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Case report

Beyond adenocarcinoma: Pancreatic adenosquamous carcinoma, report of a rare case

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Abstract

Introduction: Pancreatic adenosquamous carcinoma is an uncommon exocrine neoplasm that represents between 1% and 4% of pancreatic tumors. It is characterized by the presence of glandular and squamous components and is associated with highly aggressive behavior and poor prognosis. Diagnosis usually occurs at advanced stages because of its nonspecific clinical presentation and rapid progression. **Case presentation:** We present the case of an 82-year-old female patient with abdominal pain, jaundice, and constitutional syndrome. Laboratory studies showed cholestasis, cytolysis, and direct hyperbilirubinemia. Computed tomography and abdominal magnetic resonance imaging showed a solid-cystic lesion in the tail of the pancreas with involvement of adjacent structures and multiple liver lesions suggestive of metastases. Endoscopic ultrasound with biopsy confirmed the diagnosis of adenosquamous carcinoma through histopathological and immunohistochemical studies (p63 positive in the squamous component and carcinoembryonic antigen positive in the glandular component). The patient had an unfavorable clinical course and died two months after diagnosis. **Discussion:** This tumor subtype is associated with a high rate of early dissemination, lymphovascular invasion, and perineural invasion, which limits therapeutic options. Although surgical resection is the treatment of choice in early stages, most cases are unresectable at diagnosis. No standardized chemotherapy regimen exists, reflecting the limited available evidence. **Conclusion:** Pancreatic adenosquamous carcinoma is a rare entity with a poor prognosis, and its timely recognition and histological confirmation are essential. Additional studies are required to optimize its diagnostic and therapeutic approach, consultation, and information at the time of managing this pathology, as it is rare and poorly known.

Keywords

Pancreatic neoplasms, endoscopic ultrasonography, elderly, biopsy, case reports.

INTRODUCTION

Pancreatic cancer is one of the leading causes of death from malignant tumors, and adenosquamous carcinoma has a poorer prognosis than pancreatic ductal adenocarcinoma[(1)]. Most pancreatic cancers are pancreatic ductal adenocarcinomas, whereas only 0.4% to 4% are of the adenosquamous subtype. The identification of squamous cell histology in pancreatic tissue raised the possibility of metastatic disease from a second primary lesion. However, the absence of primary squamous tumors and the presence of a glandular component complicated the diagnostic picture. The history of this cancer is not well understood, but numerous theories have been proposed to explain the histopathogenesis of adenosquamous carcinoma. It is known that 50% of pancreatic adenosquamous carcinoma cases are associated with synchronous changes of subclinical chronic pancreatitis. Although its rarity makes it difficult

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to determine prognostic factors for adenosquamous carcinoma as a whole, patients have a poorer prognosis than those with pancreatic ductal adenocarcinoma.

The patient presented with a clinical picture of obstructive jaundice, weight loss, nausea, and anorexia, depending on the tumor location. The diagnostic methods of choice are computed tomography and magnetic resonance imaging. Adenosquamous carcinoma has the same staging and resectability characteristics as pancreatic ductal adenocarcinoma. It is associated with a higher rate of lymph node metastases and poorly differentiated histopathology than pancreatic ductal adenocarcinoma. Surgical resection is the mainstay of treatment for adenosquamous carcinoma. Adjuvant therapy is being used to further improve resectability and survival.

CASE PRESENTATION

The patient was an 82-year-old woman with a medical history of chronic gastritis and a surgical history of cholecystectomy for cholelithiasis and two cesarean deliveries. She presented with a two-week history of diffuse, colicky abdominal pain and watery stools and subsequently underwent medical evaluation. She was hemodynamically stable. Physical examination revealed dermal and scleral icterus, a soft and depressible abdomen, and tenderness to deep palpation in the epigastric region and right upper quadrant. Bowel sounds were present, with no signs of peritonitis.

