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NECROLYTIC MIGRATORY ERYTHEMA AS A DIAGNOSTIC CLUE: A RARE REPORT OF GLUCAGONOMA

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Abstract: Introduction: Glucagonomas are pancreatic neuroendocrine tumors that arise from well-differentiated neuroendocrine cells in the pancreatic islets. They are considered harmful neoplasms and are commonly small in size due to their endocrine excretion. **Case Report:** We present a case of a glucagonoma whose initial symptoms included necrolytic migratory erythema, hyperglycemia, weight loss, lethargy, a mass in the pancreatic tail, and thrombosis in the left common iliac vein. Specifically, a confounding factor was identified as a focus of endometriosis in the abdominal wall. The pancreatic mass was resected, and two years after surgery, the patient presents with good clinical and laboratory evolution. **Conclusion:** Glucagonoma is a rare pancreatic neuroendocrine tumor with significant malignant potential and difficult diagnosis.

Keywords: neuroendocrine tumor, glucagonoma, pancreatic tumor.

INTRODUCTION

Glucagon is a 29-amino acid polypeptide hormone produced by the alpha cells of the pancreas, responsible for regulating the metabolism of glucose, amino acids, and lipids[1].

Frequently, at diagnosis, it presents with locoregional and distant lymph node metastases, mainly hepatic or bone[2].

Glucagonoma syndrome is caused by this glucagon-secreting pancreatic neuroendocrine neoplasm, with variable presentation, which includes typical signs and symptoms characterized by painful glossitis, cheilitis, weight loss, chronic anemia, recently onset or worsening diabetes mellitus, deep vein thrombosis, depression, and necrolytic migratory erythema, the process in the skin of which can be explained by superficial epidermal necrosis, formation of fragile blisters, crusts, and scarring with hyperpigmentation [3,4,5]. Different stages of skin lesions may be present simultaneously[5].

This report aims to describe a case of glucagonoma diagnosed and treated at our service (Maria Aparecida Pedrossian Hospital (HUMAP) of the Federal University of Mato Grosso do Sul (UFMS) - Brazilian Hospital Services Company - EBSERH), located in the city of Campo Grande, MS. We describe information related to the challenges in clinical presentation, confounding factors, diagnoses, and surgical treatment, thus providing knowledge for better decision-making in similar cases that may arise in the daily clinical practice of general practitioners, psychiatrists, dermatologists, endocrinologists, and others.

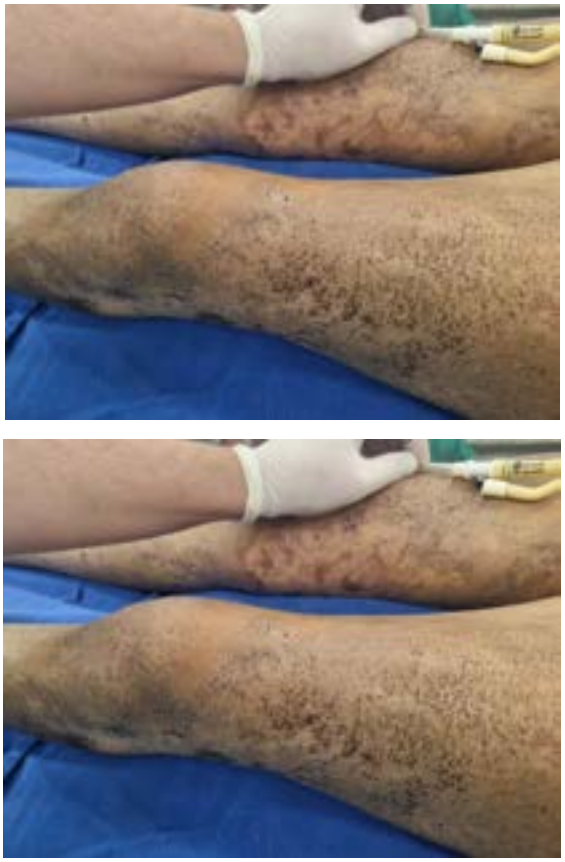
CASE REPORT

A 32-year-old white female patient, a physiotherapy student at UFMS, previously healthy, from the interior of the state of Mato Grosso do Sul, reports that at age 30, in October 2022, she presented with pruritic lesions that began on her left foot, which evolved with crusts after scratching. Subsequently, the lesions became disseminated in the form of plaques, with lamellar desquamation, becoming diffuse, affecting her thighs, perineal region, back, flanks, and face (Figures 1 and 2). Her past medical history includes using gliclazide (oral hypoglycemic agent) for recently developed diabetes, cholecystectomy, G1PC1A0. When seeking dermatological medical assistance

in her hometown, she underwent oral and topical treatment for scabies, fungal lesions, and pemphigus, without success.

