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Approach to the Patient with Hepatomegaly and Splenomegaly: A Review Study

Approach to the Patient with Hepatomegaly and Splenomegaly: A Review Study

Vera Ambrozina Delgado de Brito de Pina
Lucas Neves Solon Petrola
Nathan Portela de Oliveira
Lucas Carvalho Vasconcelos
Beatriz Castelo Branco Rocha

Summary

Hepatomegaly and splenomegaly are important clinical findings, often associated with multiple systemic and hepatic conditions. This review covers the anatomy and functions of the liver, the main physical and complementary diagnostic methods, and the various causes of liver and spleen enlargement. Anatomical and physiological parameters, anatomical variations, pathological mechanisms, and investigation strategies, including laboratory and imaging tests, and, when indicated, liver biopsy, are discussed. The appropriate clinical approach to patients with hepatomegaly and splenomegaly requires a thorough evaluation, correlating clinical findings and complementary tests to identify the etiology and define the most appropriate course of action.

Keywords: Hepatomegaly; Splenomegaly; Diagnosis; Liver.

Abstract

Hepatomegaly and splenomegaly are relevant clinical findings often associated with multiple systemic and hepatic conditions. This review study addresses the anatomy and functions of the liver, the main diagnostic methods—both physical and complementary—as well as the various causes related to liver and spleen enlargement. It discusses anatomical and physiological parameters, anatomical variations, pathological mechanisms, and investigation strategies, including laboratory tests, imaging techniques, and, when indicated, liver biopsy. An appropriate clinical approach to patients with hepatomegaly and splenomegaly requires a thorough evaluation, correlating clinical findings and complementary tests to identify the underlying etiology and define the best management strategy.

Keywords: Hepatomegaly; Splenomegaly; Diagnosis; Liver.

LIVER: ANATOMY AND FUNCTIONS

The liver is the largest organ in the human body, representing about 2% of the total body mass of an adult human (1). The mature liver is located primarily in the right hypochondriac and epigastric of the abdominal cavity, below the diaphragm and under the protection of the rib cage. In adults, a healthy liver weighs approximately 1400–1600 g and extends along the midclavicular line from the right fifth intercostal space to just below of the costal margin. The anterior border of the liver then extends medially and crosses the line median just below the xiphoid process. A small portion of the organ projects across the midline and lies in the left upper abdominal quadrant. (1, 2). The liver has two lobes, the right lobe being the largest, 4 to 6 times the size of the left lobe. The right and left are separated anteriorly by the falciform ligament, posteriorly by the fissure of the ligamentum venosum, and inferiorly by the fissure of the round ligament. (2)

It has a dual blood supply: 70% delivered by the portal vein, which drains the intestine, and the remainder by the hepatic artery (2,3). It is the central organ of intermediary metabolism, performing multiple functions, including the metabolism of food products ingested, production of amino acids to form proteins, detoxification of medications ingested, conversion of nitrogenous substances from the intestine into urea, formation of factors coagulation, bilirubin metabolism, processing of lipids absorbed from the intestine and excretion of its products as bile. It also stores glycogen, which is a source of glucose, and helps contain infections by removing bacteria from the bloodstream (2,3).

The location, vascularization and functions of the liver make it susceptible to various conditions that result in hepatomegaly, defined as enlargement of the liver beyond its normal size normal.

HEPATOMEGALY

Liver dimensions vary with gender, body mass and size of the individual. In men, normal liver measurement ranges from 10 to 15 cm; while in women, it ranges from 9 to 14 cm, with the liver normally being palpable between 1 and 2 cm below the right costal margin (2). It can if hepatomegaly or an increase in liver size is identified, by physical examination or by imaging tests:

Physical examination - To determine the extent of the liver, we percuss and palpate the liver in the mid-clavicular line with the patient in the supine position (12,13,14)

- **Percussion:** With the patient in a supine position and starting at the third intercostal space, the examiner uses percussion while moving inferiorly until dullness suggests the edge upper part of the liver (usually located in the fifth intercostal space). Then, the percussion is performed below the umbilicus in an area of the tympanic membrane, and the examiner moves superiorly until the dullness indicates the inferior border of the liver (15). If the distance from the border superior to the percussed edge of the liver is <13 cm, hepatomegaly is unlikely.

