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Rendu-Osler-Weber Syndrome: Literature Review and Clinical Case

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Abstract

Hereditary hemorrhagic telangiectasia (HHT) is a rare autosomal dominant disorder characterized by vascular dysplasia. Research in the field of genetics and regulation of angiogenesis has made a significant contribution to understanding the etiology and pathogenesis of HHT. Screening examination for HHT includes: physical examination, determination of hemoglobin and ferritin levels in the blood, radiology and endoscopic methods - the choice of method depends on the area of the suspected lesion. Treatment of HHT requires a multidisciplinary approach.

A clinical case of a 69-year-old patient who was diagnosed with Rendu-Osler-Weber disease for 15 years is presented. No surgical interventions were performed during this time, dynamic observation was carried out. Currently, she noted an attack of pain in the right hypochondrium radiating to the back. The examination revealed the following changes: Arteriovenous malformations (AVMs) of the liver (Rendu-Osler-Weber disease). Variant of development of the celiac-mesenteric basin. Aneurysms of the common hepatic and splenic arteries. Thrombosis of the superior mesenteric vein. Hypervascular areas in the tail of the pancreas should be differentiated between the bypass zone and neuroendocrine tumors. Signs of liver cirrhosis. Hepatosplenomegaly. Portal hypertension. Moderate intrahepatic biliary hypertension. Varicose veins of the esophagus, abdominal cavity and small pelvis. Spleen hemangioma. Lateral abdominal hernia. Diverticulosis of the colon. Compression atelectasis of the basal segments of both lungs. Cardiomegaly.

The following treatment tactics were determined. The first stage is endovascular occlusion of arteriovenous intrahepatic aneurysms, the second stage is surgical treatment for hepatic artery aneurysm. Celiacography, superior mesentericography, endovascular occlusion of the branches of the phrenic artery and the right and left hepatic arteries were performed. Control angiograms showed that the blood flow in the left and right hepatic arteries was slow, all hepatic arteries were contrasted in the antegrade direction. Control echocardiography showed positive dynamics. The sizes of the heart cavities and the pulmonary artery trunk decreased. The patient was discharged in a satisfactory condition. A follow-up examination at the Center's outpatient clinic in 3 months to decide on a repeat session of the endovascular occlusion.

The tactics of treating liver AVMs, unlike AVMs of other organs, remains insufficiently defined. A radical method of treating liver AVMs is liver transplantation, but it is associated with a shortage of donor organs. Endovascular occlusion of AVMs seems to be a promising and pathogenetically justified method of treating liver AVMs, but requires further multicenter studies.

Keywords: *Rendu-Osler-Weber disease, hereditary hemorrhagic telangiectasia, arteriovenous malformations (AVMs) of the liver, hepatic artery aneurysm, diagnostics, treatment, endovascular occlusion, literature review.*

1. INTRODUCTION

Rendu-Osler disease (Rendu-Osler-Weber), Osler syndrome, familial hereditary telangiectasia, hereditary hemorrhagic telangiectasia (HHT), hemorrhagic angiomatosis is a rare familial hereditary disease, which is based on the inferiority of the vascular endothelium, as a result of which multiple angiomas and telangiectasias (vascular anomalies) are formed in different areas of the skin and mucous membranes of the lips, mouth, and internal organs, which bleed [1-4]. It is named after Sir William Osler, Henri Jules Louis Marie Rendu and Frederick Parkes Weber, who described it in the late 19th - early 20th centuries [5].

Several 19th-century English physicians, beginning with Henry Gawen Sutton (1836–1891) [6], then Benjamin Guy Babington (1794–1866) [7] and John Wickham Legg (1843–1921) [8, 9], described the most common features of HHT, particularly recurrent epistaxis and the hereditary nature of the disease. The French physician Henri Jules Louis Marie Rendu (1844–1902) observed lesions of the skin and mucous membranes and distinguished the condition from haemophilia [10]. Canadian-born Sir William Osler (1849–1919), then at Johns Hopkins Hospital and then at Oxford University, made an additional contribution with a 1901 report in which he described the characteristic lesions of the alimentary tract [11]. The English physician Frederick Parkes Weber (1863–1962) reported this disease in a series of cases in 1907 [12]. The term "hereditary hemorrhagic telangiectasia" was first used by the American physician Frederick M. Haynes (1883–1946) in a 1909 article about this disease [13].

Studies of populations from many regions of the world have shown that HHT occurs at roughly the same frequency in almost all populations: somewhere between 1 in 5,000 and 8,000 [2, 14]. In some regions, it is much more common; for example, in the French region of Haut Jura, the rate is 1 in 2,351 – twice as common as in other populations. This is explained by a founder effect, in which a population descended from a small number of ancestors has high levels of a particular genetic trait because one of those ancestors had that trait.[15] In the Haut Jura, this has been shown to result from a specific ACVRL1 mutation (called c.1112dupG or c.1112_1113insG). [16] The highest incidence of HHT is 1:1331, reported in Bonaire and Curaçao, two Caribbean islands in the Netherlands Antilles [2].