In early 2023, she began experiencing progressive weight loss, approximately 30 kg in 3 months, hair loss, anemia, listlessness, drowsiness, and lack of appetite.

During the persistence of a severe and recurrent erythematous skin rash of undetermined cause, she sought medical attention from the dermatology department of HUMAP-EBSERH, where she was hospitalized for investigation.



Figures 1 and 2: Hyperchromic macules on lower limbs and trunk with different stages simultaneously.

Skin biopsy revealed mild chronic spongiotic dermatitis with moderate parakeratosis associated with mild inflammatory infiltrate, with no signs of malignancy visualized in the material.

Laboratory tests showed normocytic normochromic anemia, alpha-fetoprotein, amylase, tumor markers (CA 125, CA 19.9, CA 15.3) negative, serologies negative, direct Coombs test negative, glucagon > 522 pg/mL (reference value: less than 208 pg/mL)

In imaging studies, ultrasound showed a mass located in the left flank region, posteroinferior to the pancreatic tail and anteromedial to the left kidney, of undetermined etiology, probably neoplastic (Figures 3A and 3B). As a confounding factor, the ultrasound examination revealed a hypoechoic nodular image in the subcutaneous tissue of the right pelvic wall, of indeterminate appearance according to the method, initially suspected to be an endometriotic implant or a secondary neoplastic implant (Figure 4). No adjacent lymphadenopathy suggestive of secondary neoplastic involvement was visualized.

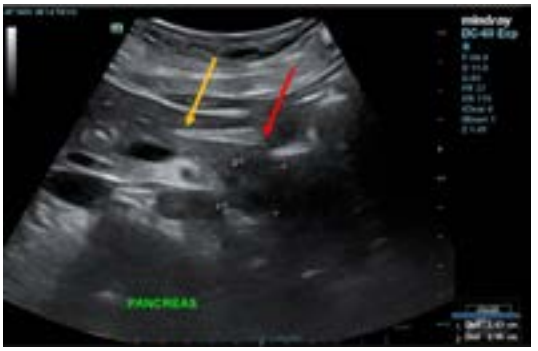


Figure 3A: B-mode ultrasound image demonstrating a hypoechoic nodular mass in the left flank (red arrow) and pancreatic body (yellow arrow).

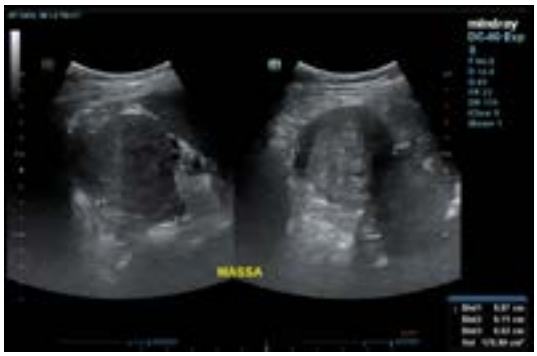


Figure 3B: B-mode ultrasound image demonstrating a hypoechoic nodular mass in the left flank, measuring 8.8 x 6.1 x 6.0 cm, with an approximate volume of 170 cm^3.

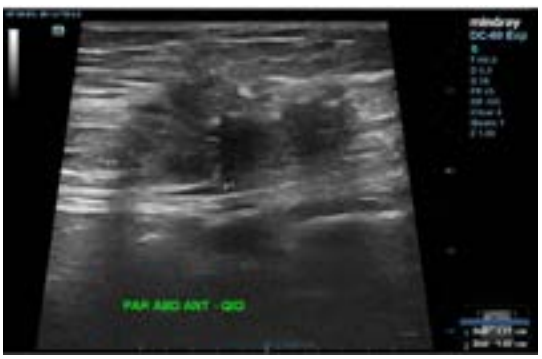


Figure 4: Hypoechoic nodular image in the subcutaneous tissue of the right pelvic wall, of indeterminate appearance according to the method.

Following clinical, laboratory, and radiological evaluation, with a high suspicion of pancreatic malignancy, a total abdominal computed tomography (CT) scan was indicated for multidisciplinary staging planning and biopsy/surgical treatment.

The total abdominal computed tomography scan with iodinated contrast infusion revealed a heterogeneous retroperitoneal mass without a clear cleavage plane with the pancreatic tail, with a suspected neoplastic etiology (Figure 5), as well as a second heterogeneous, predominantly cystic nodular image in the body of the pancreas (Figure 6) and thrombosis of the left common iliac vein (Figure 7).

