

Downhill esophageal varices associated with superior vena cava syndrome – A case report

Varizes esofágicas descendentes associadas à síndrome de veia cava superior – Relato de caso

Várices esofágicas descendentes asociadas a síndrome de la vena cava superior – Reporte de un caso

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Mariana Almeida Hein

ORCID: <https://orcid.org/0000-0002-9958-0564>
Universidade Federal do Triângulo Mineiro, Brazil
E-mail: mariana.hein@hotmail.com

Danielle Duarte Silva

ORCID: <https://orcid.org/0000-0002-9919-7717>
Universidade Federal do Triângulo Mineiro, Brazil
E-mail: danielleduarte92@yahoo.com.br

Otávio Romanini Lopes

ORCID: <https://orcid.org/0000-0003-2933-5456>
Universidade Federal do Triângulo Mineiro, Brazil
E-mail: otavio.r.lopes@hotmail.com

Matheus Soares Braga

ORCID: <https://orcid.org/0000-0003-0309-2134>
Universidade Federal do Triângulo Mineiro, Brazil
E-mail: matheusbraga338@gmail.com

Anderson Lubito Simoni

ORCID: <https://orcid.org/0000-0002-9937-9676>
Universidade Federal do Triângulo Mineiro, Brazil
E-mail: andersonsimoni@gmail.com

Bruno Doriguetto Couto Ferreira

ORCID: <https://orcid.org/0000-0001-9263-8439>
Universidade Federal do Triângulo Mineiro, Brazil
E-mail: dorigas@hotmail.com

Luis Ronan M. F. de Souza

ORCID: <https://orcid.org/0000-0002-4634-8972>
Universidade Federal do Triângulo Mineiro, Brazil
E-mail: luis.souza@uftm.edu.br

Geisa Perez Medina Gomide

ORCID: <https://orcid.org/0000-0002-6657-5515>
Universidade Federal do Triângulo Mineiro, Brazil
E-mail: geisa.gomide@uftm.edu.br

Ana Flávia Carrijo Chiovato

ORCID: <https://orcid.org/0000-0002-3184-3399>
Universidade Federal do Triângulo Mineiro, Brazil
E-mail: ana.chiovato@uftm.edu.br

Abstract

Objective: Esophageal varices are an important cause of digestive bleeding, with uphill varices secondary to portal hypertension being the most common cause. Downhill esophageal varices are rare, are related to superior vena cava obstruction, and require investigation as to their etiology, as appropriate treatment is related to the underlying cause and is essential to reduce the risk of complications. **Methodology:** A review of the patient's chart was carried out, as well as an extensive literature search on downhill esophageal varices, with a detailed study of their etiology, pathophysiology, diagnosis, and treatment. The correlations between the case and the findings in the literature are also presented. **Case report:** A 52-year-old patient presented with clinical manifestations of superior vena cava syndrome and endoscopic findings of downhill esophageal varices. A complementary investigation with computed tomography of the chest was performed, and chronic thrombosis of the superior vena cava with extensive collateral circulation was diagnosed. The investigation of thrombophilia was negative, and the etiology of the thrombosis was defined as idiopathic. **Conclusion:** The importance of recognizing, diagnosing downhill esophageal varices, and understanding their pathophysiology for adequate etiological investigation and early treatment, as well as reducing the risks of gastrointestinal bleeding, are highlighted in this case.

Keywords: Superior Vena Cava Syndrome; Esophageal varices; Gastrointestinal hemorrhage; Case report.

Resumo

Objetivo: As varizes esofágicas são importante causa de sangramento digestivo, sendo as varizes ascendentes, secundárias à hipertensão portal, as mais comuns. As varizes descendentes são raras, estão relacionadas à obstrução da veia cava superior e necessitam de investigação quanto à sua etiologia, uma vez que o tratamento apropriado está relacionado à causa de base e é fundamental para reduzir o risco de complicações. **Metodologia:** Realizado revisão do prontuário do paciente, bem como extensa pesquisa bibliográfica sobre as varizes esofágicas descendentes, com estudo aprofundado da sua etiologia, fisiopatologia, diagnóstico e tratamento, bem como correlação dos achados na literatura com o caso apresentado. **Relato de caso:** Paciente de 52 anos com manifestações clínicas da síndrome de veia cava superior e achados endoscópicos de varizes esofágicas descendentes. Realizada investigação complementar com tomografia computadorizada de tórax e diagnosticada trombose crônica da veia cava superior com extensa circulação colateral. A investigação de trombofilias foi negativa, sendo a etiologia da trombose definida como idiopática. **Conclusão:** Ressalta-se neste caso a importância do reconhecimento, diagnóstico das varizes esofágicas descendentes e compreensão da sua fisiopatologia para adequada investigação etiológica e tratamento precoce, reduzindo os riscos de hemorragia digestiva.