HHT is a genetic disorder with an autosomal dominant inheritance pattern. People with symptoms of HHT who have no relatives with the disorder may have a new mutation [17]. Homozygosity is fatal in utero [18]. Five genetic types of HHT have been proven. Of these, three are associated with specific genes, and the remaining two are currently associated only with a specific locus. More than 80% of all cases of HHT are associated with mutations in ENG or ACVRL1 [2]. In total, more than 600 different mutations are known. It is likely that one type or another predominates in certain populations, but the data are contradictory. As already mentioned, the leading role in the pathogenesis of HHT is played by anatomical and functional changes in the vessels - dysplasia of the vascular wall, its thinning with a tendency to recurrent bleeding. In the overwhelming majority of cases, the wall of small vessels consists of only endothelium. In this regard, even minor mechanical and thermal damage can disrupt its integrity and lead to profuse bleeding [19]. As a result of mutation of the gene encoding the endothelial cell protein endoglin, the transforming growth factor β is bound. This leads to a defect in the muscular and elastic layers of the vessels, destruction of contacts between endothelial cells, dilation and fragility of the capillaries, and loss of the supporting properties of the vessels [20-22]. As a result, multiple saccular dilations of the capillary vessels appear in the upper layers of the mucous membrane (or dermis), the walls of which consist of only endothelium and are surrounded by loose connective tissue [1-23].

Telangiectasias (small vascular malformations) can occur on the skin and mucous membranes of the nose and gastrointestinal tract. The most common problem is nosebleeds, which often occur in childhood and occur in about 90–95% of people with HHT. Lesions on the skin and mouth are less likely to bleed but may be considered cosmetically unsightly; they affect about 80% of patients. Skin lesions typically occur on the lips, nose, and fingers, as well as on the skin of the face in sun-exposed areas. They appear suddenly and increase in number over time [4, 16–18].

Gastrointestinal bleeding is the most common symptom after epistaxis; it occurs in about 13–30% of patients with HHT and most often begins after age 50 [24]. There are numerous case reports and case series published in the literature describing patients with overt or occult gastrointestinal bleeding, however, there are still no specific data regarding the occurrence of gastrointestinal bleeding associated with HHT

[25, 26]. The article by C. Canzonieri et al. describes a cohort of 22 patients with HHT who underwent gastroduodenoscopy, capsule endoscopy and colonoscopy. The aim of the study was to evaluate the distribution, number, size and type of telangiectasias depending on the HHT genotype (ENG or ACVRL1 mutation). They showed that gastrointestinal lesions in patients with HHT are more common in the duodenum [27]. M. Ingrosso et al. performed gastroscopy and capsule endoscopy in patients with HHT and found telangiectasia of the small intestine in 56% of patients [25]. Currently, most of the data accumulated in the literature are clinical casdes or case series. To date, no large multicenter randomized trials have been conducted on the treatment of this special group. Gastrointestinal bleeding is rarely significant enough to be noticed (as hematemesis or black stools), more often the vascular lesions bleed intermittently, but this may eventually lead to depletion of iron stores in the body, leading to iron deficiency anemia [4, 16-18].

Arteriovenous malformations (AVMs, larger vascular malformations) occur in large organs, predominantly the lungs (pulmonary AVMs) (50%), liver (30-70%) and brain (cerebral AVMs, 10%), and rarely (<1%) AVMs in the spinal cord [4, 16-18].

Many patients with diagnosed or undiagnosed HHT may have anemia without evidence of overt bleeding, and in these cases other sites of bleeding such as the gastrointestinal tract should be sought. Other manifestations, again in diagnosed or undiagnosed HHT, may result from hepatic AVMs with clinical manifestations of portal hypertension, splenomegaly, ascites, and encephalopathy. For these reasons, the role of the gastroenterologist is very important in the management of patients with HHT [28].

A very small proportion of patients (those with SMAD4 (MADH4) mutations) have multiple benign polyps in the colon, which may bleed or progress to colorectal cancer. An equally small proportion have pulmonary hypertension, a condition in which the pressure in the pulmonary arteries increases, putting pressure on the right side of the heart and causing peripheral edema (swelling of the legs), fainting, and attacks of chest pain. It has been noted that the risk of thrombosis (especially venous thrombosis in the form of deep vein thrombosis or pulmonary embolism) may be increased. It is suspected that people with HHT may have mild immunodeficiency and therefore be at slightly increased risk of infections [18].

Guidelines have been developed for the diagnosis, screening, and treatment of people living with HHT. The initial guidelines were published in 2011 and covered the diagnosis of HHT, nosebleeds, cerebral vascular malformations, pulmonary AVMs, gastrointestinal bleeding, and hepatic vascular malformations [4]. The second edition of these principles was published in 2020 with updated data on epistaxis, gastrointestinal bleeding, and hepatic vascular malformations, as well as new guidelines on anemia and anticoagulation, pediatrics, pregnancy, and childbirth [17].

Accordance to the international recommendations, as well as the result of the analysis of the largest HHT cases series, examination of patients with suspected HHT includes the following diagnostic methods: physical examination, determination of the level of hemoglobin, blood ferritin, radiology methods of examination - the choice of method depends on the area of the suspected lesion (echocardiography and ultrasound duplex scanning of the liver, MSCT of the lungs, MRI of the brain), endoscopic methods (esophagogastroduodenoscopy, nasopharyngeal endoscopy or laryngoscopy, capsule endoscopy).