- **Palpation:** With the patient in the supine position, the examining hand is placed below the level of dullness observed on percussion in the mid-clavicular line, parallel to the rectus muscle. The liver is palpated during deep inspiration as it moves inferiorly to meet the examiner's fingertips. The edge of the liver may be tender in patients with liver inflammation (e.g., acute hepatitis) or congestion (e.g., liver failure) congestive heart disease). Alternatively, the liver edge may appear firm and nodular in patients with cirrhosis and/or malignancy. (15).

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Hepatomegaly is defined as an increase in the right lobe of the liver with more than 2 cm below the costal margin, which is detected during physical examination during palpation and percussion, absolute hepatic dullness greater than 14 cm is detected (5).

A non-enlarged liver may be palpable on physical examination due to the existence of the variant anatomical, in which an increase in the right lobe is observed, without alteration in function or enzymes liver, without other appreciable changes in imaging methods, known as Riedel's lobe, more common in women (2, 16, 17).

The liver can still be palpable, without an increase in its size, in emphysema. pulmonary, in chronic bronchitis, in diseases that cause paralysis of the right diaphragm and in homolateral pleural effusion, situations that determine lowering of the diaphragm, displacing the liver downwards, which may simulate hepatomegaly, however hepatimetry is normal (2,).

CAUSES

There are several causes and mechanisms that determine an increase in liver volume (2) **-(Table** 1):

Table 1- Causes of Hepatomegaly

Acute/Chronic Liver Diseases
Acute Hepatitis: viral, drug-induced, toxic, biliary Chronic Hepatitis: alcohol, viral, Autoimmune Hepatitis, Primary Biliary Cholangitis, Metabolic dysfunction-associated steatohepatitis (MASH), Wilson's disease, Hemochromatosis, Alpha1-Antitrypsin Deficiency, Primary Sclerosing Cholangitis, Caroli's Disease, Early-Stage Cirrhosis
Infectious
Liver abscess: amoebic, pyogenic, fungal Viral Hepatitis, Schistosomiasis, Kala-azar, Infectious Mononucleosis, Cytomegalovirus (CMV), Dengue, Cholangitis, Sepsis, Malaria, Toxoplasmosis, Typhoid Fever, Yellow Fever, Leptospirosis, Hydatidosis
Vascular
Congestive Heart Failure Constrictive Pericarditis Suprahepatic Vein Thrombosis (Budd-Chiari Syndrome) Veno-occlusive disease Inferior Vena Cava Occlusion
Metabolic/Infiltrative
Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

Gestational steatosis

Iron Deposition (Primary or Secondary Hemochromatosis)

Wilson's Disease (Copper Accumulation Due to Altered Biliary Excretion)
Amyloidosis

Alpha 1-antitrypsin deficiency
Porphyria

Fibrotic Infiltration

Glycogen Storage — Glycogenoses (I to IX)

Mucopolysaccharidoses

Lipid deposition, Gaucher disease, Niemann-Pick

Extracellular Erythropoiesis

Granulomatous Diseases

Immunological: Sarcoidosis, Granulomatosis with polyangiitis, Chronic Granulomatous Disease, Giant Cell Hepatitis

Infectious: Tuberculosis, Syphilis, Leishmaniasis, Schistosomiasis, Leprosy, CMV, Epsteins-Barr,
Mycobacterium avium-intracellulare in patients with HIV, Toxoplasmosis, Hepatitis C, Brucellosis,
Typhoid Fever, Tularemia,
Yersiniosis, Histoplasmosis, Blastomycosis, Coccidiomycosis, Q Fever, Cat Scratch Disease
Medications: Allopurinol, Penicillin, Diphenylhydantoin
Neoplastic: Hodgkin's and Non-Hodgkin's Lymphoma, Hypernephroma

Biliary Obstruction

Primary Biliary Cirrhosis, Secondary Biliary Cirrhosis

Primary Sclerosing Cholangitis

Extrahepatic obstruction: Gallbladder, Common bile duct, papilla, pancreas tumor and metastases