Laboratory testing revealed leukocytosis, neutrophilia, mild anemia, elevated pancreatic enzymes (amylase and lipase) greater than three times the upper limit of normal, cytolysis, cholestasis, and hyperbilirubinemia predominantly involving the direct fraction, as well as abnormal nitrogenous waste parameters and hyponatremia. An abdominal ultrasound was therefore performed and revealed a pancreatic lesion. A noncontrast and contrast-enhanced abdominal CT scan was subsequently obtained. It showed a 3.9 × 3.6 × 3 cm space-occupying lesion arising from the pancreatic tail. The lesion was predominantly cystic and multiseptated, with irregular walls, particularly along its medial aspect, where it demonstrated heterogeneous enhancement. There was loss of the cleavage plane with the anterior border of the spleen and the left adrenal gland, which could correspond to a primary neoplasm. The liver also showed multiple hypoenhancing nodular lesions in both lobes, measuring up to 2.4 cm in segment VI. A noncontrast abdominal MRI was subsequently performed. It showed a 4.1 × 3.1 × 3 cm lesion with a neoplastic appearance adjacent to the pancreatic tail, with no apparent cleavage plane from the splenic region, as well as multiple nodular hepatic lesions consistent with probable metastatic disease (**Figure 1**).

The patient was therefore referred to Hospital Solca, Quito Branch, for biliopancreatic endoscopic ultrasonography with biopsy. Endoscopic and endosonographic examination showed a normal-appearing papilla, a normal pancreatic head and body with a normal main pancreatic duct (Wirsung duct), and a solid-cystic tumor in the pancreatic tail measuring 39 × 40 mm in diameter. The lesion involved the splenic artery and vein and was in contact with the spleen. Qualitative elastography suggested malignancy. No lymphadenopathy was observed, the celiac trunk was free of involvement, and the main pancreatic duct was probably involved. A 19-gauge biopsy needle was used to puncture the previously described lesion twice through the gastric window. Adequate tissue was obtained and sent to pathology, with no complications. The common bile duct was normal (**Figure 2**). Biopsy of the solid-cystic lesion in the pancreatic tail was positive for malignancy (adenosquamous carcinoma), confirmed by immunohistochemistry (P63 positive in foci of squamous epithelium, CEA positive in areas of adenocarcinoma, and P53 negative) (**Figure 3**). The patient died two months after diagnosis without receiving therapy.

DISCUSSION

Pancreatic adenosquamous carcinoma is an extremely rare subtype of ductal carcinoma (less than 1%), most frequently located in the pancreatic tail[2], and accounts for 1% to 4% of all exocrine pancreatic neoplasms[3]. This neoplasm is characterized by aggressive biological behavior, which poses significant challenges for its diagnosis and management[3]. Its prognosis is less than 6 months in advanced disease and 11 to 20 months in localized disease[4]. However, there are also several fundamental challenges in recognizing and treating this type of cancer. An important aspect of the case is identifying and characterizing the tumor's morphology and growth pattern, which helps distinguish it from other similar tumors, particularly conventional ductal adenocarcinoma[5]. In particular, adenosquamous carcinoma is identified by dual cellular differentiation comprising glandular and squamous components, with the latter accounting for at least 30% of the tumor[6]. Identifying these features may contribute to the development of new strategies for improved diagnosis and treatment of these tumors. Likewise, early recognition of these features may have a substantial impact on therapeutic decisions, underscoring the importance of an accurate and timely diagnosis[7].

Another important aspect highlighted by this case is the prognosis associated with adenocarcinoma. The condition has a notably unfavorable clinical course due to the high frequency of early spread, which occurs in approximately