The use of genetic diagnostic methods is indicated in children with no clinical manifestations of the disease if the parents have HHT [29].

Diagnostic tests can be performed for various reasons. Some tests are needed to confirm or refute the diagnosis. Others - to identify possible complications [4].

Due to the rarity of HHT in general and liver damage, we present a clinical case of a 69-year-old woman, who was treated at A.V. Vishnevsky National Medical Research Center of Surgery with a diagnosis of Rendu-Osler-Weber disease and the presence of AVMs of the visceral vessels.

Complaints: moderate pain in the right hypochondrium.

2. ANAMNESIS

Rendu-Osler-Weber disease was diagnosed about 15 years ago. No surgical interventions were performed during this time, dynamic observation was carried out. In March, she noted an attack of pain in the right hypochondrium radiating to the back. She was hospitalized. An ultrasound scan revealed an aneurysm of the right hepatic artery. A course of therapy with

antispasmodics was administered, after the attack was relieved, she was discharged. Esophagogastroscopy: varicose veins of the esophagus stage 1-2, chronic gastritis, duodenitis.

After 3 months, an outpatient examination was performed at A.V. Vishnevsky National Medical Research Center of Surgery.

3. MSCT

Free fluid in the abdominal cavity is not detected. A minimal amount of delimited fluid is traced along the posterior surface of the spleen.

The liver is enlarged, measuring 20.6 x 12.6 x 15.5 cm, with a density of 57 HU, and with distinct tuberous contours. Hypertrophy of segments I, II, and IV of the liver is noted. When contrasting in the arterial phase, diffuse heterogeneous enhancement of the parenchyma is noted, against which multiple tortuous dilated vessels are contrasted. Arteriovenous shunts are determined in the liver between the portal vein system and the hepatic arteries (Fig. 1 a, b). The changes are more pronounced in the right lobe. In the delayed phase, the parenchyma is contrasted uniformly, the vessels are isodense to the parenchyma. The portal vein is dilated to 20 mm. In the superior mesenteric vein, a parietal thrombus is determined over a length of 40 mm to the level of confluence with the splenic vein (Fig. 1c). Splenic vein up to 13 mm in diameter. Varicose tortuous veins up to 14 mm in diameter are found in the abdominal cavity, along the posterior wall of the esophagus, in the pelvic cavity. The inferior vena cava is intact.

The superior mesenteric artery (SMA) is dilated to 13 mm. The celiac trunk is represented by the left gastric, splenic and gastroduodenal arteries GDA. The common hepatic artery departs from the superior mesenteric artery at a distance of 40 mm from the orifice of SMA, with a diameter of 12 mm. At a distance of 11 mm from the orifice of the common hepatic artery (CHA), an aneurysm is determined (Fig. 2), measuring 63x54 mm, walls up to 3 mm, adjacent tissue is compacted, distally the lumen of the CHA is 17 mm in diameter.

Intrahepatic bile ducts with a diameter of up to 4 mm, common bile duct up to 10 mm. The transverse size of the gallbladder is 37 mm, a kink is determined in the neck area. The walls are not thickened, the contents are homogeneous.

The splenic artery is up to 9 mm in diameter; in the distal part of the splenic artery, two aneurysms with calcified walls are determined: proximally, a fusiform aneurysm up to 17 mm in diameter (Fig. 3a) and distally, a saccular aneurysm 10 mm in diameter (Fig. 3b).

The spleen has smooth, clear contours, is enlarged, and measures 133x70x190 mm. Contrast parameters are normal. On the medial surface at the level of the sinus, a round hypodense lesion with a density of 30 HU, 13 mm in diameter, is determined in the splenic parenchyma, centripetally accumulating the contrast agent more in the delayed phase. The spleen somewhat compresses the left kidney. The pancreas is correctly located, the head is somewhat compressed by an aneurysm of the inferior pancreaticoduodenal artery. Dimensions: head 20 mm, body 17 mm, tail 11 mm, density is unchanged: 51 HU in the native phase. The contours of the gland are clear and uneven. In the arterial and venous phases, hypervascular areas measuring 11x6 mm and 2 mm are determined in the tail of the pancreas (Fig. 4). In the delayed phase, the density of these areas is similar to the density of the pancreatic parenchyma. The pancreatic duct is not dilated. The parapancreatic tissue is not infiltrated. The parapancreatic lymph nodes are not enlarged.

The adrenal glands are usually located, unchanged. The kidneys are of normal shape, size, location, the contours are clear, smooth. Radiopaque stones are not determined. The calyceal-pelvic system, the upper sections of the ureters are not dilated. The excretory phase is unchanged.

Along the left lateral surface, there is a divergence of the abdominal wall muscles, the width of the hernial orifice is 42 mm. The contents of the hernial sac are fatty tissue and varicose veins.

In the walls of the large intestine, diverticula up to 10 mm in diameter are determined along the entire length.