Primary/Metastatic Tumors

Hepatocellular Carcinoma and Fibrolamellar Variant
Autoimmune Hemolytic Anemia, Hereditary Anemias

Myelodysplastic Syndrome

Myeloproliferative Diseases

Benign Neoplasms

Giant Hemangiomas
Adenomas

Cysts: simple, complex, cystadenomas, cystadenocarcinomas

Miscellaneous

Vasculitis

POEMS (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal Gammopathy,
Skin Pigmentation

COMPLEMENTARY EXAMS

- Laboratory:

The initial evaluation of liver disease involves a battery of blood tests, which

can evaluate hepatic necroinflammation (serum aminotransferases), cholestatic dysfunction of the

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biliary tract (alkaline phosphatase, ÿ-glutamyl transpeptidase), excretory function (bilirubin) and synthetic function (coagulation factors, albumin) (3). These are tests performed to look for abnormalities in liver biochemistry or function, including:

•Serum aminotransferases: alanine aminotransferase (ALT) and aspartate aminotransferase (AST)

•Alkaline phosphatase

•Gamma Glutamyl Transferase

•Total bilirubin and fractions

•Serum albumin

•Prothrombin time/international normalized ratio

- Image:

Ultrasound – Ultrasound is a common method for assessing liver size and pathology (12,18). Hepatomegaly is defined as a longitudinal liver diameter at the midcostal line greater than 15 cm, visualized by ultrasound (5). It should be the initial investigation. It can confirm dilated bile ducts in patients with biliary obstruction and can often identify the cause, such as a pancreatic mass or a gallstone lodged in the bile duct common. Ultrasound can also determine whether the liver parenchyma is diffusely abnormal, as in acute viral hepatitis; may identify bright hepatic echo texture in non-alcoholic fatty liver disease or a coarse echo texture in cirrhosis. In addition to confirm the presence of ascites. Ultrasound can identify other signs of hypertension portal veins, such as splenomegaly or intra-abdominal varices. A Doppler flow study can assess blood flow through the portal and hepatic vessels. An ultrasound study can identify liver masses and distinguish a cystic mass from a solid lesion (3).

Computed tomography (CT) or magnetic resonance imaging (MRI) – Both CT and MRI MRIs can be used to determine liver size and volume. They add more details on the evaluation of hepatic vasculature, liver masses and hepatic vascular structures. MRI can obtain a detailed cholangiogram (3).

- Liver biopsy

Liver biopsy still retains an important role in the diagnosis of hepatitis autoimmune and drug hepatotoxicity. However, due to their potential complications, such as intra-abdominal bleeding, biopsy is recommended only when less severe tests are performed. invasive tests do not produce a definitive diagnosis or prognosis or when information

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additional, such as the quantitative determination of hepatic copper in Wilson's disease or iron hepatic in hemochromatosis, are necessary for a definitive diagnosis. Liver biopsy under radiographic guidance is also indicated if a liver mass cannot be characterized as benign or malignant by non-invasive methods (3)

APPROACH TO THE PATIENT WITH HEPATOMEGALY

The initial evaluation of a patient with hepatomegaly includes obtaining a history to identify symptoms suggestive of underlying systemic disease and risk factors for liver disease, performing a physical examination to look for clues to the etiology and signs of liver disease, and obtaining biochemical data and function tests and Doppler ultrasound. Subsequent tests are determined based on information gathered from the history and physical examination, as well as the pattern of abnormalities in laboratory tests, if any. present. Figure 1 shows the suggested approach to the patient with hepatomegaly.

