Clinical Case Report

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Glucagonoma syndrome with severe erythematous rash

A rare case report

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Abstract

Rationale: Glucagonoma is a rare neuroendocrine tumor of the pancreas. Glucagonoma syndrome is often misdiagnosed as other skin lesions by clinicians due to a typical clinical sign of necrolytic migratory erythema (NME) with severe erythematous rash.

Patient concerns: A 48-year-old female patient was admitted to our department because she presented with unclear recurrent severe erythematous rash. The patient was diagnosed as skin disease.

Diagnoses: Histopathologic examination revealed a pancreatic glucagonoma. Immnohistochemical staining of tumor tissue was positive for glucagon.

Interventions: The distal pancreatectomy plus splenectomy was performed in 2017.

Outcomes: The skin lesions disappeared after surgery. She was followed up and showed no recurrence until now.

Lessons: Clinicians should consider the diagnosis of glucagonoma according to the typical initial symptoms. Early diagnosis is very important to provide a better prognosis. A multidisciplinary approach is effective in patients with unresectable metastatic tumors.

Abbreviations: GS = glucagonoma syndrome, NME = necrolytic migratory erythema.

Keywords: glucagonoma, necrolytic migratory erythema, pancreas, severe erythematous rash

1. Introduction

Pancreatic endocrine tumors are usually accompanied by gastrinoma and insulinoma, and glucagonoma and VIPoma are found in approximately 3% and 1% of the pancreatic endocrine tumors, respectively.[1] Glucagonoma was first identified and reported in 1966 by McGavran et al.[2] It can be found in approximately 65% to 75% of the multiple endocrine neoplasia type 1 patients.[3] We here report a case of recurrent glucagonoma, which is even rarer.

2. Case report

A 48-year-old woman presented with erythematous rash with bullae and erosion on both her feet in 2017. The lesions progressed to the gluteal sacral region and upper extremities (Fig. 1). The patient was admitted to the dermatological department in our hospital. The symptoms included anorexia, glossitis, and angular stomatitis. Blood biochemical examination showed anemia, hypoalbumin, and hyperglycemia. Preoperative hemoglobin level was 90 g/L (115–150 g/L), albumin level was 32.8 g/L (40–55 g/L), and serum glucagon level was 7.2 mmol/L (3.9–6.1 mmol/L). Computed tomography (CT) revealed a cystic and solid mass located in the pancreatic tail (Fig. 2). The size of the mass was about 5 × 8 cm (Fig. 3). The patient was then transferred to our department. The distal pancreatectomy plus splenectomy was performed in 2017. Histopathologic examination revealed a pancreatic glucagonoma (Fig. 4A and B). Immnohistochemical staining of tumor tissue was positive for glucagon, synaptophysin (Syn), and chromogranin A (CgA), but negative for insulin, gastrin, and somatostatin (Fig. 4C–E). Ki-67 index was 1%. The patient was diagnosed with malignant pancreatic glucagonoma (Fig. 4F). The skin lesions disappeared after surgery (Fig. 5). Blood test was performed 1 week after operation. Hemoglobin level was 104 g/L (115–150 g/L), albumin level was 31.6 g/L (40–55 g/L), and serum glucagon level was 5.7 mmol/L (3.9–6.1 mmol/L). She was followed up and showed no recurrence until now. The patient has provided informed consent for publication of the case.

3. Discussion

Glucagonoma is a rare pancreatic neuroendocrine tumor, which originates from the alpha cells of the pancreatic islet.[4] Necrolytic migratory erythema (NME) is the most typical clinical symptom. NME is present in about 70% of the patients with glucagonoma syndrome. Other possible symptoms include diabetes mellitus, weight loss, glossitis, cheilitis, and diarrhea.[5] As this patient, blood biochemical examination showed anemia, hypoalbumin,

Editor: N/A.

This study was funded by the National Natural Science Foundation of China (grant number: 81560384).

The authors report no conflicts of interest.

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How to cite this article: Wang ZX, Wang F, Zhao JG. Glucagonoma syndrome with severe erythematous rash. Medicine 2019;98:37(e17158).