On the scans included in the study area, compression of the posterobasal segments of both lungs is noted (more on the left). Calcifications are detected against the background of hypoventilation zones and in the bronchial walls. The heart is significantly enlarged (CTI=0.67) (Fig. 5).

Conclusion. AVMs of the liver (Rendu-Osler-Weber disease). Variant of the celiac-mesenteric basin. Aneurysms of the common hepatic and splenic arteries. Thrombosis of the superior mesenteric vein. Hypervascular areas in the tail

of the pancreas should be differentiated between the bypass zone and neuroendocrine tumors. Signs of liver cirrhosis. Hepatosplenomegaly. Portal hypertension. Moderate intrahepatic biliary hypertension. Varicose veins of the esophagus, abdomen and pelvis. Hemangioma of the spleen. Lateral abdominal hernia. Diverticulosis of the colon. Compression atelectasis of the basal segments of both lungs. Cardiomegaly.

4. ECHOCARDIOGRAPHY

Increased size of all heart cavities. Left ventricular myocardial hypertrophy. Impaired diastolic function of the left ventricle, type 1. Aneurysmal dilation of the trunk and branches of the pulmonary artery. Slightly increased pressure gradient on the mitral valve due to remodeling of the left cavities. No blood shunts. Minor mitral, aortic and tricuspid regurgitation. Contractile function of the left ventricle is moderately reduced. No data on pulmonary hypertension.

The patient was hospitalized at A.V. Vishnevsky National Medical Research Center of Surgery for further examination and treatment.

Anamnesis of life: bronchial asthma since 30 years of age (?).

5. ULTRASOUND WITH DUPLEX SCANNING

Free fluid in the abdominal cavity is not detected.

The liver is enlarged in size: the size of the right lobe is 170x165 mm, the left lobe is 120x96 mm. The contours of the liver are smooth, clear, the parenchyma is of increased echogenicity, heterogeneous structure. The vascular pattern of the liver is changed, the branches of the portal vein and hepatic artery at all levels are dilated, tortuous, multiple small cystic cavities are determined - arteriovenous shunts (Fig. 6). Against this background, data on the presence of additional focal changes in the liver parenchyma were not obtained.

In the projection of the liver hilum, there is an aneurysm of the common hepatic artery measuring up to 70 mm.

In the projection of the confluence, a parietal thrombus (Fig. 7) up to 12 mm thick is determined in the lumen of the vein, the passable lumen is up to 7 mm.

Intra- and extrahepatic bile ducts are not dilated, the hepaticocholedoch is 5.7 mm in diameter, the lumen is free. The gallbladder is enlarged, its dimensions are 78x34 mm, the walls are 1.2 mm, the contents are homogeneous.

The pancreas is not enlarged in size: the head is 20 mm, the body is 14 mm, the tail is 21 mm. The contours of the gland are smooth and clear, the parenchyma is of increased echogenicity, the structure is homogeneous. The pancreatic duct is not dilated.

The spleen is not enlarged, measuring 146 x 48 mm, S = 72 cm^2, contours are smooth, clear, the structure of the parenchyma is heterogeneous due to the presence of a rounded lesion of slightly reduced echogenicity in the gate, measuring mm, blood flow in the structure is not localized (most likely due to the insignificant size of the lesion).

Conclusion. Ultrasound signs of multiple AVMs of the liver (Rendu-Osler-Weber disease), portal hypertension, mural thrombosis in the projection of the portal vein confluence.

Duplex scanning of the brachiocephalic arteries

Conclusion. Bilateral deformation of the anatomical course of the ICA.

Duplex scanning of the arteries of the lower extremities

Conclusion. Atherosclerosis of the arteries of the lower extremities.

Duplex scanning of the veins of the lower extremities

Conclusion. The examined superficial and deep veins of both lower extremities are passable.

Based on the examination data, a ***consultation*** was held. The patient has Rendu-Osler-Weber disease with multiple intrahepatic portoarterial fistulas, a large aneurysm of the hepatic artery (branching from the SMA). Cardiomegaly with dilation of the right and left cavities of the heart (the cause of which is arteriovenous intrahepatic shunting of blood). There are no signs of pulmonary hypertension. The patient requires the first stage of endovascular occlusion of arteriovenous intrahepatic aneurysms, the second stage is surgical treatment for the hepatic artery aneurysm. The identified hypervascular areas in the tail of the pancreas should be differentiated between the bypass zone and neuroendocrine tumors (most likely AV-shunts), dynamic observation is advisable. Previously diagnosed bronchial asthma may be (?) a manifestation of pulmonary hypertension.

The Patient Underwent Surgery: Celiacography, Superior Mesentericography, Endovascular Occlusion of the Branches of the Phrenic Artery and the Right and Left Hepatic Arteries

Under combined anesthesia, the left brachial artery was punctured and catheterized, a TR 5F

introducer was installed, angiography of the celiac trunk and superior mesenteric artery was performed using a 0.035" hydrophilic guidewire and a 5F multipurpose catheter. A 5F multipurpose catheter was inserted alternately through the phrenic artery, then into the hepatic arteries branching off from the superior mesenteric artery. Angiography was performed. endovascular occlusion of the afferent branches was performed using cylindrical emboli of 0.6 mm - 3 fl. (90 pcs.) and 0.75 mm - 2 fl. (60 pcs.), as well as spherical emboli Contour (PVA) 1000-1180 microns - 3 bottles and Contour (PVA) 710-1000 microns - 2 bottles.