Palavras-chave: Síndrome da Veia Cava Superior; Varizes esofágicas; Hemorragia gastrointestinal; Relato de caso.

Resumen

Objetivo: Las várices esofágicas son una causa importante de sangrado digestivo, siendo las várices ascendentes secundarias a hipertensión portal las más frecuentes. Las venas varicosas descendentes son raras, están relacionadas con la obstrucción de la vena cava superior y requieren investigación en cuanto a su etiología, ya que el tratamiento adecuado está relacionado con la causa subyacente y es fundamental para reducir el riesgo de complicaciones. **Metodología:** Se realizó una revisión del prontuario del paciente, así como una extensa investigación bibliográfica sobre las várices esofágicas descendentes, con un estudio profundo de su etiología, fisiopatología, prevalencia, diagnóstico y tratamiento. **Caso clínico:** Paciente de 52 años con cuadro clínico de síndrome de la vena cava superior y hallazgos endoscópicos de várices esofágicas descendentes. Se realizó estudio complementario con tomografía computarizada de tórax y se diagnosticó trombosis crónica de la vena cava superior con circulación colateral extensa. La investigación de los trastornos de hipercoagulabilidad fue negativa y la etiología de la trombosis se definió como idiopática. **Conclusión:** En este caso, se destaca la importancia del reconocimiento, diagnóstico de las várices esofágicas descendentes y el conocimiento de su fisiopatología para una adecuada investigación etiológica y tratamiento precoz, reduciendo los riesgos de hemorragia digestiva.

Palabras clave: Síndrome de la Vena Cava Superior; Várices esofágicas; Hemorragia gastrointestinal; Informe de caso.

1. Introduction

Gastrointestinal varices are enlarged veins that can occur throughout the digestive tract, particularly in the esophagus, stomach, and rectum. They account for approximately 23% of cases of upper gastrointestinal bleeding and are associated with high morbidity and mortality, with esophageal varices being the most common. Gastrointestinal endoscopy is the gold standard for diagnosis, including determination of caliber and risk of bleeding (Kovacs & Jansen, 2019).

Gastrointestinal varices can develop in the context of venous hypertension of the upper systemic circulation due to obstruction of the superior vena cava (SVC). These are often located in the proximal third of the esophagus and known as downhill esophageal varices (DEV) (Neguyen et al, 2016).

DEVs were first described in 1964 by Felson and Lessure after reporting a case of SVC obstruction secondary to mediastinal fibrosis in a patient with metastatic lung cancer (Uceda et al, 2021). They received this denomination due to the cephalocaudal direction of their blood flow. This is a rare cause of upper gastrointestinal bleeding; however, DEVs can be associated with severe and life-threatening bleeding, and early recognition is essential (Ali, A.A et al, 2021).

Acute or chronic obstruction of the SVC can result in the development of superior vena cava syndrome (SVCS), manifesting with a set of signs and symptoms. SVCS can develop due to extrinsic compression or thrombosis, secondary to malignancy in 90% of cases, with relevance to lung carcinomas and lymphomas (Bellefqih et al, 2014). The most common symptoms are facial plethora, edema, upper-limb edema, cyanosis, dyspnea, and collateral circulation in the thoracic and cervical regions (Wan & Bezjak, 2009).

