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SPLEEN, ITS GENERAL STRUCTURE, AND DEVELOPMENT

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Annotation:

This thesis highlights the external and internal morphological structure of the spleen, its importance as a lymphoid organ, its physiological functions, and its role in hematopoiesis.

Keywords:

Embryonic hematopoiesis, spleen, liver, aorta–gonad–mesonephros, erythro- and granulocytopoiesis, extravascular hematopoiesis, mesenchyme, extramedullary hematopoiesis, hematopoietic progenitor, blood depot, yolk sac.

Relevance:

Immune cells are formed in the spleen. More precisely, this process represents the formation, growth, maturation, and specialization of blood cells from hematopoietic stem cells through hematopoietic progenitor cells into specific blood cells. This process is strictly regulated by several elements of the bone marrow microenvironment, such as growth factors, transcription factors, and cytokines. During embryonic and fetal development, hematopoiesis occurs in various organs, including the yolk sac, the aorta–gonad–mesonephros region, lymph nodes, fetal liver, and embryonic or fetal spleen.

Research purpose:

The spleen plays an important role in metabolism and cell migration, being a key component of the portal circulation that contains reticuloendothelial structures. The liver performs secretory functions, but under certain conditions, it can compensate for bone marrow insufficiency and, together with the spleen, help prevent a deficiency of functional blood cells. The spleen is an organ with high metabolic activity; one of its functions is to recycle blood cells and iron and filter atypical blood cells. It removes aged erythrocytes, damaged platelets, and apoptotic cells through phagocytosis, produces and stores antibodies, and supports the immune system by producing and activating T and B lymphocytes that fight infections.

The spleen bud first appears in the 5th–6th week of embryonic development, arising from a dense aggregation of mesenchymal cells within the developing greater omentum. The vascular system of the spleen differentiates earlier, and reticular cells form between the blood vessels, among which stem cells of the blood are located. By the 7th–8th week, macrophages appear in the spleen; by the 11th–12th week, B lymphocytes develop. Up to the 5th month of embryonic development, granulocytopoiesis, erythropoiesis, and thrombocytopoiesis actively occur in the spleen. Meanwhile, lymphocytopoiesis gradually intensifies — during the 3rd–5th months, T lymphocytes accumulate around arteries (T-zone or periarteriolar zone), followed later by B lymphocytes, forming the white pulp of the spleen. The reticular

tissue between them, together with large sinusoidal blood vessels, forms the red pulp. During the first half of embryonic life, all hematopoietic cells develop in the spleen.

Materials and methods:

The liver bud appears during the 3rd–4th weeks of embryonic development. From the fifth week onward, the liver becomes the main site of blood formation in the embryo. The formed blood cells develop from stem cells, which transform into primary blood cells and then produce secondary erythrocytes. Alongside mature erythrocytes, mature granulocytes—mainly neutrophils and eosinophils—are also observed in the liver. Hematopoiesis occurs extravascularly along capillaries as mesenchymal tissue grows into hepatic lobules. The source of blood formation is the stem cells derived from the yolk sac, which differentiate into secondary erythrocytes and granulocytes. In addition, megakaryocytes also develop. Unlike in adults, this process bypasses intermediate stages, and mature neutrophils and eosinophils are produced without completing the myeloblast and promyelocyte stages.Schematically, the maturation of granulocytes proceeds as follows: from primary blood cells to mature granulocytes. Furthermore, giant megakaryocyte cells also develop in the liver. All these elements develop outside the blood vessels, i.e., extravascularly. Gradually, hematopoiesis in the liver decreases and completely ceases by the end of embryonic development. Thus, in the post-embryonic period, blood formation no longer occurs in the liver.