Received: 30 January 2019 / Received in final form: 21 July 2019 / Accepted: 20 August 2019

http://dx.doi.org/10.1097/MD.0000000000017158

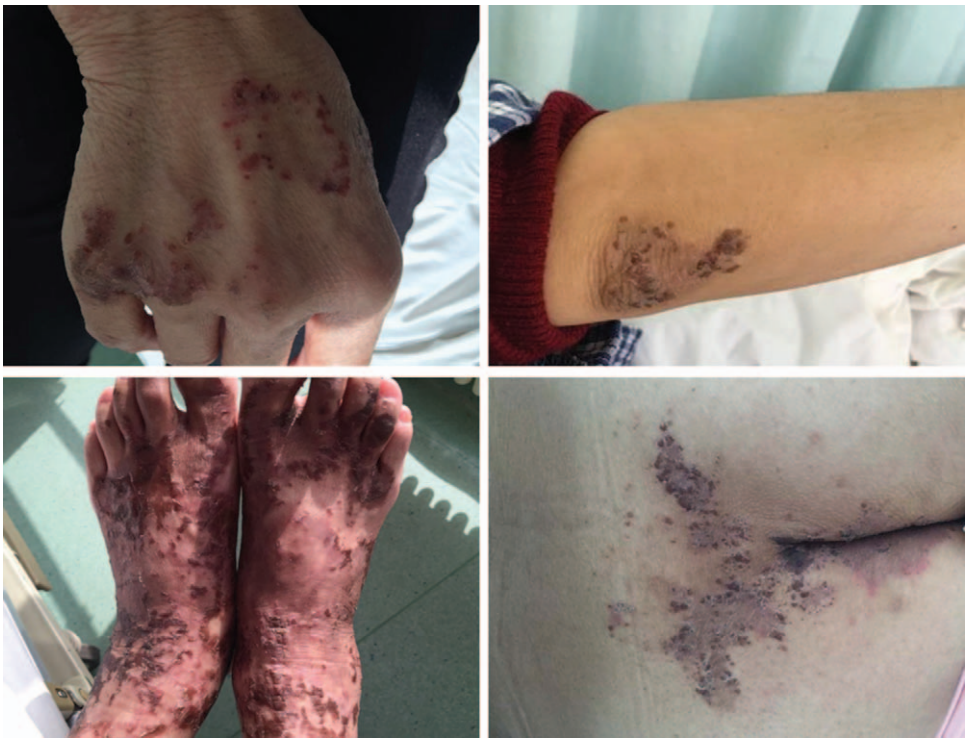

Figure 1. Erythematous rash with bullae and erosion on her hand, arm, buttock region, and feet.

and hyperglycemia. NME is mostly found in the inguinal and gluteal regions and the lower extremities. Erythema and bubble appear initially and scar was formed eventually. The symptoms may occur repeatedly.[6] In the present case, the patient had glossitis and erythematous rash and was misdiagnosed with skin disease. Usually glucagonoma is located in the pancreas, but there are exceptions. Poggi *et al* reported a case of primary malignant hepatic glucagonoma confirmed by immunohistochemistry and histopathological examination after autopsy.[7]

Glucagonoma often had liver metastasis when it was diagnosed.[8] Thus, early diagnosis is very important for early operation and better prognosis. This disease should be taken into consideration when the patients present with typical erythematous rash. The imaging diagnostic methods, including

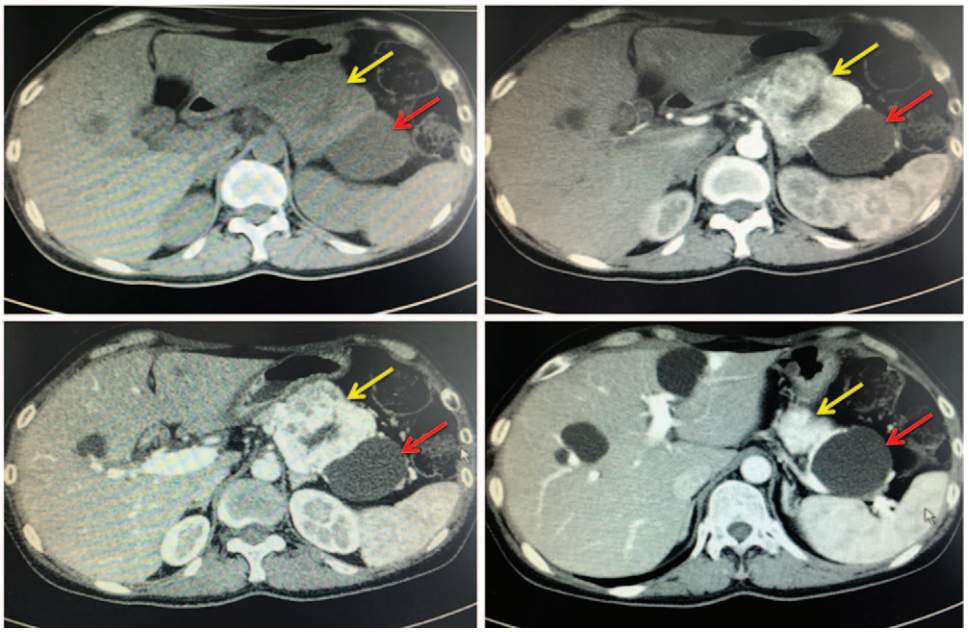

Figure 2. Computed tomography showed a cystic and solid mass located in the pancreatic tail. Yellow arrow: a solid lesion. Red arrow: a cystic lesion.