The present report aimed to present to the scientific community the case of a patient with clinical manifestations of

SVCS and endoscopic findings of DEV in the absence of signs of chronic liver disease and portal hypertension. After 11 years of evolution, superior vena cava thrombosis was lately diagnosed, to the point that it was not possible to institute adequate therapy because of the chronicity of the condition, extensive collateral circulation, and risk of complications. However, the patient did not experience gastrointestinal bleeding during this period. Thus, the the main goal of this paper was to publish a case recognizing DEV, elucidate its pathophysiology and etiologies, and perform the necessary complementary investigation for the institution of appropriate early treatment, thereby reducing the risk of complications for the patient.

2. Methodology

The present report is a retrospective study of the clinical case of a patient undergoing outpatient follow-up at the Hospital de Clínicas, Universidade Federal do Triângulo Mineiro. The study was conducted in accordance with current bioethical standards and was submitted to the Research Ethics Committee for analysis and prior approval (CAAE: 59936922.6.0000.8667; Approval No. 5.529.666). After the necessary instructions and clarifications were provided, the patient signed a Free and Informed Consent Form.

The methodology of the report and case study was divided into four phases: 1) analysis of the patient's chart and data collection of clinical findings; 2) evaluation of complementary examinations and review of tomographic images by the radiology and vascular surgery team; 3) bibliographic review with the establishment of the main findings related to the patient's pathology, its prevalence, signs and symptoms, diagnosis, and treatment; and 4) analysis and correlation of findings found in cases with those described in the literature.

The authors were divided into two groups: one was responsible for reviewing the medical records, collecting data, and evaluating the complementary exams, while the other was responsible for the literature review. Subsequently, correlations were made between the patient's clinical condition and the findings described in the literature; these were interpreted and elaborated on for publication of the case report.

3. Results

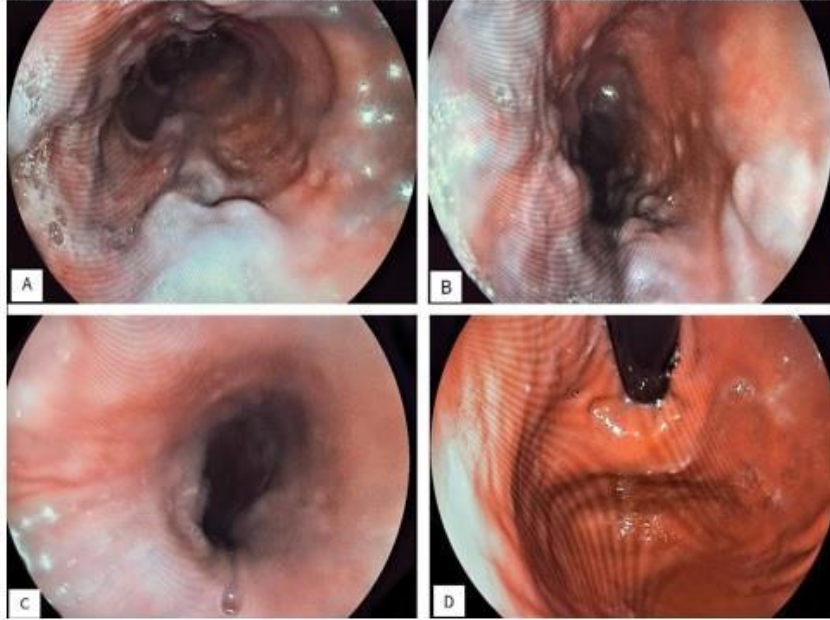
Case Report

A 52-year-old man started outpatient follow-up at the Hospital das Clínicas of the Universidade Federal do Triângulo Mineiro in 2010 due to the presence of dyspeptic symptoms, post-feeding abdominal discomfort, and constipation with defecation effort. The patient had experienced partial improvement in his condition through the use of symptomatic drugs. At that time, irritable bowel syndrome with constipation and dyspeptic syndrome was considered as a hypothetical diagnosis. Given the persistence of the patient's dyspeptic symptoms, upper digestive endoscopy (UDE) was requested. Grade II esophageal varices and mild chronic gastritis were observed with UDE, and portal hypertension was then considered. Abdominal ultrasound was performed, without signs suggestive of chronic liver disease or portal hypertension.

