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Case Report: Situs Inversus Totalis

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ABSTRACT

Background: The formation of human body organs is not symmetrical. Even though the human heart begins its formation in the midline of the embryo, its formation will move to the left side of the thoracic cavity and looping will occur on the right. The spleen is found alone on the left side of the abdomen, the right liver lobe is formed predominantly on the right side of the abdomen, the colon will loop from right to left in the abdominal cavity, and the right lung has one more lobe than the left lung. situs inversus is a condition where the internal organs (viscera) occur in the thorax and abdomen.

Case Description: An adult male cadaver during dissection found abnormalities in the location of organs in the thoracic and abdominal cavities. It appears that this cadaver has a heart located on the right, 3 lung lobes on the left side and 2 lung lobes on the right side of the thoracic cavity. The location of the liver is also visible on the left side of the abdominal cavity, as well as the position of the stomach and spleen which are located on the right side of the abdominal cavity. This can be related to congenital abnormalities, namely autosomal recessive genetic disorders.

Conclusion: The cadaver in this case experienced situs inversus totalis, which is a condition where internal (visceral) organs occur in the thorax and abdomen, which is also accompanied by dextrocardia. From the case analysis, several possible causes of situs inversus totalis were found, namely an autosomal recessive disorder inherited from both parents who are carriers. This genetic disorder is inherited by parents who are carriers and is related to disturbances in the formation of the left and right axes of the body during the formation of the embryo in the womb.

Keywords: situs inversus totalis, congenital abnormality, autosomal recessive genetic disorder

INTRODUCTION

Situs inversus is taken from the Latin expression " situs inversus viserum " which means the upside down position of the internal organs (visceral)[4], which was first described by Leonardo da Vinci in 1452-1519 and then by Marco Severin in 1643, and for more than 100 years later described by Matthew Ballie.[5] situs inversus is a condition where the internal organs (viscera) occur in the thorax and abdomen.[2] If this condition involves the heart in a position next to the right (dextrocardia) then this disorder is called situs inversus totalis. If the heart is in normal condition or remains on the left side of the body, it is called situs inversus with levocardia or situs inversus incomplete. situs inversus is generally an autosomal recessive genetic disorder. People with situs inversus totalis are not aware of the anatomical abnormalities they have until they go to the doctor to be checked for diseases that are not related to this condition. The situs inversus that occurs is usually accompanied by dextrocardia. A 3-5% incidence of heart defects is found in situs inversus with

dextrocardia, usually with transposition of the great vessels.[3] In these patients 80% have the aortic arch on the right side. situs inversus with levocardia (the heart remains on the left) is very rare (1:22,000 population) and usually this condition is almost always associated with congenital heart defects.[3] Approximately 50% of patients with situs inversus totalis also experience bronchiectasis and chronic sinusitis due to ciliary abnormalities (Cartagener syndrome). The formation of human organs is not symmetrical. Although the human heart begins its formation in the midline of the embryo, its formation will move to the left side of the thoracic cavity and looping will occur on the right. The spleen is found alone on the left side of the abdomen, the right lobe of the liver is formed predominantly on the right side of the abdomen, the colon will loop from right to left in the abdominal cavity, and the right lung has one more lobe than the left lung.[1] situs inversus is a condition of transposition of internal organs (viscera) in the thorax and abdomen.[2]

The condition that underlies this ciliary disorder is primary ciliary dyskinesia (PCD). PCD is a dysfunction of the cilia that occurs during embryonic development. Normally functioning cilia determine the position of visceral organs during embryonic development, and therefore individuals with PCD have a 50% chance of developing situs inversus. Interestingly, under normal circumstances, cilia are present on the ventral surface of the primitive node and may be involved in the formation of left-right patterning during gastrulation. Another left-right abnormality condition is known as laterality sequence. Patients suffering from this condition do not have complete situs inversus, but appear to show a bilateral predominance of the left or right side.[2]