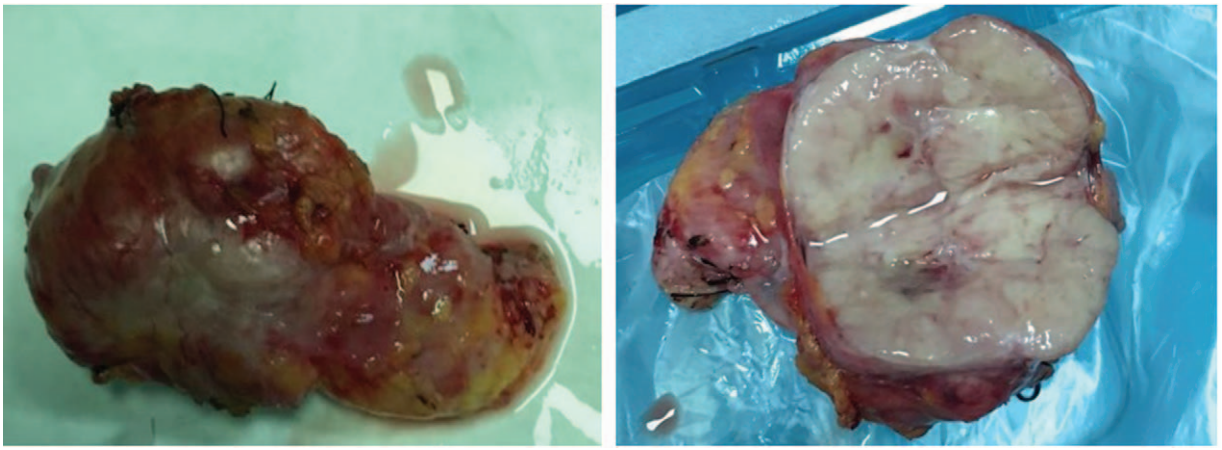

Figure 3. The tumor was about 5x8 cm in size. A mixed cystic lesion was shown.