The patient missed several follow-up consults and returned to the hospital 11 years later with comorbidities of grade I obesity, migraine, recurrent nephrolithiasis, and stage III chronic kidney disease. They had symptoms secondary to irritable bowel syndrome; however, hyperemia, plethora, cyanosis of the face, and dyspnea were triggered by flexing the trunk and lowering the head. The patient denied any episodes of digestive bleeding, jaundice, ascites, or encephalopathy. There was no edema of the upper or lower limbs, orthopnea, or paroxysmal nocturnal dyspnea. On physical examination, they showed no signs of chronic liver disease, such as jaundice, ascites, telangiectasias, palmar erythema, or splenomegaly. However, collateral circulation in the right hypochondrium was noted. Thus, we decided to perform UDE once more, and two small- and medium-sized varices were observed, without premonitory signs of bleeding, in the proximal and middle thirds of the esophagus,

compatible with downhill esophageal varices (Figure 1). An abdominal ultrasound with Doppler of the portal system was performed, without signs of chronic liver disease or portal hypertension, in addition to an echocardiogram, which displayed results within normal limits. Cervical ultrasound was also performed, with normal results.

Figure 1: Upper digestive endoscopy with the presence of downhill esophageal varices.

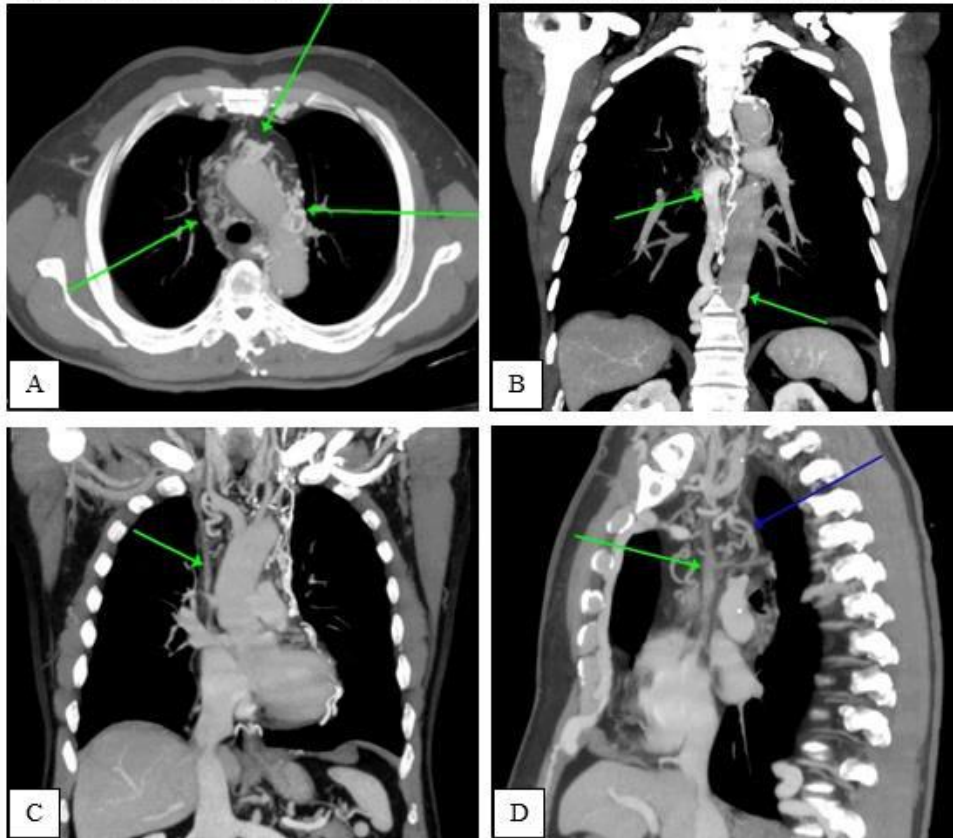


Source: Digestive Endoscopy Unit. Hospital de Clínicas - UFTM (2022).

In the upper images (A and B), the presence of downhill esophageal varices in the proximal and middle thirds of the esophagus is evident. In the lower left image (C), the distal third of the esophagus without varices is shown. On the right (D), we observed a gastric fundus without varices.

