CASE REPORTS

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Pancreatic panniculitis associated with periampullary duodenal diverticulum

Panikulitis pankreasa udružen sa periampularnim divertikulumom duodenuma

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Abstract

Introduction. Pancreatic panniculitis (PP) is a rare type of lobular panniculitis that manifests as painful erythematous nodules on the skin of the lower extremities. Subcutaneous fat necrosis caused by the release of pancreatic enzymes is the underlying cause of the disease, affecting around 2–3% of patients with pancreatic diseases. **Case report.** We present a case of a 58-year-old male patient who was admitted to our clinic due to the appearance of painful erythematous nodules on the lower extremities and trunk. Laboratory results revealed increased levels of pancreatic enzymes, amylase, and lipase, as well as heightened levels of glucose and inflammation markers. The histological analysis of the skin lesion biopsy revealed the presence of predominantly lobular panniculitis in the hypodermis, with areas of fatty tissue necrosis/saponification and remnants of adipocytes ("ghost cells"). Abdominal computed tomography scan demonstrated periampullary diverticulum (PD) of the duodenum, with no signs of pancreatitis or other pancreatic abnormalities. Esophagogastroduodenoscopy showed a wide opening of PD in the D2 segment of the duodenum. The patient was successfully treated with pancreatin therapy, resulting in a significant reduction of skin lesions and decreased levels of pancreatic enzymes. **Conclusion.** Duodenal PDs can be the cause of PP, most likely due to the pressure they exert on the pancreatic duct, which can lead to elevated values of pancreatic enzymes. Depending on the individual characteristics of the patient, symptomatic duodenal PD may be treated with operative or non-operative measures. Treatment of PP primarily involves addressing any underlying medical condition.

Key words:
diagnosis; diverticulum; endoscopy, gastrointestinal; histological techniques; pancreatin; pancreatitis; panniculitis; tomography, x-ray computed.

Apstrakt

Uvod. Panikulitis pankreasa (PP) je retka forma lobularnog panikulitisa koja se manifestuje pojavom eritematoznih bolnih nodusa na koži predominantno donjih ekstremiteta. U osnovi ovog oboljenja je supkutana masna nekroza uzrokovana oslobađanjem pankreasnih enzima koja se viđa kod 2–3% bolesnika sa bolestima pankreasa. **Prikaz bolesnika.** Prikazujemo 58-godišnjeg bolesnika koji je primljen u našu kliniku zbog pojave bolnih, eritematoznih nodusa na koži donjih ekstremiteta i trupa. Laboratorijske analize pokazale su povišene vrednosti pankreasnih enzima, amilaze i lipaze, povišene vrednosti glukoze i markera zapaljenja. Histopatološkom analizom bioptirane lezije kože pokazano je prisustvo pretežno lobularnog panikulitisa u hipodermu, sa poljima nekroze/saponifikacije masnog tkiva i ostacima adipocita („ćelijama-duhovima"). Kompjuterizovanom tomografijom abdomena utvrđeno je postojanje periampularnog divertikuluma (PD) duodenuma, bez znakova pankreatitisa ili drugih abnormalnosti pankreasa. Ezofagogastroduodenoskopijom viđen je širok otvor PD u D2 segmentu duodenuma. Bolesnik je uspešno lečen pankreatinom i došlo je do početne regresije promena na koži, uz sniženje nivoa pankreasnih enzima. **Zaključak.** Duodenalni PD mogu biti uzročnici PP, najverovatnije zbog pritiska koji vrše na izvodni kanal pankreasa, što može dovesti do povišenih vrednosti pankreasnih enzima. U zavisnosti od individualnih karakteristika bolesnika, terapija PD može biti hirurška i nehirurška. Lečenje PP podrazumeva lečenje oboljenja i stanja koja se nalaze u njegovoj osnovi.

Ključne reči:
dijagnoza; divertikulum; endoskopija, gastrointestinalna; histološke tehnike; pankreatin; pankreatitis; panikulitis; tomografija, kompjuterizovana, rendgenska.

