagus and may affect up to 10 % of patients with ALSA (Natsis *et al*., 2017).

Regarding the pathophysiological mechanisms involved, aortic tears or dissections may be more likely to occur during trauma in patients with ALSA. Injury to the inferior laryngeal nerve is a major complication of thyroid and parathyroid surgery. An abnormal anatomical situation, such as an undetected NRLN, increases the risk of nerve injury and vocal fold paralysis. Patients with undetected NRLN have a nearly six-fold increased risk of intraoperative nerve injury (Toniato *et al*., 2004). To minimize these surgical risks, preoperative identification of ALSA and NRLN is crucial. For this purpose, the computed tomography, ultrasonography, and intraoperative neurophysiological monitoring are recommended (Iijima *et al*., 2022). For interventions or surgeries affecting the aortic arch, a thorough understanding of the bicarotid trunk is crucial (Rogers *et al*., 2011).

Previously, *Situs inversus totalis* was thought to be associated with primary ciliary dyskinesia, a recessive genetic disorder caused by mutations affecting the function of motile cilia. Although primary ciliary dyskinesia can occur in combination with *Situs inversus totalis*, the probability of this condition is only 41 % in cases of *Situs inversus totalis* (Postema *et al*., 2020). Kartagener syndrome occurs when primary ciliary dyskinesia occurs together with *Situs inversus totalis*, chronic sinusitis, and bronchiectasis. However, various studies have shown that the genes involved in Primary Ciliary Dyskinesia are not significantly correlated with the occurrence of *Situs inversus totalis*, which is caused by more complex genetic factors. Genes such as LRRC6, DNAH11, DNAAF1, CCDC114, DNAH5, PKD1L1, CFAP52 (also known as WDR16), ZIC3, and CCDC11 are known to cause *Situs inversus totalis* without Primary Ciliary Dyskinesia. Some of these genes can cause partial collapse of visceral laterality, resulting in heterotaxia or situs ambiguus (Postema *et al*., 2020).

Regrettably, in the present case, detailed medical history records of the patient could not be obtained, aside from the cause of death. However, considering her lifespan of 83 years, it is speculated that she may have experienced minimal symptoms associated with *Situs inversus totalis*.

In this report, we presented a case of SIT with ALSA, NRLN, and bicarotid trunk. This case report can contribute to surgical planning and provide insights into the complexities of SIT and associated anomalies.

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RESUMEN: El *Situs inversus totalis* es una afección congénita poco frecuente que se caracteriza por la posición invertida de los órganos internos. Puede presentarse de diversas formas, incluida la inversión total o parcial, y a menudo se descubre de manera accidental mediante imágenes médicas o un examen post mortem. En algunos casos, también puede estar acompañado de anomalías vasculares. Este informe describe un caso poco frecuente de *Situs inversus totalis* en un cadáver femenino de 83 años (causa de muerte: insuficiencia orgánica múltiple) durante una disección realizada por un estudiante de medicina. El cadáver mostró una posición reflejada de los órganos toracoabdominales y los vasos sanguíneos, junto con variaciones en los vasos. Entre las anomalías adicionales más notables se encontraba la presencia de una arteria subclavia derecha aberrante y un tronco bicarotídeo, la ausencia de un tronco braquiocefálico y de un nervio laríngeo recurrente. Se analizó la rara anomalía anatómica del *Situs inversus totalis*, que implica la transposición de los órganos en imagen especular, y se destacaron las anomalías adicionales. Por lo tanto, se espera que este informe mejore la comprensión de la correlación entre el *Situs inversus totalis* y las anomalías asociadas y proporcione información útil para un diagnóstico preciso y procedimientos quirúrgicos relevantes.

PALABRAS CLAVE: ***Situs inversus totalis*; Anormalidades; Arteria subclavia; Nervio laríngeo recurrente.**

REFERENCES

Casey, B. Two rights make a wrong: human left-right malformations. *Hum. Mol. Genet., 7(10)*:1565-1571, 1998.