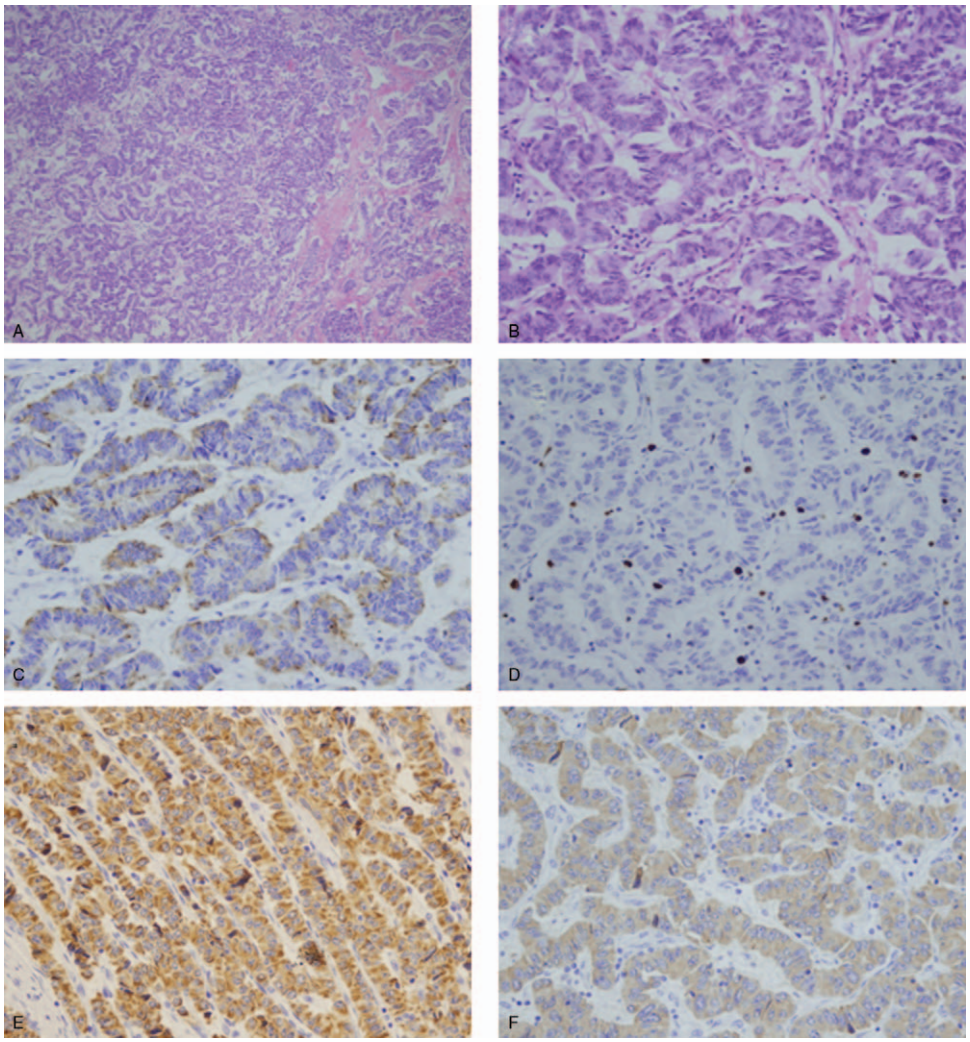

Figure 4. (A, B) Histologic analysis demonstrated gyrus-arranged adenoid cells, median nucleus, eosinophilic and fine granular cytoplasm, rich blood vessels and amyloid substance in mesenchyma (hematoxylin and eosin staining: A, ×100; B, ×400). (C, D, E) Immunohistochemical staining was positive for glucagon, synaptophysin, and chromogranin A (hematoxylin and eosin staining: x 400). (F) Ki-67 index was 5% (hematoxylin and eosin staining: ×400).

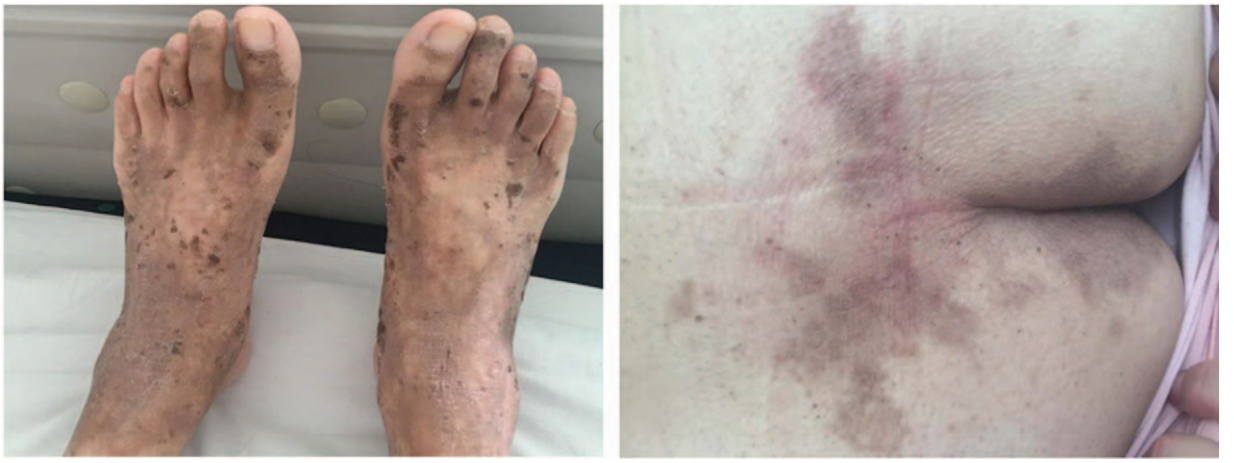

Figure 5. The skin lesions disappeared after operation.

ultrasonograhpy, CT, and MRI, are commonly used.[9] CT scan plays a critical role in assessing location, infiltration, and metastasis of the tumor. In this case, CT showed a pancreatic mass. High blood glucose level can be found in 80% of the patients with glucagonoma syndrome as glucagon can inhibit both the endocrine and exocrine functions of the pancreas.[10] In this case, serum glucagon level of patient was slightly high. So serum glucagon level test and pancreatic somatostatin receptor scintigraphy are also useful in the diagnosis of glucagonoma. Positron emission tomography-CT can be a complementary technique in identifying the metastasis of glucagonoma. Selective visceral angiography is highly sensitive, but it is an invasive test.[10] Skin biopsy is also a helpful diagnostic method.

Surgery is the most effective treatment for glucagonoma.[11] Distal pancreatectomy and pancreaticduodenenctomy are often chosen depending on the location of the tumor. The distal pancreatectomy plus splenectomy was performed in this patient. Focal ablation should be considered if the tumor is small. As the tumor grows slowly, patients with multimetastasized tumors should be treated by surgery, chemoembolization, and long-acting octreotide.[12] Long-acting somatostatin analogues have been proven effective in suppressing glucagon secretion from glucagonomas and in controlling the metastatic growth.[13] Follow-up is necessary and special precaution should be taken if the patients have typical skin rash again.

Clinicians should consider the diagnosis of glucagonoma according to the typical initial symptoms, which might be misdiagnosed as skin diseases. Early diagnosis may provide a better prognosis. A multidisciplinary approach is effective in patients with unresectable metastatic tumors.

Author contributions

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