During the endovascular occlusion, the patient complained of difficulty breathing, after which verbal contact was not available - intensive therapy was started, it was decided to complete the intervention. Control angiography was performed. Catheters and introducer were removed. Hemostasis with the TR-Band device.

On the angiograms, the celiac trunk (CT) has uneven contours, homogeneous contrast, the branches of the celiac trunk are dilated. The CT is divided into the splenic and GDA. The proper hepatic artery originates from SMA, is dilated to 2.5 cm, tortuous, and divides into the left and right hepatic arteries. The branches of the left and right hepatic arteries are highly tortuous and dilated. At a distance of 1 cm from the mouth of the proper hepatic artery, an aneurysm with a diameter of up to 7 cm is determined; distal to the aneurysm, the artery can be traced with a diameter of up to 2 cm. In the projection of the left and right lobes of the liver, hypervascular lesions with a discharge of contrast into the portal vein for 2-3 sec are determined (Fig. 8a). The lesions are also contrasted from the diaphragmatic arteries and overflows from the GDA basin (Fig. 8b). On control angiograms, the blood flow in the left and right hepatic arteries is slowed (Fig. 9), all hepatic arteries are contrasted in the antegrade direction. There are no signs of intimal dissection and distal embolism. SMA and its branches have smooth contours and are contrasted homogeneously.

Conclusion. AVMs of the liver. Direct arteriovenous fistulas of the hepatic arteries. Condition after endovascular occlusion of the right and left hepatic arteries branches.

Intraoperatively, transient loss of consciousness and hemodynamic instability were noted, due to which the patient was transferred to the intensive care unit. Consciousness was restored on its own against the background of non-invasive ventilation. According to control studies, no data for pulmonary embolism were found.

The further course of the postoperative period is uneventful.

Control Echocardiography showed positive dynamics. The sizes of the heart cavities and the pulmonary artery trunk have decreased. Left ventricular myocardial hypertrophy. There are no local contractility disorders. Hemodynamically insignificant transvalvular regurgitations. Pulmonary hypertension of 1-2 degrees. No blood shunts. The contractile function of the left ventricle is normal.

Laboratory parameters are within normal limits.

The patient is discharged from the department in satisfactory condition for outpatient observation (surgeon, gastroenterologist, cardiologist). Follow-up examination at the Center's outpatient clinic in 3 months to decide on a repeat session of the endovascular occlusion.

6. Discussion

The most common symptom of HHT is recurrent nosebleeds, which often lead to severe anemia. Laboratory examination does not reveal any changes in blood coagulation parameters, platelets, clot retraction, or bleeding time [30, 31]. The first symptoms of the disease may appear during the first 12 months after birth, but the manifestation of the disease can occur at any age [23, 32]. Among patients who have reached the age of 16, signs of the disease appear in 71%, and among individuals aged 40 years - in more than 90% of patients [33]. The diagnosis of HHT remained clinical until a research group at Duke University Medical Center identified the genetic defects causing the pathology in 1994 and 1996, respectively [34, 35]. In 2000, the International Scientific Advisory Committee on the Treatment of HHT, formerly known as the HHT Foundation International, published the currently widely used Curaçao criteria [30].

No studies have been conducted to assess the sensitivity and specificity of the Curasao criteria, but experts believe that they have a greater diagnostic value than genetic testing. The use of genetic diagnostic methods is indicated in children with no clinical manifestations of the disease if their parents have HHT [29].

The diagnosis can be made depending on the presence of four criteria from the Curaçao criteria [30]. If three or four criteria are met, the patient has "definite HHT", and two give "possible HHT", less than two criteria - "doubtful HHT":

- recurrent spontaneous nosebleeds;
- multiple telangiectasias on the skin and mucous membranes;
- arteriovenous aneurysms of internal organs (lungs, brain and spinal cord, liver, gastrointestinal tract);
- the presence of a first-degree relative who meets the first three criteria.

Despite the "possible" designation, someone with a visceral AVMs and a family history but no nosebleeds or telangiectasias is still highly likely to have HHT, as these AVMs are very rare in the general population. However, the same cannot be said for nosebleeds and rare telangiectasias, which occur in people without HHT in the absence of an AVMs. Over the course of one's life, one's diagnostic status may change, as young children may not yet exhibit all the symptoms; at age 16, thirteen percent are still uncertain, while at age 60, the vast majority (99%) have a definite diagnostic classification. Thus, children of patients with confirmed HHT may be labeled "possible HHT", as up to 50% may develop HHT during their lifetime [36]. Treatment of HHT is symptomatic (treats symptoms, not the disease itself), since there is no therapy that would directly stop the development of telangiectasias and AVMs. In the treatment of HHT, two main principles are followed.

- control of local and general symptoms (bleeding of various localizations and their consequences);
- prevention of complications associated with the presence of AVMs in various organs.

Treatment of HHT requires an interdisciplinary approach involving a hematologist, otolaryngologist, pulmonologist, interventional surgeon, neurologist, neurosurgeon, geneticist, cardiologist.