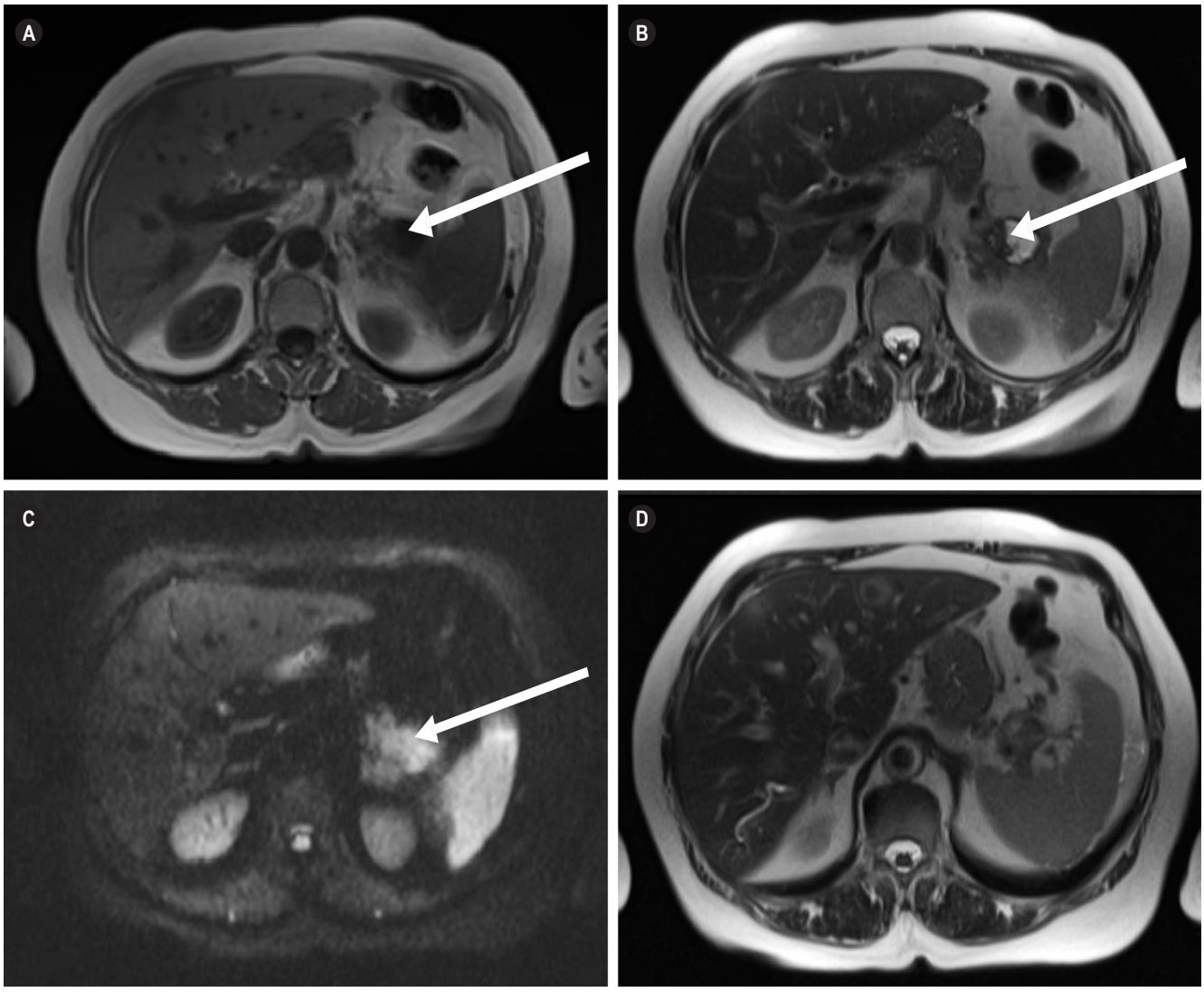


Figure 1. Magnetic resonance imaging. Obtained from external studies of the patient. **A.** T1-weighted axial MRI sequence: hypointense mass in the pancreatic tail. **B.** T2-weighted axial MRI sequence: hyperintense mass in the pancreatic tail. **C.** Diffusion-weighted axial MRI sequence: mass with slight restriction of signal intensity in the pancreatic tail. **D.** T2-weighted axial MRI sequence: multiple hypointense hepatic lesions with a hyperintense halo (MET). Images courtesy of the authors.