CASE REPORT

An adult male cadaver with situs inversus totalis at the FKUKI anatomy museum. From the ventral side, it can be seen that the heart (cor) is on the right side of the thoracic cavity, the pulmo with 3 lobes is on the left side of the thoracic cavity, and the pulmo with 2 lobes is on the right side of the thoracic cavity. Also visible in the abdominal cavity, the liver occupies the left side of the abdominal cavity. The stomach is on the right side of the abdominal cavity. The spleen is not visible in the image, but in reality there is a spleen on the right side of the abdominal cavity. The location of visceral organs such as the colon is also reversed. The ascending colon starts on the left side of the body and runs transversely to the right side of the body. In the photo above the colon is not visible because there was a flaw in taking the photo

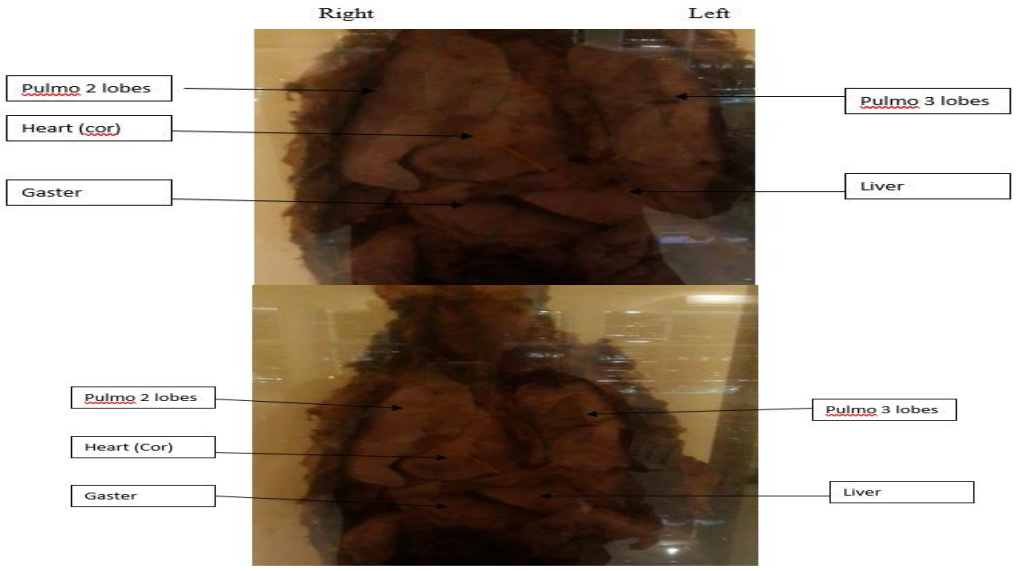

Figure 1. Cadaver viewed from the ventral side

DISCUSSION

situs inversus totalis is associated with disorders of the formation of the right-left axis of the body during gastrulation in the 3rd week of pregnancy.[2] situs inversus totalis is a rare case, the incidence rate is 6 in 8,000 live births, and is an autosomal recessive genetically inherited disorder.[5]

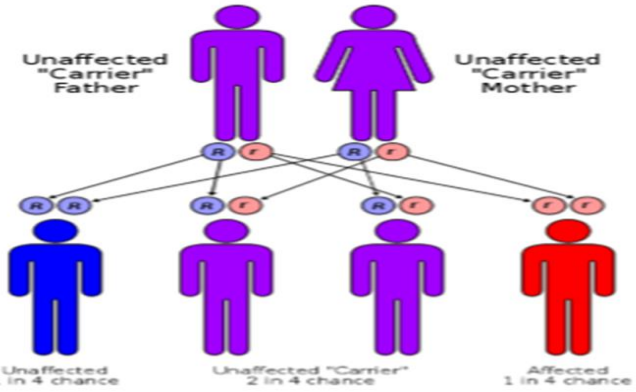

Figure 2. An autosomal recessive genetic pattern of inheritance in situs inversus

Sometimes this autosomal recessive genetic disorder can be x-linked and is also found in identical twins. An autosomal recessive genetic disorder related to immotile cilia syndrome (ICS), where there is abnormal cilia movement and impaired mucociliary clearance. Defects in the function and structure of the cilia result in reduced motility of the cilia, resulting in abnormal mucociliary clearance. Approximately 50% of sufferers are associated with situs inversus.[5]