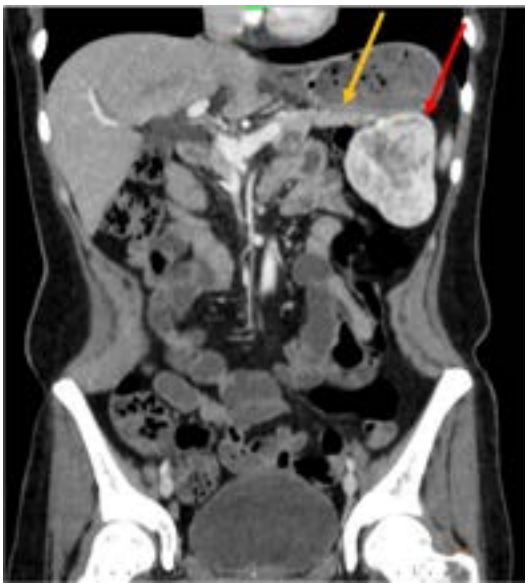


Figure 5: Coronal plane image of the total abdominal CT scan in the arterial phase, demonstrating a large hypervascular mass (red arrow) without a clear cleavage plane with the pancreatic tail, which is tapered (yellow arrow).

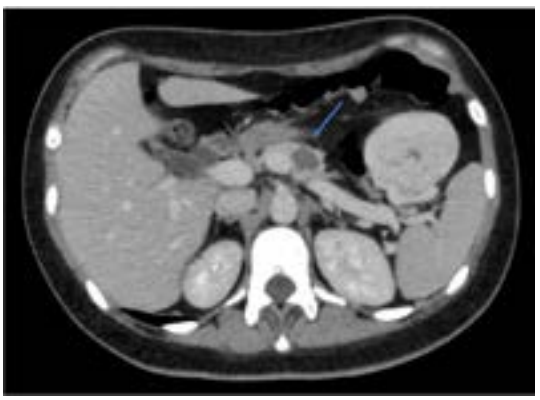


Figure 6: Axial image of a total abdominal CT scan in the portal phase, demonstrating an expansive formation with a predominantly cystic appearance in the pancreatic body, without enhancement by iodinated contrast medium (blue arrow).

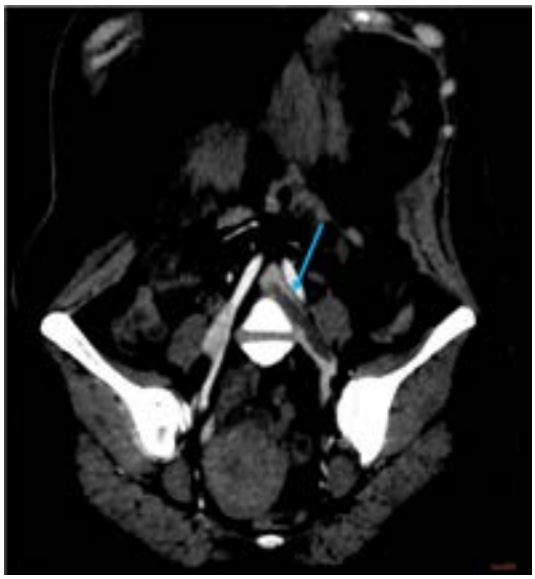


Figure 7: Coronal plane image of a total abdominal CT scan in the portal phase, demonstrating a filling defect by the iodinated contrast medium in the left common iliac vein, indicating thrombosis (blue arrow).

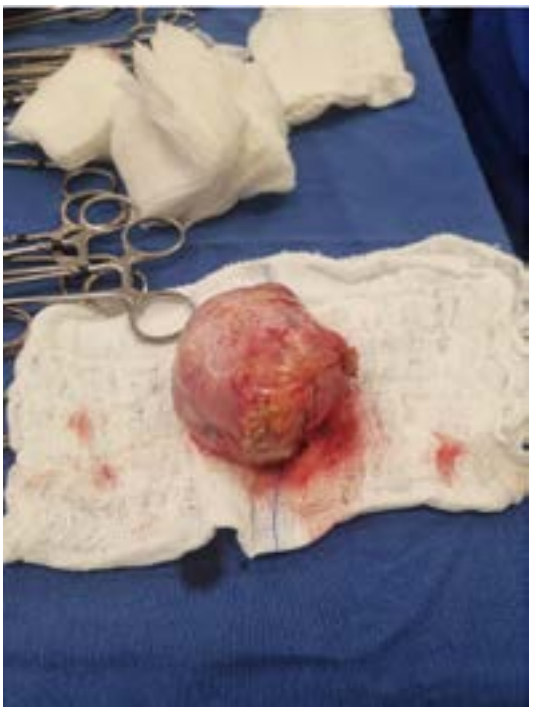


Figure 8: Macroscopic view of the anatomical specimen, characterized by a large, brownish, and highly vascularized expansive formation.