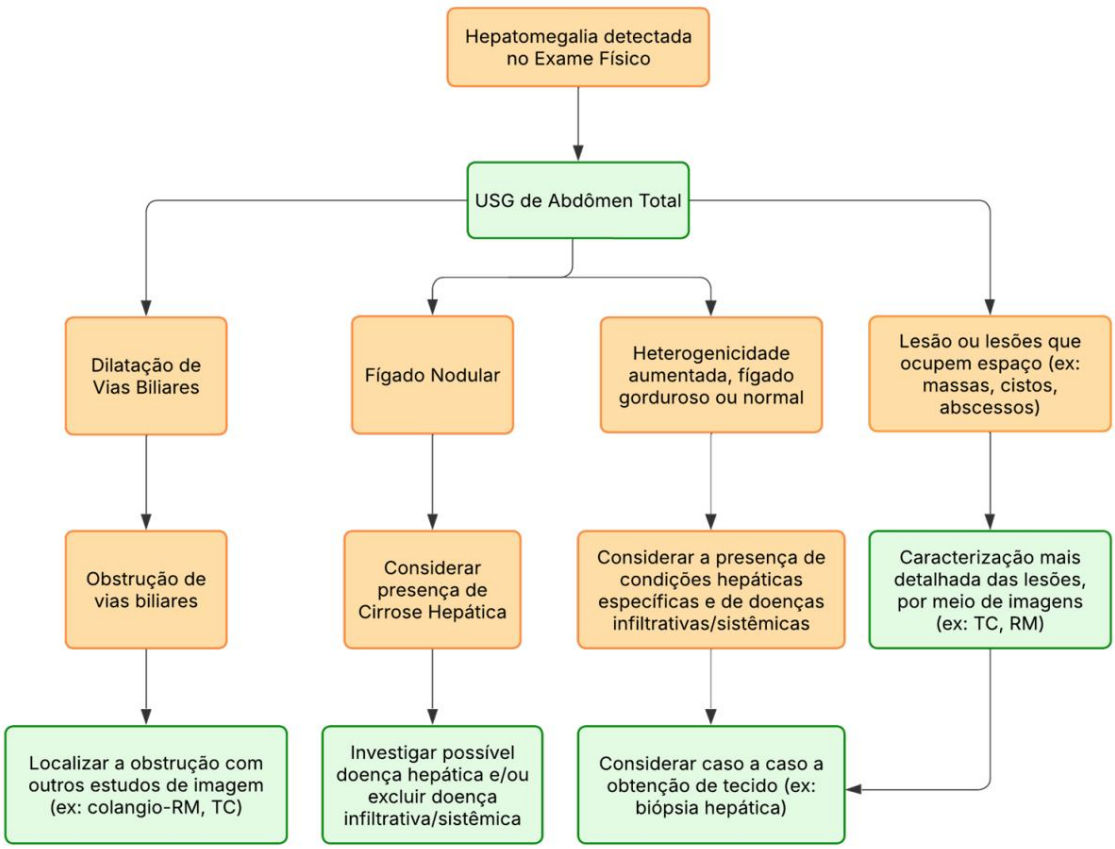

Fig. 1 Approach to the patient with hepatomegaly (MARTIN, P, 2020, In Cecil medicine)

SPLEEN: ANATOMY AND FUNCTIONS

The spleen is a reticuloendothelial organ that has its embryological origin in the mesogastrium dorsal around 5 weeks of gestation. It appears in a series of prominences, migrates to

its normal location in adults, in the left upper quadrant (LEQ). When the prominences do not unite into a single mass of tissue, accessory spleens appear in about 20% of individuals (7). It is located within the peritoneal cavity, in the posterior portion of the upper left quadrant, below the diaphragm and adjacent to the lower ribs (9 to 11), to the stomach, to the splenic flexure of the colon and to the left kidney, with its hilum in close proximity to the tail of the pancreas. The spleen is connected to the stomach and kidney by the gastrosplenic and splenorenal ligaments, respectively (7)

Two areas are distinguished, the white pulp and the red pulp, with anatomy and functions distinct. The red pulp is composed of blood-filled sinuses or sinusoids, cords splenic reticular fibers and marginal zone surrounding the white pulp. The white pulp is composed of nodules, called Malpighian corpuscles, composed of "follicles lymphoids" (or "follicles"), rich in B lymphocytes and the periarteriolar lymphoid sheath (PALS) rich in T lymphocytes (2,4,7).

The splenic artery, derived from the celiac artery, supplies arterial blood to the spleen (7). The vein splenic vein combines with the superior mesenteric vein to become the portal vein. The spleen has a series of functions that can be broadly divided into filtration, immunological and hematopoietic processes (19, 20, 21):

Filtration - through the sinusoids in the red pulp, the spleen removes unsuitable materials of blood, including senescent red blood cells (hemocateresis), defective red blood cells (acquired or congenital), cellular particles (e.g., nuclear debris, metabolic remnants, etc.) (2).