half of affected individuals. In addition, angiolymphatic and perineural invasion further worsen the prognosis[8]. Therefore, the findings of this case emphasize the need for a more aggressive therapeutic approach. Although aggressive surgical resection with negative margins remains the cornerstone of therapy, the implementation of preoperative and postoperative treatments could improve long-term outcomes[7]. In addition, recognizing these determinants helps to understand the malignant processes involved in this type of tumor growth. Another crucial message from the case is the value of immunohistochemical marker studies. The use of markers from multiple cell lineages helps determine whether the tumor has squamous or glandular differentiation, which is crucial for accurate diagnosis and comprehensive treatment planning[5]. Loss of expression of the P16 protein (CDKN2A), loss of the SMAD4 protein (DPC4), and strong nuclear P53 immunoreactivity have been described, while the squamous component also expresses P63, P40, and low-molecular-weight cytokeratins. Because of its higher proliferative rate, there is increased Ki-67 staining on immunohistochemistry, and a subset of tumors expresses programmed death-ligand 1 (PD-L1), which is restricted to the squamous cell carcinoma component[9].

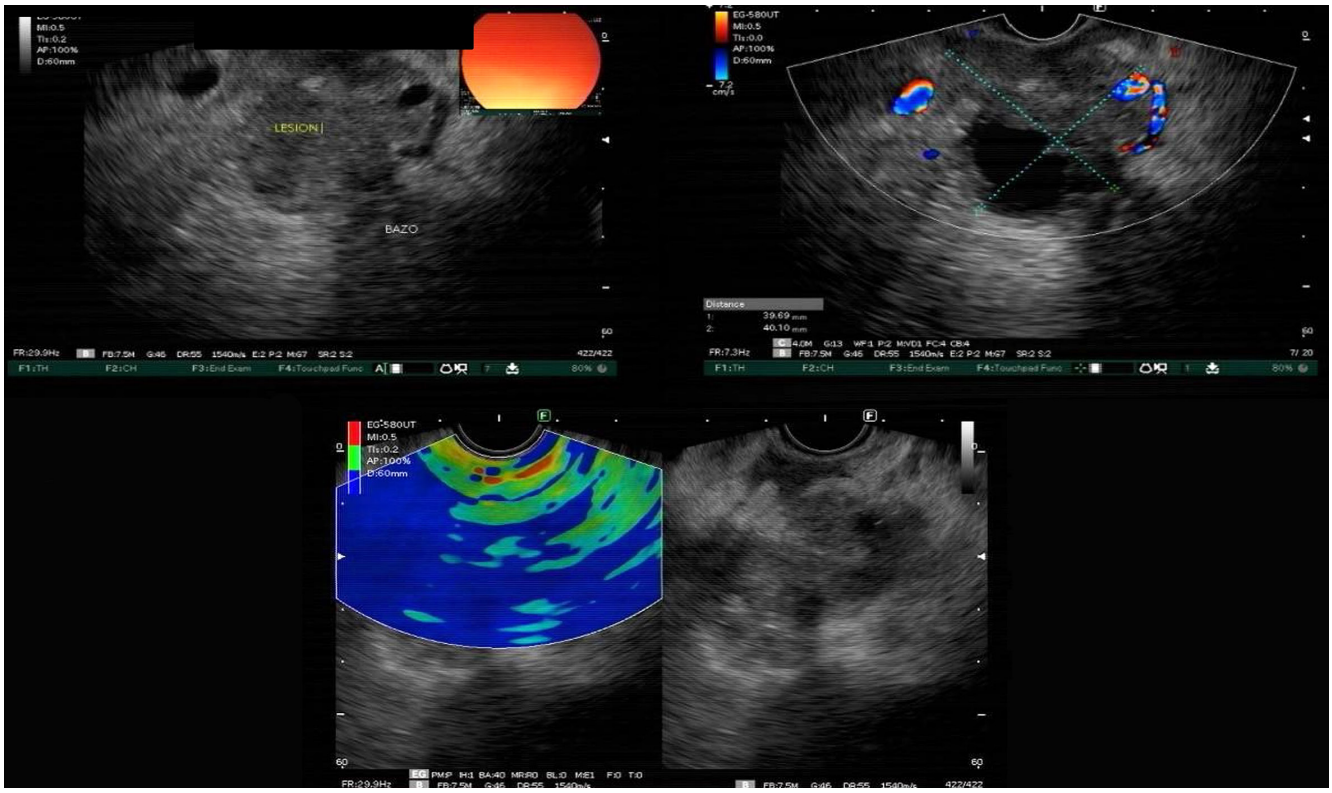


Figure 2. Endoscopic ultrasonography of the patient. Obtained from the archives of Hospital Solca, Quito Branch, Quito, Ecuador.