In view of the presence of downhill esophageal varices and a clinical picture compatible with SVCS, chest venous computed tomography angiography was requested, which identified a reduced-caliber SVC, filiform flow associated with periesophageal, mediastinal, and diaphragmatic collateral circulation. In addition, in the chest and abdominal walls, the findings were suggestive of chronic partial thrombosis of the SVC (Figure 2). The patient had no history of other thrombotic events, and a hematological investigation was performed to rule out thrombophilia, which resulted in normal results (negative factor V Leiden and prothrombin gene mutation; antithrombin III, protein C, protein S, homocysteine, and anticardiolipin IgM and IgG measurements within the normal range). Thus, the patient's chronic SCV thrombosis was defined as idiopathic.

Figure 2: Chest tomography with chronic thrombosis of the superior vena cava.

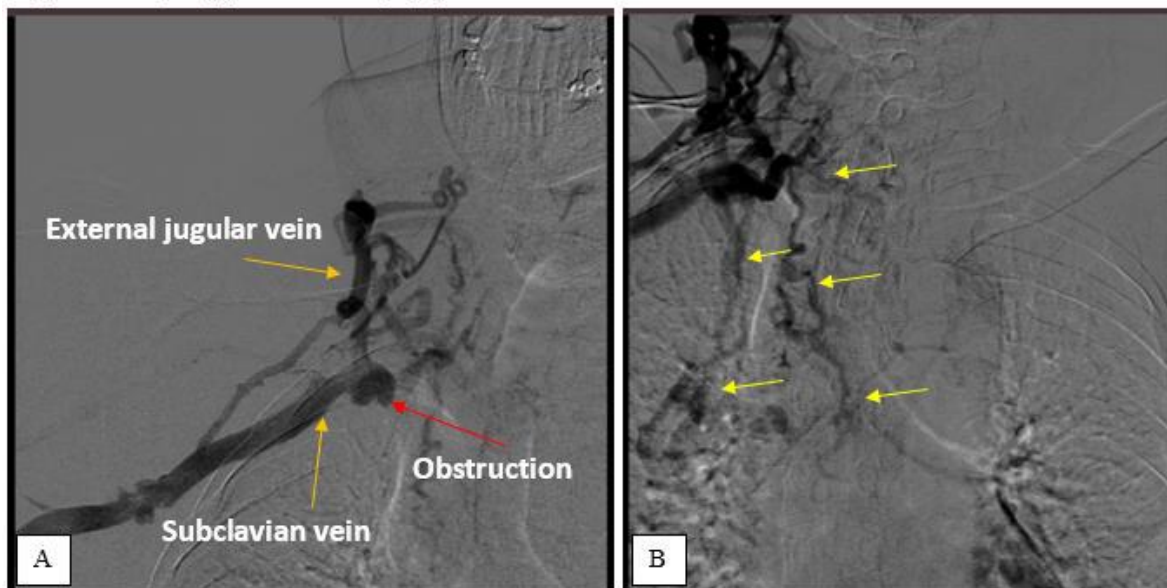


Source: Radiology Unit. Hospital de Clínicas – UFTM (2021)

In the upper-left image (A), an axial image of the chest is observed with extensive collateral circulation (arrows) in the anterior, middle, and posterior mediastinal compartments. On the right (B), marked ectasia of the azygos (left arrow) and hemiazygos (right arrow) veins is observed. In the lower left image (C), the superior vena cava is shown as a fibrous cord due to chronic thrombosis/fibrosis (arrow). On the right (D), the superior vena cava is shown as a fibrous cord due to chronic thrombosis/fibrosis (green arrow) and extensive pericaval collateral circulation (blue arrow).

Considering the patient's chronic thrombosis of the SVC, negative history of thrombosis in other sites, presence of significant collateral circulation, absence of hemodynamic repercussions, negative investigation for thrombophilia, and association with risk of digestive bleeding, an anticoagulant therapy was not indicated to start. After evaluation by vascular surgery using venography, risks and benefits were considered, and endovascular treatment was not indicated owing to 1) the chronicity of the condition; 2) the extensive thrombosis with obstruction of the right and left brachiocephalic veins as well as the SVC (Figure 3); and 3) the risks of the procedure. In addition, endoscopic therapy was not performed, which is mainly indicated in the presence of gastrointestinal bleeding due to the lower risk of bleeding from the DEV and higher rates of complications associated with the procedure. We opted for expectant management and outpatient follow-ups.