Fetal (embryonic) hematopoiesis includes two main stages: primitive and definitive. In this article, we explored in depth the primitive hematopoiesis occurring in the spleen and liver, i.e., the secondary functions of these organs during embryonic development. The spleen is often regarded as the “forgotten organ” among clinicians and radiologists. Nevertheless, it plays a role in various congenital and acquired diseases and can be clearly visualized using computed tomography (CT) and magnetic resonance imaging (MRI) of the abdominal cavity. Because the spleen is a highly variable organ, radiologists frequently encounter its normal variants, which can sometimes be mistaken for pathological conditions. For example, splenic clefts on the surface of the spleen may occasionally be misinterpreted as splenic lacerations in patients with abdominal trauma. Moreover, medical literature contains numerous reports of accessory spleens, especially those located near the liver or the tail of the pancreas, being mistaken for lymphadenopathy or intra-abdominal tumors. To fully understand the normal morphology of the spleen, it is essential to use precise terminology describing its developmental stages and anatomical variations. The natural depressions on the surface of the spleen have been referred to by various names — clefts, notches, or fissures — though these terms are used inconsistently across different sources, and a unified definition has yet to be established.

Therefore, in this article, we use only the term “cleft” to denote the natural depressions on the splenic surface. According to previous studies, such clefts are found on the superior border of the spleen in 40–98% of adults, with 4–5 clefts generally considered a normal finding.

If the number of clefts is excessively high or if they are located on other surfaces of the spleen — such as the diaphragmatic (superior-facing) or visceral (organ-facing) surfaces — this is considered abnormal.

In addition, accessory spleens are also common. These are small nodules separated from the main spleen, found in 10–30% of cases during autopsy. Variations in the shape of the adult spleen are often explained by the hypothesis that the organ develops through the fusion of multiple embryonic splenic primordia. It is believed that if one or more of these primordia fail to fuse with the main body, an accessory spleen develops.

During fetal development, the spleen appears lobulated, and the natural surface depressions are thought to represent areas where the embryonic buds did not completely fuse. Consequently, the clefts observed in the adult spleen are interpreted as remnants of the lobulated structure present during fetal life.

Obtained results and analysis

The term “fetal lobulation” of the spleen lacks a clear and universally accepted definition, and there are very few original scientific studies devoted to examining the normal surface morphology of the human fetal spleen. The only well-documented study was conducted by Ungör and colleagues, who examined 141 fetal spleens. They found clefts in 95% of cases along the superior border, 7.8% on the diaphragmatic surface, and 3.5% on the visceral surface.

These results are very similar to those observed in adults, calling into question whether there is any real difference between the fetal and adult surface morphology of the spleen. Another important issue is that the hypothesis of the spleen’s “multifocal origin” has never been directly demonstrated in human or animal embryos. Such views appear only in secondary sources, while primary observations provide no supporting evidence for this concept.

Therefore, we propose the following hypothesis:

The spleen develops from a single embryonic bud (a single center of origin), and the morphological variations on its surface emerge during the course of development. These variations occur naturally both in fetuses and adults.

In this study, we first analyze the development of the spleen from the embryonic stage based on histological sections. Then, we compare the number of clefts in fetal and adult spleens to determine their differences through statistical analysis.

Development of the embryonic spleen

The splenic clefts were classified according to their anatomical location (based on Netter’s classification) as follows:

- Superior border
- Inferior border
- Anterior extremity

- Posterior extremity
- Diaphragmatic surface
- Visceral surface

Each cleft was required to be identified in at least two imaging planes and to appear in several consecutive sections in at least one plane. Clefts located around the splenic hilum, where blood vessels enter or exit, were excluded from the analysis.

Conclusion:

For many years, radiologists have widely accepted the view that splenic surface clefts (notches, fissures, clefts) are remnants of fetal lobulation. However, the findings of our study, based on an analysis of human splenic development, refute this long-standing assumption.

Our results demonstrate that:

- The morphology of the spleen is highly variable;
- This variability is not related to age or developmental stage;
- The clefts of the spleen, regardless of their number or location, should be regarded as normal anatomical variants.

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