With the discovery of the genetic basis of HHT, the attention of researchers focused on drug therapy aimed at angiogenesis. Bevacizumab is one of such drugs. It inhibits the biological activity of vascular endothelial growth factor (VEGF) and is currently used as a chemotherapeutic drug [37]. However, despite the ongoing research in the field of conservative treatment of the disease, preference is currently given to surgical methods of treatment, including minimally invasive ones.

In the above clinical case, the patient's liver was predominantly affected. In case of liver damage, the differential diagnosis of HHT should be made with telangiectasias in cirrhosis, as well as with hemophilia, thrombocytopenic purpura, and diffuse angiokeratoma of the Fabry trunk. Currently, there is no effective therapy for HHT manifestations in the liver. According to a number of authors, the indication for transarterial embolization of AVMs is a combination of liver AVMs with severe heart failure. According to international recommendations, AVMs embolization is performed in the presence of contraindications to liver transplantation and is associated with a high level of postoperative complications and mortality. However, according to A. Chavan et al., mortality after liver AVMs embolization is comparable to mortality after liver transplantation, but is associated with fewer complications [38-40]. A radical method of treating hepatic AVMs is liver transplantation, and the main indications for it are severe heart failure, biliary ischemia, portal hypertension, and lack of effect from embolization. Postoperative mortality is 10% [41-43].

According to Z.-C. Liu et al., ligation of the common hepatic artery and/or one of its branches provides correction of symptoms of heart failure and portal hypertension and improves the quality of life of patients. Indications for ligation of the hepatic artery are resistant heart failure (stages III-IV according to NYHA) and portal hypertension with ascites and/or bleeding from esophageal varices in patients with a dilated hepatic artery or its aneurysm with preserved liver function. However, these are data from a single-center retrospective study with a limited number of patients [44].

In our clinical case, in connection with multiple lesions of the liver vessels (both intra- and extrahepatic) and pronounced dilation of the heart cavities caused by arteriovenous intrahepatic blood flow in the liver, a decision was made to perform staged endovascular treatment.

7. Conclusion

HHT is a rare autosomal dominant disorder characterized by vascular dysplasia. Research in the field of genetics and regulation of angiogenesis has made a significant contribution to understanding the etiology and pathogenesis of HHT. Screening examination for HHT includes: physical examination, determination of hemoglobin and ferritin levels in the blood, radiology and endoscopic methods - the choice of method depends on the area of the suspected lesion. Treatment of HHT requires a

multidisciplinary approach. The tactics of treating liver AVMs, unlike AVMs of other organs, remains poorly defined. A radical method of treating liver AVMs is liver transplantation, but it is associated with a shortage of donor organs. Endovascular occlusion of AVMs seems to be a promising and pathogenetically justified method of treating liver AVMs, but requires further multicenter studies.

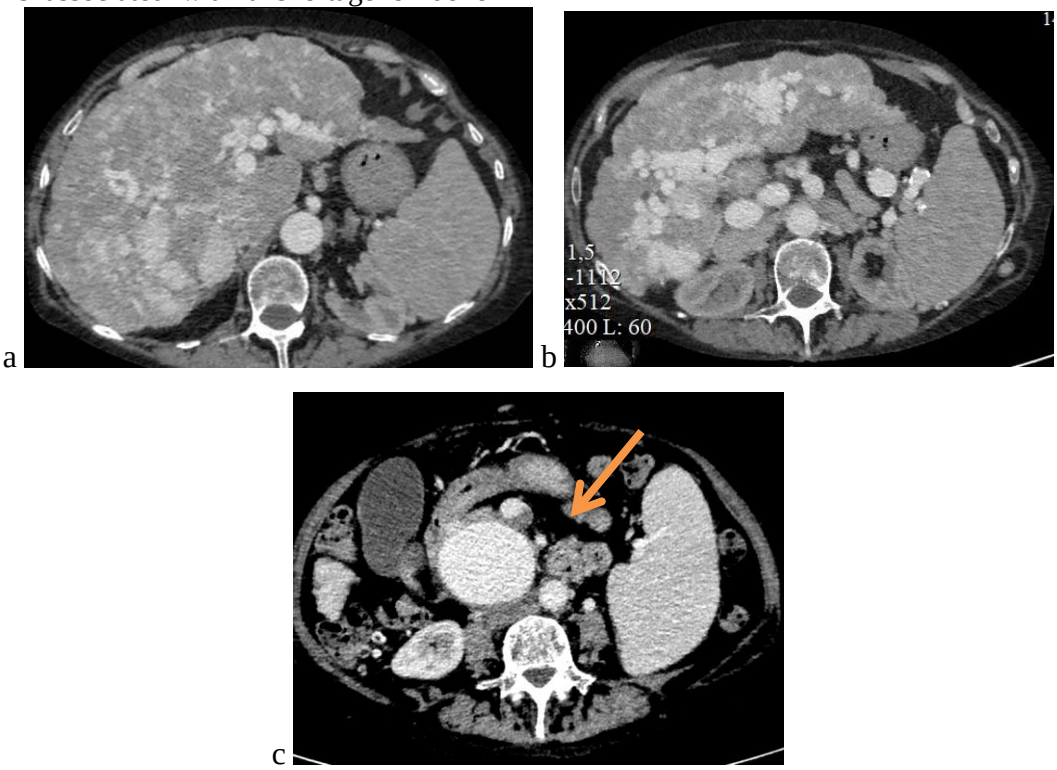

Fig 1. *MSCT images, arterial phase: a, b - arteriovenous shunts between the portal vein system and hepatic arteries at different levels; c - a mural thrombus is determined in the superior mesenteric vein (indicated by the arrow)*