Immunity - In the white pulp reside the lymphoid follicles rich in B lymphocytes, and the sheath periarteriolar lymphoid, rich in T lymphocytes that are part of the monocytic-macrophagic system and that make up the immune system against infections (2)
In it, which is a secondary lymphoid organ, B lymphocytes, T lymphocytes and plasma cells mature and reside in the white pulp. Mature B cells interact with T cells in the spleen during the antigen-dependent phase humoral immune response, which leads to the production and release of antibodies (4).

Hematopoiesis – While the bone marrow is the primary site of hematopoiesis in adults, the spleen has an important hematopoietic function until the fifth month of pregnancy, which can be resumed after birth in the presence of hematological diseases (e.g., Agnogenic Myeloid Metaplasia, hemoglobinopathies) (2, 7).

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Another function of the spleen is to store formed elements of the blood, it contains approximately one-third of total body platelets, as well as a significant number of marginated neutrophils. These cells will be available when needed to respond to bleeding or infection (2,7). An increase in these normal functions can result in splenomegaly (7).

Splenomegaly

Spleen size correlates with a person's height, weight, and sex; it is slightly larger in taller, heavier individuals and in men than in women (22).
In an adult, it weighs about 150 g and measures 12 cm long, 7 cm wide, and 3 cm thick (2.9). It is located deep within the splenic cavity. It is limited superiorly with the upper margin of the 9th rib in the left posterior axillary line and inferiorly with the lower margin of the 11th rib, so the normal spleen is usually not palpable because it is located below the rib cage in the upper left abdomen (2). The splenomegaly or enlargement of the spleen, as seen by physical examination or imaging tests:

Physical examination - in the physical examination of the spleen, palpation and percussion.
- **Palpation:** palpation can be performed by bimanual palpation, rejection and palpation from from above (Middleton maneuver). In bimanual palpation, as reliable as other techniques, the patient should lie on his back with his knees bent. The doctor places his hand left over the lower part of the rib cage and pull the skin towards the costal margin, allowing the fingertips of the right hand to feel the tip of the spleen as it descends while the patient inhales slowly, smoothly and deeply. Palpation begins with the right hand in the lower left quadrant, with gradual movement towards the margin left costal, thus identifying the lower border of a massively enlarged spleen.
When the tip of the spleen is felt, the finding is recorded in centimeters below the margin left costal, at some arbitrary point, i.e., 10 to 15 cm from the midpoint of the umbilicus or the xiphisternal junction (7). A palpable spleen usually implies splenomegaly significant.
- **Percussion:** percussion for splenic dullness is performed using any of the three techniques described by Nixon, Castell or Barkun:

Nixon method: The patient is placed on the right side so that the spleen is in above the colon and stomach. Percussion begins at the lower level of the pulmonary tympanic sound, in the posterior axillary line, and continues diagonally along a perpendicular line in towards the mid-anterior costal margin. The upper edge of the dullness is normally 6 to 8 cm above the costal margin. A dullness > 8 cm in adults is presumed to indicate splenomegaly (7).

Castell method: with the patient in the supine position, percussion in the intercostal space inferior, in the anterior axillary line (eighth or ninth space) produces a resonant sound if the spleen is of normal size. This occurs during expiration or full inspiration. A dull sound on percussion during full inspiration suggests splenomegaly (7).

Percussion of Traube's semilunar space: the borders of Traube's space are the sixth rib superiorly, the left midaxillary line laterally and the left costal margin inferiorly. The patient is placed in a supine position with the left arm in a slight abduction. During normal breathing, this space on the medial margin is percussion to the side, obtaining a normal tympanic sound. A dull note to percussion suggests splenomegaly (7). However, this finding is not extremely sensitive or specific. False Positives may occur with liver enlargement or a recent meal, and false negatives may occur in obese individuals (23).