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Introduction

Pancreatic panniculitis (PP) is a skin condition that affects a small percentage (2–3%) of individuals with pancreatic diseases [1]. While the exact cause is unknown, some studies suggest that pancreatic enzymes may trigger the condition by releasing fatty acids from the fat beneath the skin, leading to fat necrosis [1, 2].

PP can be linked to several pancreatic conditions, such as acute and chronic pancreatitis, pancreatic tumors, and cysts [1–4]. The skin symptoms can occur before, during, or after the development of pancreatic disease [2, 4].

The condition typically presents as painful, red nodules beneath the skin, mostly observed on the lower legs, although other body areas can also be affected. In more severe cases, the symptoms can lead to skin ulcers and other complications [3].

Case report

A male 58-year-old patient was hospitalized in our clinic due to the presence of painful erythematous nodules on his lower extremities and trunk, that persisted for two months. The patient did not exhibit any constitutional symptoms. Initial treatment with systemic antibiotics on an outpatient basis did not yield a therapeutic response.

In his personal medical history, the patient reported that he suffered from acute pancreatitis in 2011. The patient also reported cigarette smoking with no previous history of alcohol consumption.

During the physical examination, numerous subcutaneous nodules, measuring 1.5–4.0 cm in diameter, displaying erythematous coloration and fluctuation, were observed primarily on the lower legs, thighs, and trunk (Figure 1). Additionally, mild edema of both feet and ankles was present, and the patient's abdomen was found to be soft and non-tender. He did not report abdominal pain, nausea, vomiting, or any other gastrointestinal symptoms.

Abnormal laboratory findings showed increased sedimentation rate [106 mm/h, reference range (RR) < 20 mm/h], increased leucocyte count (14.47 × 10^9/L, RR 4–10 × 10^9/L), increased levels of C-reactive protein (280.57 mg/L, RR 0–5 mg/L), glucose (10.5 mmol/L, RR 4.1–5.9 mmol/L), urea (13.1 mmol/L, RR 2.5–7.5 mmol/L), creatinine (139 mmol/L, RR 62–115 mmol/L), amylase (133 U/L, RR 30–115 U/L), lipase (1,041 U/L, RR 73–393 U/L), alpha-1 antitrypsin (2.88 g/L, RR 0.78–2 g/L) and decreased levels of iron (3 μmol/L, RR 8–30 μmol/L), erythrocytes (3.68 × 10^{12}/L, RR 4.5–6.5 × 10^{12}/L), and hemoglobin (101 g/L, RR 130–180 g/L). Serum tumor marker levels of carcinoembryonic antigen, CA 19.9, and alpha-fetoprotein were within the RR. Immunologic analyses: anti-nuclear antibodies - ANA, C3, C4, extractable nuclear antigen - ENA screening, antineutrophil cytoplasmic antibodies - ANCA with a cytoplasmic staining pattern (cANCA), perinuclear ANCA - pANCA, cryoglobulins, and circulating immune complexes were undetectable.

The histological analysis of the skin lesion biopsy revealed the presence of predominantly lobular panniculitis in the hypodermis, characterized by a mixed inflammatory infiltrate, areas of fatty tissue necrosis/saponification, and remnants of adipocytes ("ghost cells") (Figure 2). Granuloma formation or atypical cells were not observed, and the pathological findings were consistent with subcutaneous nodular fat necrosis.

The culture of the skin tissue sample showed no presence of deep fungal infection or acid-resistant bacteria.

Additional diagnostic procedures were done. Abdominal ultrasound showed signs of liver steatosis. Computed tomography (CT) of the chest, abdomen, and pelvis demonstrated the periampullary diverticulum (PD) of the duodenum adjacent to the pancreatic head. CT scans showed no signs of pancreatitis, pancreatic neoplasm, or any other pancreatic disease. Esophagogastroduodenoscopy showed a wide opening of PD in the D2 segment of the duodenum.