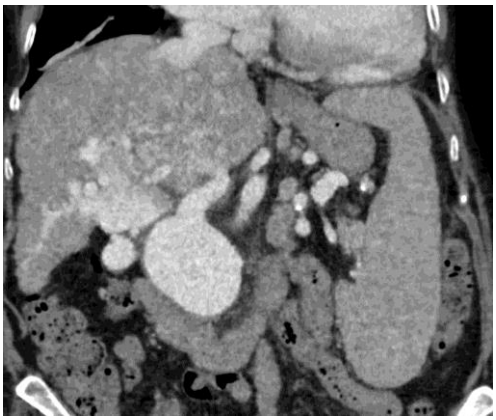

Figure 2. *MSCT image of a common hepatic artery aneurysm*

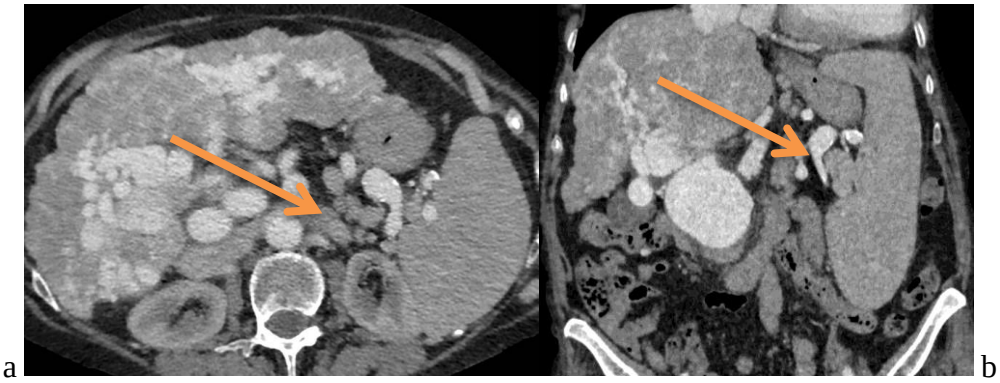

Figure 3. *MSCT images of splenic artery aneurysms (indicated by arrows): a - fusiform, b – saccular*

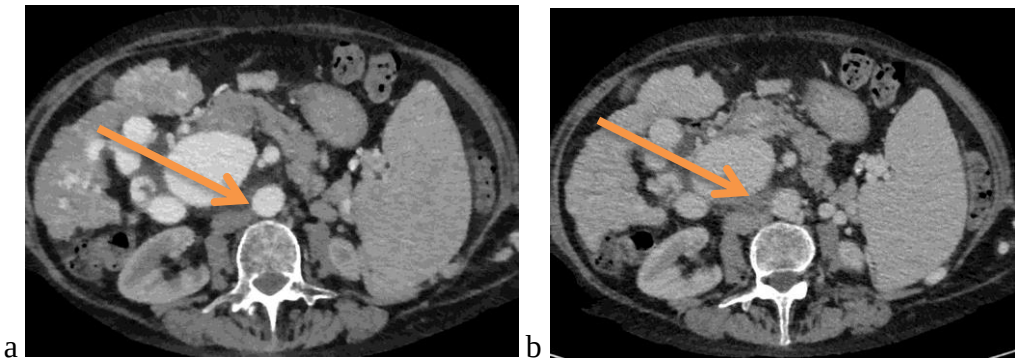

Figure 4. *MSCT image of a hypervascular area in the pancreas tail (indicated by an arrow): a – arterial phase, b – venous phase*