The mechanism for determining the right-left side involves the cilia on the cells in the node moving to create a Nodal gradient towards the left or through a signal-forming gradient produced by gap junctions and small ion transport.[2]

In mammals, the distinction between left and right sides is initiated by the ciliary cells of the Nodal. These ciliary cells cause fluid in the nodes to flow from right to left. There is a gene that codes for a ciliary motor protein called dynein. If there is an abnormality in dynein, the ciliary nodes will not move and the location (lateral position) of each asymmetrically located organ will be scrambled. This finding is connected with other data. First, it has long been known that humans with dynein deficiency have immotile cilia and random changes in the heart on the left or right side of the body. Second, when the iv (inversus visitrum) gene was cloned, it was found that this gene would code for the ciliary dynein protein. Third, culture is carried out on mouse embryos with a medium speed flow made from left to right, resulting in a reversal of the left-right axis.[1]

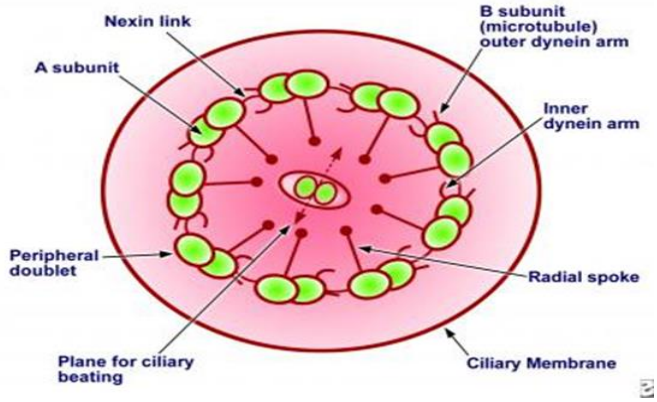

Figure 3. The anatomical structure of ciliary cells which have dynein protein in them.[6]

Nodal fluid flow was able to regulate the polarity of the body's left-right axis in experiments on mutant mice, where the cilia experienced immotility. Nodal fluid flow is very important for left-right asymmetry because there are small particles (± 1µm) attached to the membrane called nodal vesicular parcels (NVPs). These particles contain the sonic hadgehog (SHH) protein and retinoic acid (RA), which are secreted from nodal cells under the influence of FGF signaling. Cilia flow will carry NVPs to the left side of the body, if FGF signals are inhibited, NVPs will not be secreted and left-right asymmetry of the body will fail to form. One of the results of transport from NVPs is an increase in calcium ions on the left side of the node.[1]

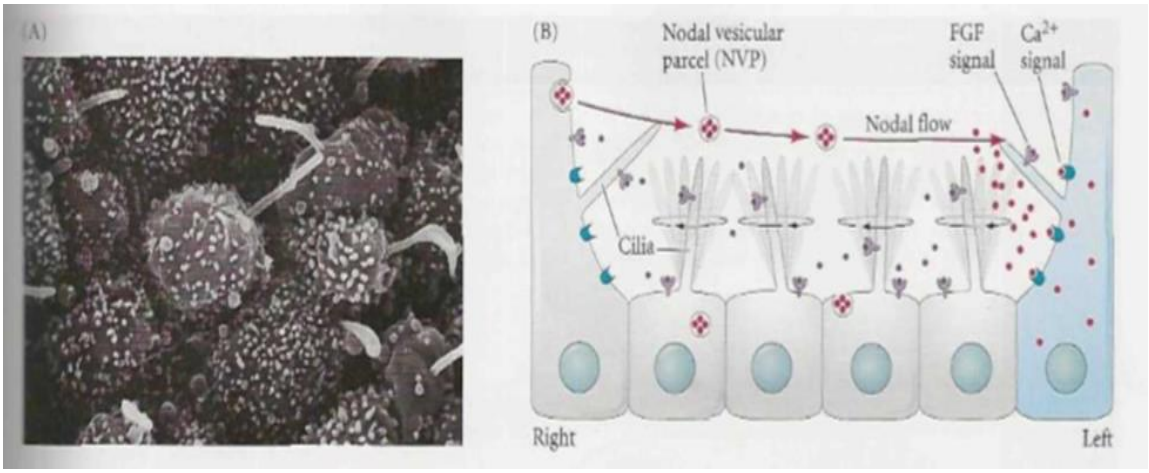

Figure 4. (A) shows ciliary cells in mammalian nodal cells, (B) shows the movement of cilia which move from the left side to the right side and cause nodal flow carrying the nodal vesicular parcel (NVP) under the influence of FGF signals and Ca2+ ions