Initially, before obtaining the results of histologic analysis for skin lesions, systemic antibiotic therapy (intravenous metronidazole and meropenem for seven days) and topical corticosteroids (betamethasone dipropionate 0.05%) were started twice a day for skin lesions along with bed rest and leg elevation, with insufficient therapeutic effect. Since the diagnoses of PD and PP were established and pancreatic enzymes were elevated, a gastroenterologist was consulted, and pancreatin 10,000 IU was administered three times a day.

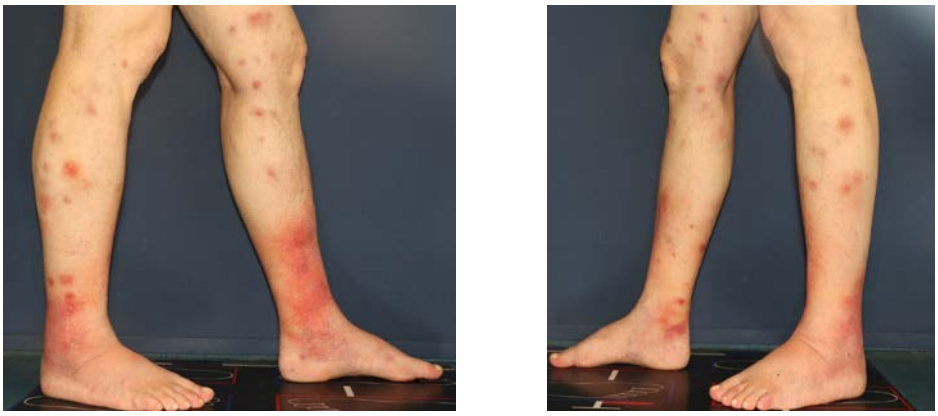

Fig. 1 – Multiple fluctuant erythematous subcutaneous nodules measuring 1.5–4 cm in diameter on both lower legs and thighs.

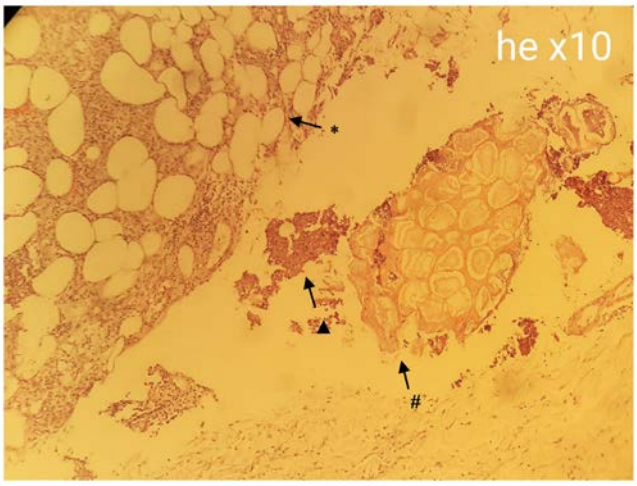

Fig. 2 – Predominantly lobular panniculitis (*) with "ghost-cells" (#), necrotic adipocytes with amorphous granular debris (▲) (hematoxylin-eosin, ×10).

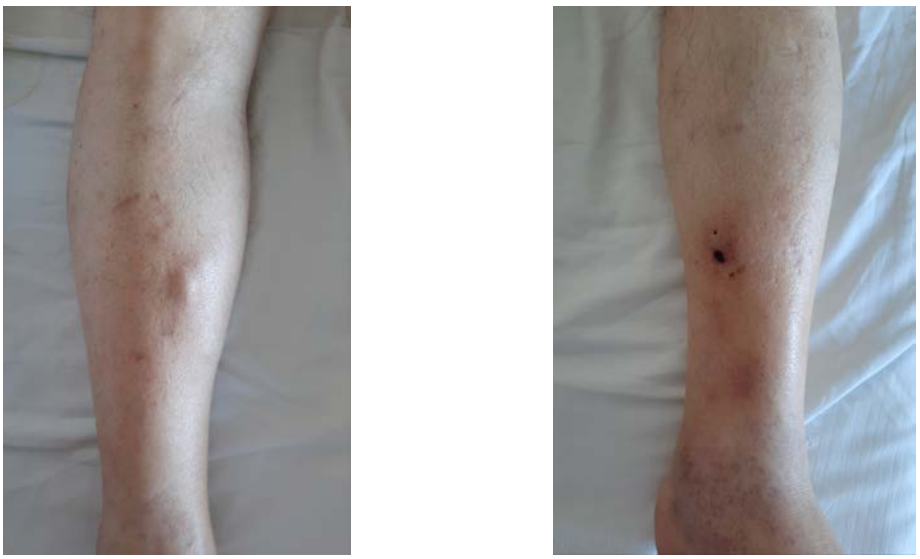

Fig. 3 – Initial regression of skin lesions.