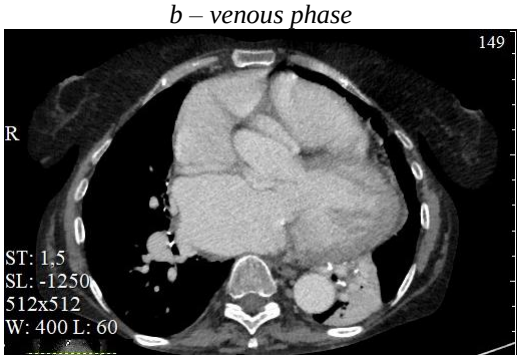

Figure 5. *MSCT image of an enlarged heart*

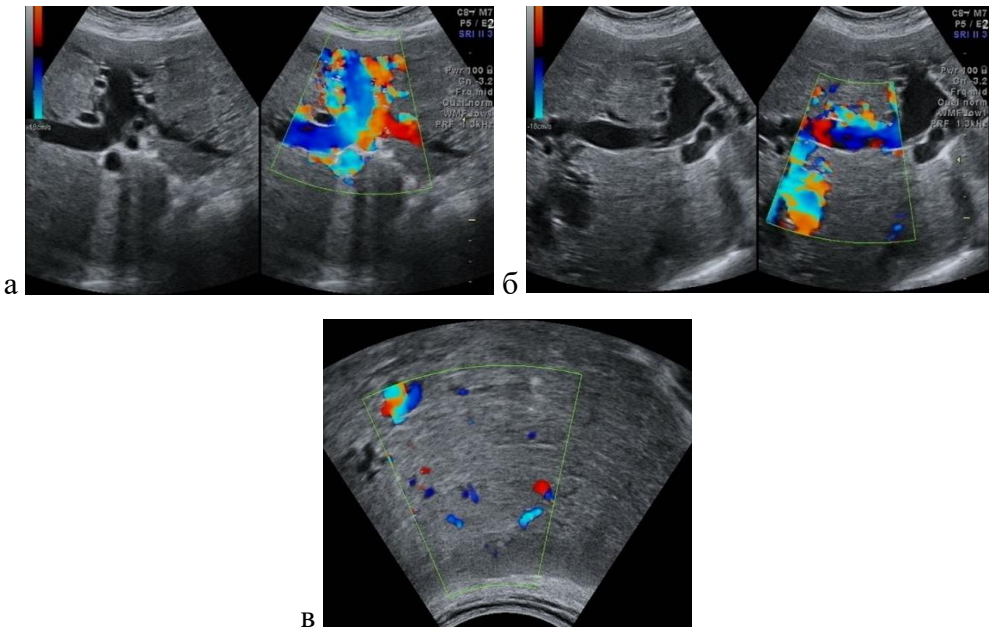

Figure 6. *Ultrasound images of the liver in Color Doppler Imaging: a – left branch of the portal vein with multiple AV-shunts; b – right branch of the portal vein with multiple AV-shunts; c – AV-shunts on the liver periphery*

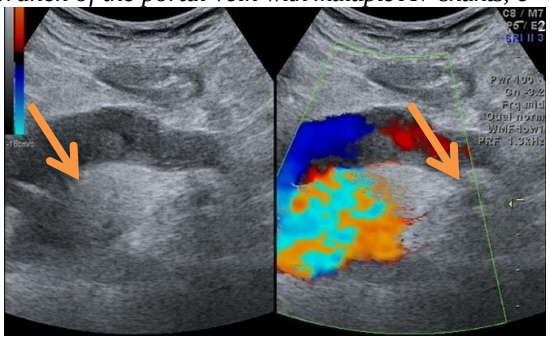

Figure 7. *Ultrasound image of a mural thrombus in the superior mesenteric vein (indicated by the arrow) in Color Doppler Imaging*

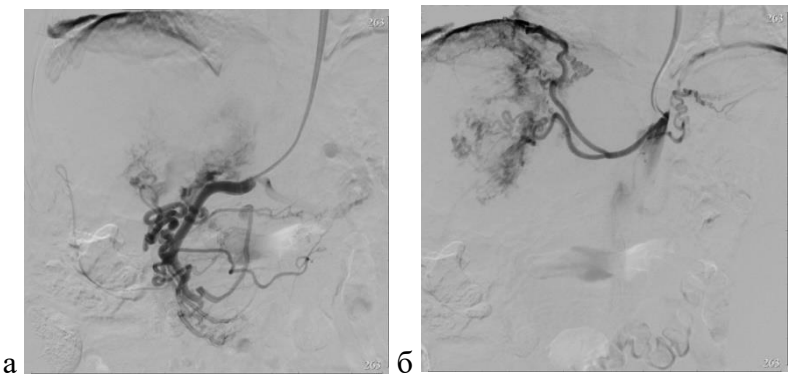

Figure 8. *Selective angiograms before endovascular occlusion: a - afferent branches of the GDA to the liver with AV-shunt; b - afferent branches from the phrenic artery with direct AV-shunt*

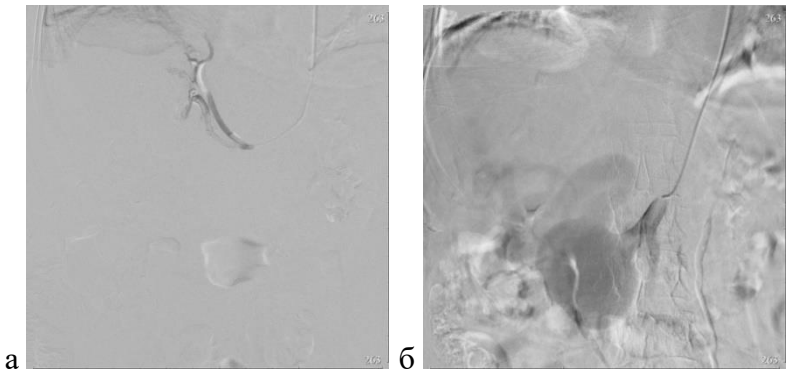

Figure 9. *Selective angiograms after endovascular occlusion: a - diaphragmatic artery; b - SMA, blood flow through the left and right hepatic arteries is slowed, significant decrease in AV-shunt*

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