Figure 3: Right upper limb venography.



Source: Unit of Hemodynamics and Interventional Cardiology. Hospital de Clínicas – UFTM (2022)

In the image above, venography of the right upper limb was performed, and occlusion of the right and brachiocephalic vein, as well as the superior vena cava, was observed (A); thus, superior venous drainage occurred through the collateral veins and azygos system (B).

4. Discussion

4.1 Epidemiology

DEV is an uncommon condition, with little data on its prevalence and etiology; therefore, current publications are limited to case reports (Ayvaz et al, 2018). DEVs have a low incidence, corresponding to 0.5% of patients undergoing UDE, and are responsible for 0.4% to 10% of variceal upper gastrointestinal bleeding cases (Ali A.A et al, 2021). They have a lower risk of bleeding than uphill esophageal varices, which may be explained by their location in the submucosa and their decreased exposure to gastroesophageal reflux (Loudin et al, 2016). This was observed in the case in question, in which the patient had never experienced gastrointestinal bleeding, even with a clinical evolution of at least 11 years, and had been performing blowing exercises during their leisure activities such as playing the saxophone.

Although rare, DEVs are highly associated with SVC obstructions. Asymptomatic patients diagnosed with benign or malignant SVC obstruction were described in 30% of the patients undergoing screening by UDE. When associated with upper gastrointestinal bleeding, downhill varices have stenosis of the main etiology secondary to a long-term hemodialysis catheter, a complication that occurs in almost 30% of these patients (Siegel et al, 2015). The higher incidence of bleeding in such cases can be explained by uremic coagulopathy related to kidney disease as well as the use of anticoagulants in hemodialysis sessions (Ali, H et al, 2021).

4.2 Pathophysiology

Venous drainage of the esophagus occurs predominantly through the azygos system in the upper and middle thirds and by the porta system in the lower third. Esophageal veins are usually not evident in UDE; they are present in obstructive or hypertensive processes that lead to the formation of collaterals with the portal system and azygos that reach the systemic circulation, resulting in the formation of esophageal varices (Areia et al, 2006).

Esophageal varices are classified based on the direction of their venous flow as uphill, downhill, or idiopathic. The

most common are uphill or distal esophageal varices secondary to portal hypertension (Neguyen et al, 2016). Downhill or proximal varicose veins are rare and are a consequence of obstruction of the SVC, with blood flow diverted by mediastinal collaterals towards the inferior vena cava to return to the right atrium (Uceda et al, 2021). In this way, a collateral pathway from the azygos and hemiazygos veins can develop, resulting in increased blood flow in the esophageal plexus and the formation of descending varices (Ennaifer et al, 2015). If the obstruction is located above the azygos vein, venous hypertension and varices form in the upper third of the esophagus, as in the case presented here. In the presence of obstruction below or involving the azygos vein, venous drainage occurs through the esophageal plexus, with the formation of varices along its entire length (Gessel & Alcorn, 2015).

The most common etiology of DEV in the literature is compression of the SVC by mediastinal tumors such as thymoma, lymphoma, or lung cancer, corresponding to approximately 60% of the cases described. Despite being the most common etiology, malignancies are associated with a lower incidence of variceal hemorrhage (Siegel et al, 2015). They can also be secondary to benign causes, such as thrombosis, central venous catheter-associated stenosis, mediastinal fibrosis, heart disease, postoperative complications (Inoue et al, 2013), pulmonary arterial hypertension (Harwani et al, 2014), and goiter (Van der Veld et al, 2006), in addition to hypercoagulable states, such as factor V Leiden mutation (Gómez-Aldana & Gómez-Zuleta, 2017). In the present case, despite exhaustive investigation, the etiology of the thrombosis was not found. The long-term evolution of the condition rules out neoplasms as the etiology of the thrombosis and DEV presented by the patient.

4.3 Clinical Presentation

Clinical symptoms resulting from DEV, such as gastrointestinal bleeding (hematemesis and melena), are rare and usually associated with the underlying disease that results in the clinical picture, accounting for only 0.1% of all upper gastrointestinal bleeding (González et al. al, 2021). Patients who present with bleeding complications have a higher incidence of SVCS, such that the presence of signs and/or symptoms, such as cyanosis of the face, edema of the head and upper limbs, and dyspnea, are associated with a higher risk of variceal hemorrhage (Ayvaz et al, 2018). The case described here presented signs and symptoms of SVCS during its evolution but lacked the manifestation of upper gastrointestinal bleeding.