Recent research states that disorders of left-right axis formation are also caused by abnormalities in the Lefty gene, Nodal gene, and PITX gene. This gene mutation appears on chromosome 12.5. As we know, in humans and vertebrates, the asymmetrical formation of body anatomy occurs during embryogenesis. Lateralization (left-right) is also established early in development and is accompanied by a series of signal-forming molecules and genes. As the primitive streak forms, FGF8 is secreted by cells within the node and primitive streak, triggering Nodal expression. But only on the left side of the embryo. Furthermore, as the neural plate forms, FGF8 maintains Nodal expression in the lateral plate mesoderm, as well as Lefty-2, and both of these genes regulate PITX2 expression. PITX2 is a homeobox-containing transcription factor that plays a role in determining left-handedness, and its expression is repeated on the left side of the cardiac, gastric, and intestinal primodia because these organs determine normal asymmetric body position. Simultaneously, Lefty is expressed on the left side of the neural tube floor plate and may act as a barrier to prevent signals on the left side from passing through. Therefore, if there are abnormalities in the genes mentioned above, the asymmetric formation of the body will change. There is also a role for another protein, namely Sonic hedgehog (SHH) which can also play this role and function as a suppressor of gene expression on the left side on the right. Apart from that, there is also the Brachyury (T) gene, which codes for a transcription factor secreted by the notochord, which is also important for nodal expression, Lefty-1 and Lefty-2.2 So there are many roles for this gene in the formation of the left-right axis of the body during embryonic development.

The neurotransmitter serotonin (5HT) also plays an important role in the chain of signal formation that determines this laterality, 5HT is concentrated on the left side, possibly because 5HT is broken down by the enzyme

monoamine oxidase (MAO) on the right side, and is the beginning of the formation of the FGF8 signal. Alterations in the generation of 5HT signaling lead to situs inversus, dextrocardia and various heart defects. Recent results also show that children born to mothers taking antidepressant drugs from the selective serotonin reuptake inhibitor (SSRI) class of drugs have an increased risk of developing various heart malformations, thus providing additional evidence of the importance of 5HT in determining laterality.[2] Individuals with situs inversus totalis do not have any problems with their health, because there is no problem with the relationship between the organs which are in reverse position.[5] As can be seen in this case, all the organs in this cadaver can develop as they should until adulthood.

CONCLUSION

The cadaver in this case experienced situs inversus totalis, which is a condition where internal (visceral) organs occur in the thorax and abdomen, which is also accompanied by dextrocardia. From the case analysis, several possible causes of situs inversus totalis were found, namely an autosomal recessive disorder inherited from both parents who are carriers. This autosomal recessive disorder causes abnormalities in the cilia, so that the cilia in the nodes are immotile and cause their flow to be obstructed and the formation of the left and right axes of the body is also disturbed. It cannot be ascertained whether this cadaver only had situs inversus totalis or Kartagener's syndrome, because no medical record was found for this cadaver. The second possibility is that this cadaver experienced a mutation on chromosome 12 during the 3rd week of development in the womb, because this mutation on chromosome 12 causes abnormalities in the Lefty gene, Nodal gene, and PITX gene, all of which influence the formation of the body's left-right axis. on the fetus. The third possibility is that there is a disturbance in the neurotransmitter serotonin (5HT) which can be caused by consuming SSRI antidepressant drugs such as Fluoxetine (Prozac), Sertraline (Zoloft), Proxetine (Paxil), Fluvoxmine (Luvox), Escitalopram (Cipralex) in the second week. -3 pregnancies.

Declaration by Author

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