Iijima, Y.; Ishikawa, M.; Iwai, S.; Yamagata, A.; Motono, N.; Tsuji, H. & Uramoto, H. Usefulness of intraoperative nerve monitoring for giant type AB thymoma combined with an aberrant right subclavian artery: a case report. *J. Cardiothorac. Surg., 17(1)*:300, 2022.

Kamitani, S.; Tsutamoto, Y.; Hanasawa, K. & Tani, T. Laparoscopic cholecystectomy in *Situs inversus totalis* with "inferior" cystic artery: a case report. *World. J. Gastroenterol., 11(33)*:5232-4, 2005.

Koo, C. H.; Shim, J. K.; Kim, N.; Ki, Y.; Park, J. & Kim, J. C. Anesthetic considerations for a patient with *Situs inversus totalis* undergoing cardiac surgery: A case report. *Anesth. Pain Med., 14(2)*:193-6, 2019.

Marta, M. J.; Falcão, L. M.; Saavedra, J. A. & Ravara, L. A case of complete *Situs inversus totalis*. *Rev. Port. Cardiol., 22(1)*:91-104, 2003.

Mishra, M.; Kumar, N.; Jaiswal, A.; Verma, A. K. & Kant, S. Kartagener's syndrome: A case series. *Lung India, 29(4)*:366-9, 2012.

Natsis, K.; Didagelos, M.; Gkiouliava, A.; Lazaridis, N.; Vyzas, V. & Piagkou, M. The aberrant right subclavian artery: cadaveric study and literature review. *Surg. Radiol. Anat., 39(5)*:559-65, 2017.

Polguj, M.; Chrzanowski, L.; Kasprzak, J. D.; Stefanczyk, L.; Topol, M. & Majos, A. The aberrant right subclavian artery (arteria lusoria): the morphological and clinical aspects of one of the most important variations--a systematic study of 141 reports. *ScientificWorldJournal, 2014*:292734, 2014.

Popieluszko, P.; Henry, B. M.; Sanna, B.; Hsieh, W. C.; Saganiak, K.; Pe˛kala, P. A.; Walocha, J. A. & Tomaszewski, K. A. A systematic review and meta-analysis of variations in branching patterns of the adult aortic arch. *J. Vasc. Surg., 68(1)*:298-306.e210, 2018.

Postema, M. C.; Carrion-Castillo, A.; Fisher, S. E.; Vingerhoets, G. & Francks, C. The genetics of *Situs inversus totalis* without primary ciliary dyskinesia. *Sci. Rep., 10(1)*:3677, 2020.

Rogers, A. D.; Nel, M.; Eloff, E. P. & Naidoo, N. G. Dysphagia lusoria: a case of an aberrant right subclavian artery and a bicarotid trunk. *ISRN Surg., 2011*:819295, 2011.

Sun, X. Y.; Qin, K.; Dong, J. H.; Li, H. B.; Lan, L. G.; Huang, Y.; Cao, S. & Li, Z. J. Liver transplantation using a graft from a donor with *Situs inversus totalis*: a case report and review of the literature. *Case Rep. Transplant., 2013*:532865, 2013.

Taskent, I.; Danısan, G. & Murat Aydın, A. *Situs inversus totalis* with double superior vena cava: An unusual case report. *J. Surg. Med., 3(10)*:774-6, 2019.

Toniato, A.; Mazzarotto, R.; Piotto, A.; Bernante, P.; Pagetta, C. & Pelizzo, M. R. Identification of the nonrecurrent laryngeal nerve during thyroid surgery: 20-year experience. *World. J. Surg., 28(7)*:659-61, 2004.

Corresponding author:
Ji-Hyun Lee
Department of Anatomy and Acupoint
College of Korean Medicine
Gachon University
1332 Seongnam-daero
Seongnam 13306
REPUBLIC OF KOREA

E-mail: anatomy@gachon.ac.kr