CAUSES

Various causes and mechanisms can lead to an increase in the size of the spleen and/or other organs, mainly the liver and lymphatic system (2) - **(Table** 2):

Table 2 - Causes of Splenomegaly

Congestive
Cirrhosis
Heart failure
Thrombosis of portal, hepatic, splenic, mesenteric veins
Malignancies
Lymphomas, usually indolent variants.
Acute and chronic leukemias
Polycythemia vera
Waldestrom's macroglobulinemia
Essential thrombocythemia
Agnogenic Myeloid Metaplasia

Langerhans Cell Histiocytosis
Primary Splenic Tumors (angiosarcoma)
Metastatic Solid Tumors
POEMS Syndrome

Infections
Viral - hepatitis, infectious mononucleosis, cytomegalovirus, measles, AIDS
Bacterial - salmonellosis, brucellosis, tuberculosis, lues, sepsis, typhoid fever
Parasitic - malaria, schistosomiasis, toxoplasmosis, visceral leishmaniasis
Infective Endocarditis
Systemic mycoses

Inflammatory
Sarcoidosis
Serum sickness
Systemic Lupus Erythematosus
Rheumatoid Arthritis (Felty's Syndrome)

Non-malignant infiltrative
Gaucher disease
Niemann-Pick disease
Amyloidosis
Glycogen Storage Disease
Hemophagocytic Lymphohistiocytosis

Hematological (hypersplenism)
Acute/chronic hemolytic anemias (acquired and congenital), iron deficiency
Sickle cell anemia in children (in adults, autosplenectomy occurs)
Use of recombinant human granulocyte colony-stimulating factor

Splenomegaly due to benign lesions
True cysts, pseudocyst, parasitic cyst (hydatid cyst)
Hemangioma (most common primary tumor of the spleen)
Harmatomas, lymphangiomas, splenic peliosis
Thyrotoxicosis

The possibilities of differential diagnosis become much smaller when the spleen is “massively enlarged”, > 8 cm below the left costal margin or has a drained weight of ÿ 1,000 g. The vast majority of these patients have non-Hodgkin lymphoma, chronic lymphocytic leukemia, hairy cell leukemia, chronic myeloid leukemia, (7,11) - **(Table** with myeloid metaplasia or polycythemia vera 3). myelofibrosis

Table 3 - Causes of massive splenomegaly

Diseases associated with massive splenomegaly

Chronic myeloid leukemia	Gaucher disease
Lymphomas	Chronic lymphocytic leukemia
Hairy cell leukemia	Sarcoidosis
Myelofibrosis with myeloid metaplasia	Autoimmune hemolytic anemia
Polycythemia vera	Diffuse splenic hemangiomatosis

The spleen extends > 8 cm below the left costal margin and/or weighs > 1,000 g

COMPLEMENTARY EXAMS

- Laboratory tests: the indication of laboratory and imaging tests occurs on a case-by-case basis, to perform diagnosis of the underlying disease that presents with splenomegaly as a manifestation (8).

- Complete blood count and blood smear – abnormalities on the complete blood count and blood smear may usually suggest a class of hematologic disorders (7):

• Erythrocyte count may be normal, decreased (thalassemia major syndromes, SLE, cirrhosis with portal hypertension) or increased (polycythemia vera).

•Platelet count may be normal, reduced when there is increased sequestration or destruction of platelets in the enlarged spleen (congestive splenomegaly, Gaucher disease, immune thrombocytopenia) or elevated in myeloproliferative disorders such as polycythemia vera.

• Increased granulocyte count (infections or inflammatory disease, disorders myeloproliferative).

• Cytopenias – Liver disease with hypersplenism, AIHA, ITP, Felty's syndrome or congenital disorders (e.g., hereditary hemolytic anemias)

• Immature or abnormal white blood cells (leukocytes) – Lymphoproliferative disorders or myeloproliferative

• Teardrop-shaped cells – Myelofibrosis or thalassemia

• Spherocytes – AIHA or hereditary spherocytosis

- Liver function tests are often helpful in determining the contribution of disease hepatic.

- Blood cultures are obtained if infection is suspected.

- Serologies can be used to diagnose certain pathogens.

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Subsequent examinations are guided by the acuity of symptoms and details of findings. (7).