4.4 Diagnosis

Currently, there are no guidelines that determine the protocols to be followed in cases of suspected DEV (Chakinala et al, 2018). Diagnosis is made by identifying varicose veins in the upper third of the esophagus through UDE, which is performed after upper gastrointestinal bleeding is diagnosed, or as an incidental finding during the investigation of other pathologies of the gastrointestinal tract (Yasar & Abut, 2015). In the case described here, DEV was diagnosed based on UDE performed to investigate nonspecific dyspeptic symptoms. After identification of DEV, investigation should be carried out to determine the etiology of the underlying disease, which is associated with obstruction of the SVC (Chakinala et al, 2018). Venography is the gold standard for accurately defining treatment; however, it is invasive and carries a risk of complications. In addition, machine CT angiography or magnetic examination models are useful and allow for visualization of blood flow (Hussein et al, 2008). In this way, thrombosis and stenosis, in addition to extrinsic compressions such as mediastinal neoplasms, can be identified.

When no underlying etiology is identified, a complementary workup should be performed with cervical Doppler ultrasound, thyroid ultrasound, echoendoscopy, and transesophageal echocardiography (Ayvaz et al, 2018). In the present case, an extensive complementary investigation was carried out with cervical and thyroid ultrasound, echocardiogram, and laboratory analyses to search for thrombophilia. All results were normal, and it was not possible to perform echoendoscopy due to unavailability in the hospital.

4.5 Treatment

A multidisciplinary team is required to determine the best DEV therapy; thus, there are no definitive recommendations regarding DEV management, which typically aims to treat the etiology of SVC obstructions (Yasar & Abut, 2015). When DEV is secondary to obstruction by a neoplasm, the possibility of chemotherapy, radiotherapy, or even surgical resection to reduce venous hypertension should be considered (Van & Singh, 2021). In cases associated with thrombosis or stenosis of the SVC, endovascular therapy, angioplasty with or without a stent, or revascularization surgery should be considered (Berkowitz et al, 2016), with the decision being individualized and shared with the surgical team.

Endoscopic treatment can be performed with band ligation or sclerotherapy, which is generally restricted to acute bleeding due to the risk of complications associated with fragility of the posterior wall in the upper third of the esophagus and absence of serosa (Van & Singh, 2021). Ligation is preferred, as sclerotherapy is associated with the potential risk of spinal cord infarction (Tavakkoli et al, 2006). In patients presenting with upper gastrointestinal bleeding, endoscopic treatment and balloon tamponade can be considered until definitive therapy is established. Notably, there are no benefits from splanchnic vasoconstrictors such as octreotide, which are used in bleeding from portal hypertension, or from pump inhibitors of protons (Loundin et al, 2016). The patient in question was discussed in a multidisciplinary meeting with the participation of a gastroenterologist, hematologist, radiologist, and vascular surgeon. The team concluded that the best option was conservative treatment due to the patient's risk of variceal hemorrhage related to anticoagulation and the risk of complications associated with a vascular approach due to the chronic process and extensive collateral circulation.

5. Conclusion

Downhill esophageal varices are an uncommon cause of upper gastrointestinal bleeding; however, recognizing and understanding their pathophysiology are essential, as they can manifest with severe, life-threatening bleeding and require a different management approach to uphill varices, which are the most common. Unlike varicose veins related to portal hypertension, DEVs are associated with obstruction of the superior vena cava; therefore, their identification must be followed by exhaustive complementary investigations to elucidate their etiology given their high association with mediastinal neoplasms. Most of the time, DEV patients are asymptomatic; however, they may present with symptoms of superior vena cava syndrome, and immediate clinical suspicion is essential for the early diagnosis and prevention of hemorrhagic events. Thus, diagnosing DEV, understanding its pathophysiology, and performing appropriate etiological investigations is essential to define the best therapy for the patient (according to the underlying etiology) and reduce the risk of associated complications.

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