Despite the above, the case also has certain limitations. The first is the lack of a standard treatment approach for pancreatic adenosquamous carcinoma because of the very low prevalence of this condition. Although numerous chemotherapy combinations (cytosine arabinoside, cisplatin, 5-fluorouracil, and gemcitabine) are being evaluated in research, there is no internationally recognized protocol[10]. The lack of clarity regarding treatment is another major problem. Because pancreatic adenosquamous carcinoma is uncommon, it is difficult to enroll sufficient numbers of patients in studies capable of adequately characterizing its behavior and determining whether treatments are effective. This, in turn, limits the ability to extrapolate results and reduces the validity of precise clinical recommendations regarding long-term survival and the efficacy of adjunctive therapy[11]. Therefore, comprehensive global research conducted across different regions of the world may help improve understanding of variations in incidence and neoadjuvant treatment regimens, including perioperative radiation, with the aim of assessing and improving patient response[12].

Ultimately, even with advances in diagnostic and therapeutic modalities, the outlook for individuals with adenosquamous neoplasms of the pancreas remains poor. Long-term survival is often difficult to achieve, with a high proportion of patients succumbing within the first year after diagnosis[8]. This high mortality rate is attributed to the inherent resistance of this neoplasm to standard therapies, necessitating the exploration of innovative treatment options. Without more effective treatments, the prognosis of patients will remain poor.

Overall, individuals with squamous cell neoplasms of the pancreas generally face a poor outlook, with a higher risk of metastasis and a worse prognosis than those with adenocarcinoma. This underscores the need to explore new treatment approaches[13].

In summary, this unusual pancreatic cancer illustrates how rare and rapidly growing the disease can be. Its clinical behavior and the lack of a clearly established cure pose a major challenge for physicians. Careful evaluation of the diagnosis, therapy, and prognosis of adenosquamous carcinoma is imperative to improve patient quality of life and survival.

CONCLUSION

This case of pancreatic adenosquamous carcinoma illustrates both the rarity and aggressive nature of this tumor. It represents a significant diagnostic and therapeutic challenge because of its unique biological behavior and the limited