- Image:

Ultrasound – The least invasive and least expensive approach to imaging the spleen is ultrasound, an approach that allows for sequential and accurate measurements. By the criteria of ultrasound, a spleen that is 13 cm or more in length and more than 5 cm in "thickness" qualifies as enlarged (6). It is the current procedure of choice for routine assessment of spleen size (7).

Computed tomography (CT) – by CT, splenomegaly is defined as a spleen of (8). Compared to ultrasound, CT scans length > 10 cm generally focus on the entire abdomen, not just the spleen, and provide information important that often provide an explanation for splenomegaly. The CT scans will also show whether the spleen is diffusely enlarged or enlarged due to multiple nodules (6). CT is adequate for assessing consistency and useful for identifying splenic tumors or abscesses (8).

Magnetic resonance imaging (MRI) - although CT and MRI are effective in identifying lesions focal lesions, MRI may be more useful in characterizing a lesion that has been identified and requires additional evaluation...

Scintigraphy – Gallium scintigraphy allows the identification of active infections or lymphomas, while with technetium it detects liver diseases with secondary splenic involvement (e.g., cryptogenic cirrhosis) (8).

Fluorodeoxyglucose-PET (FDG-PET) – it does not distinguish between a variety of malignancies, infections and other causes of splenomegaly, but is usually used later, to evaluate patients with lymphoid malignancies, to assess the response and not in the diagnostic evaluation of the patient with splenomegaly (6).

- Biopsy

Spleen biopsy is not performed frequently due to its extensive vascularization and associated risk of bleeding. Splenic biopsy can be used in cases of lesions isolated splenic lesions of unknown cause, for which there is no other tissue more amenable to biopsy or if biopsies from other sites have not been revealing (10). It is usually done using ultrasound or CT guidance in controlled circumstances, with surgical support available if emergency splenectomy is required due to bleeding.

APPROACH TO THE PATIENT WITH SPLENOMEGALY

The evaluation of splenomegaly depends on the patient's clinical condition and the reason for the which splenomegaly was identified. It must be differentiated whether the individual actually has a disorder involving the spleen, or if you simply have a slightly enlarged spleen, visualized in an imaging exam, without any associated pathology.

Initially, one should focus on excluding systemic disease that could explain the splenomegaly. Occult infections, hematologic diseases, and liver diseases should be investigated. occult diseases, autoimmune disease or storage disease. To do this, the patient's history must be obtained, seeking to identify symptoms suggestive of underlying systemic disease, complementing this history with a detailed physical examination, to look for clues about the etiology of the splenomegaly. Then, laboratory tests such as a complete blood count, blood smear peripheral, liver function and imaging tests should be requested to complement the history information and physical examination findings.

The presence of fever, weight loss and other symptoms requires persistence and consultation for exclude active infection or neoplasia. Bone marrow examination with culture and cytometric analysis flow, may be useful in identifying a cause in these patients. Splenectomy or biopsy of focal splenic lesions, may be the only diagnostic option in patients with symptoms persistent or progressive cytopenias. However, in the asymptomatic patient, careful observation is often preferable to splenectomy (6).

When the systemic condition is identified, treatment should be continued and reevaluate the spleen.

SPLENECTOMY

Due to the risk of surgical complications and long-term susceptibility to infection (in particular those caused by encapsulated microorganisms) in individuals splenectomized, the relative risks and benefits of the procedure must be seriously considered. considered. Once splenectomy is a possibility, immunization should proceed promptly in an attempt to reduce long-term risks (6). Splenectomy is an option for symptom control in massive splenomegaly, disease control in cases of traumatic rupture of the spleen or for correction of cytopenias in patients with hypersplenism or immune destruction of blood cellular elements (7).

Chronic manifestations of splenectomy consist of marked variation in size and shape of erythrocytes (anisocytosis, poikilocytosis), as well as the presence of

Howell-Jolly bodies (nuclear remnants), Heinz bodies (hemoglobin denatured), basophilic stippling and occasional nucleated erythrocytes in peripheral blood. When these red cell abnormalities appear in a patient whose spleen has not been removed, splenic infiltration by tumor should be suspected, interfering with its normal functions of selection and removal (7).

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