The patient underwent a partial en bloc distal pancreatectomy with the expansive formation (Figures 8). Intraoperatively, a clear cleavage plane with the spleen was observed, which was preserved. Preservation and follow-up of the cystic formation in the pancreatic body was chosen due to the patient's young age and the possibility of cure after removal of the pancreatic tail and the mass.

The patient had an excellent postoperative recovery. At the follow-up outpatient visit, complete resolution of the dermal lesions was observed, with only residual hyperpigmented macules, complete resolution of hyperglycemia, and discontinuation of oral hypoglycemic medication. Laboratory tests demonstrated resolution of anemia, and serum glucagon one month after surgery was 98 pg/mL. During oncology follow-up, no adjuvant therapies were necessary, and her latest CT scan showed the cystic lesion of the pancreatic body without significant enlargement and without late intra-abdominal complications (Figure 9).

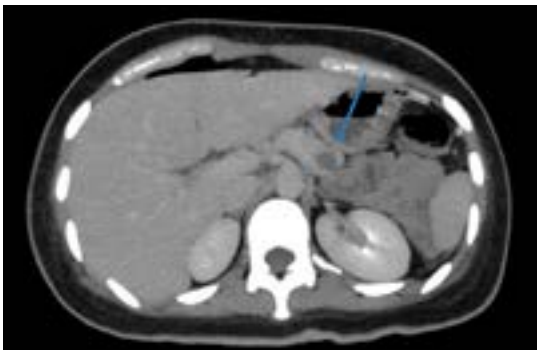


Figure 9: Abdominal computed tomography scan in axial view and venous phase of iodinated contrast medium, demonstrating the cystic lesion of the pancreatic body without significant enlargement and without late intra-abdominal complications.

Currently, she is under follow-up with clinical oncology and gynecology, where conservative treatment of the endometriotic lesion in the abdominal wall was chosen.

DISCUSSION

Glucagonomas are rare, with an incidence of one in 20 million people per year (2). They generally occur in people between 40 and 60 years of age (range 19 to 84 years) and have an equitable distribution by sex 6,7. They represent 1% of all neuroendocrine tumors and less than 5% of all primary malignant neoplasms of the pancreas.

The first case of glucagonoma was described by Becker et al[8] in 1942, in which the patient suffered from pancreatic neoplasia complicated by cutaneous erythema, diabetes mellitus, and anemia. Most glucagonomas demonstrate malignant behavior, and about three-quarters are fatal.

Glucagonoma syndrome is called the 4D syndrome [9,10,11] due to its association with dermatitis, diabetes, deep vein thrombosis, and depression. The form of dermatitis observed in glucagonoma syndrome is necrolytic erythema migrans, which occurs in more than two-thirds of patients. It consists of painful, itchy plaques that begin on the abdomen and groin and spread to the trunk and extremities. Its cause is unknown, although it is postulated that it results from a direct effect of glucagon, prostaglandin release, or a deficiency of amino acids or zinc. Other symptoms include diarrhea, glossitis, weight loss, and various neurological and psychiatric symptoms. Diabetes mellitus is present in most patients and can be mild or severe [9,11]. Glucagonoma is also associated with an increased frequency of thromboembolism, most commonly deep vein thrombosis and pulmonary embolism.

An elevated serum glucagon level, usually 10 to 20 times the normal level, is confirmatory of glucagonoma[5].

Most glucagonomas usually originate from the body or tail of the pancreas. Diagnosis is often late, and most primary tumors have a diameter greater than 5 to 6 cm. On CT and MRI, they may show hypervascular or heterogeneous enhancement, just as in our case[6,8,9,10,12.]

CONCLUSION

Pancreatic glucagonoma is an extremely rare neuroendocrine tumor, most frequently located in the body and tail of the pancreas. It generally presents with symptoms related to a paraneoplastic syndrome that is difficult to diagnose, and surgical treatment is curative when there are no metastases. We highlight here our experience

with the delay in diagnostic elucidation of two years, a time interval that could have changed the prognosis and life expectancy of the young patient, and the importance of radiological diagnosis, which defined the course of treatment in this case. Frequently, the main clue to diagnosis is a characteristic skin rash (migratory necrolytic erythema) that can affect the entire body and should be a warning sign for the attending physician to proceed with radiological and laboratory investigation. In conclusion, imaging studies are useful for determining the location and size of a glucagonoma.

Conflict of Interest

The authors declare no conflict of interest and received no financial support or grants in the production of this manuscript.

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