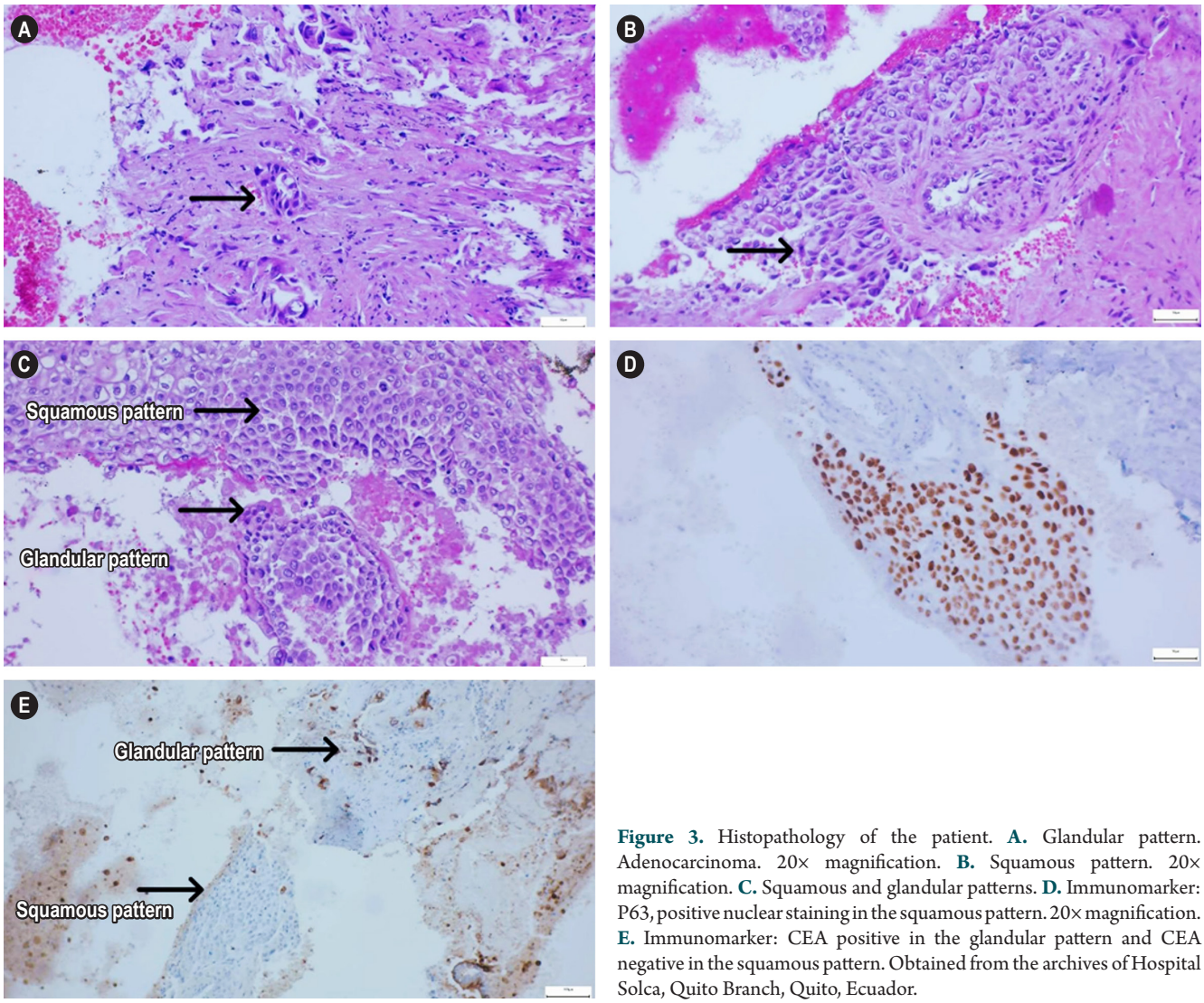


Figure 3. Histopathology of the patient. **A.** Glandular pattern. Adenocarcinoma. 20× magnification. **B.** Squamous pattern. 20× magnification. **C.** Squamous and glandular patterns. **D.** Immunomarker: P63, positive nuclear staining in the squamous pattern. 20× magnification. **E.** Immunomarker: CEA positive in the glandular pattern and CEA negative in the squamous pattern. Obtained from the archives of Hospital Solca, Quito Branch, Quito, Ecuador.

availability of robust clinical evidence to guide its management. Although the strengths of this case include accurate identification of its histological features and a multidisciplinary approach to treatment, its limitations are primarily related to the lack of standardized treatment, the scarcity of large-scale studies, and the limited generalizability of the findings. Despite advances in diagnostic and therapeutic techniques, pancreatic adenosquamous carcinoma remains a neoplasm with a very poor prognosis and an area of ongoing research that warrants further attention.

Ethical considerations

The article was reviewed and approved by the Research Department of Hospital SOLCA, Quito Branch.

Informed consent

Informed consent was obtained from the patient's daughter because the patient had died.

Conflicts of interest

The authors declare no conflicts of interest.

Use of artificial intelligence

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Author contributions

- Study design and conception: Giomara Ojeda-Peláez, Zelma Paz-Cañadas, and Lisbeth Gando-Ruiz.
- Data acquisition: Giomara Ojeda-Peláez, Zelma Paz-Cañadas, and Lisbeth Gando-Ruiz.
- Data analysis and interpretation: Giomara Ojeda-Peláez, Zelma Paz-Cañadas, and Lisbeth Gando-Ruiz.
- Manuscript drafting: Giomara Ojeda-Peláez, Zelma Paz-Cañadas, and Lisbeth Gando-Ruiz.
- Critical revision of the manuscript: Giomara Ojeda-Peláez, Zelma Paz-Cañadas, and Lisbeth Gando-Ruiz.

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