Ten days after starting pancreatin therapy, there was a significant reduction in skin lesions along with decreasing levels of pancreatic enzymes (amylase, 129 U/L; lipase, 120 U/L) (Figure 3).

Discussion

PP is an infrequent disorder that occurs when pancreatic enzymes are released in large quantities into the bloodstream, leading to the development of subcutaneous nodules and necrosis of the fatty tissue [1, 2]. This condition is an uncommon complication of pancreatic diseases, often observed in cases of acute or chronic pancreatitis, pancreatic carcinoma (specifically the acinar cell variant), and less frequently in conjunction with pancreatic pseudocysts and pancreas divisum [1–4]. Nevertheless, there have been documented cases of its occurrence linked to various other diseases and conditions like HIV infection, haemophagocytic syndrome, diabetic ketoacidosis, sepsis, liver carcinoma, and systemic lupus erythematosus [5–9]. To the best of our knowledge, this case report presents the first documented instance of PP associated with a duodenal PD.

Due to its clinical presentation, PP may have similarities with other types of septal and lobular panniculitis (erythema nodosum, erythema induratum, lupus panniculitis, etc.) [2, 4]. Therefore, it is crucial to conduct various diagnostic procedures, placing particular emphasis on performing a biopsy of skin lesions and submitting the sample for thorough histological and microbiological analysis. In the initial stages, early skin lesions may exhibit septal panniculitis without fat necrosis. On the other hand, fully developed lesions display distinct saponification and "ghost cells", which represent remnants of adipocytes with amorphous granular debris [2–4].

The presumed mechanism behind the development of skin lesions involves trypsin increasing the permeability of blood vessels in the tissue, which allows lipase to enter the subcutaneous tissue and break down fatty acids [2, 4].

Elevated serum levels of amylase, lipase, and trypsin are often observed in PP, even though the presence of elevat-

ed levels of a single enzyme without concurrent elevation in others is not uncommon. The development and severity of panniculitis do not necessarily correlate with enzyme levels [2]. In some cases, the patient may display elevated levels of serum lipase without any clinical or radiologic evidence of pancreatitis or other pancreatic diseases [8].

In this particular case, laboratory analyses revealed a 2.6-fold increase in serum lipase levels (1,043 U/L, normal < 393 U/L) with slightly increased levels of amylase (133 U/L, normal < 115 U/L). Abdominal CT indicated the presence of duodenal PD with no signs of pancreatitis or other pancreatic diseases. The patient did not report any constitutional or gastrointestinal symptoms at presentation.

PDs refer to sac-like expansions in the mucosal lining situated near the ampulla of Vater. It is worth noting that approximately 70–75% of duodenal diverticula are classified as periampullary [10]. There have been reports linking PDs with acute and chronic pancreatitis. Complications arising from these diverticula can occur when they exert pressure on the duodenal wall, common bile duct, or pancreatic duct, potentially leading to pancreatitis [10–12].

In the case presented, it is possible that distension of a diverticulum caused compression of the pancreatic duct, resulting in an asymptomatic increase in pancreatic enzymes and subsequent PP. Furthermore, elevated pancreatic enzymes were observed despite the absence of clinical examination or CT scan findings indicative of pancreatitis (CT scans have a sensitivity of approximately 92% for detecting pancreatitis) [13]. Notably, the patient had experienced an episode of acute pancreatitis ten years prior, which may have been related to the same underlying cause. In 40% of cases, lesions of PP can appear before the onset of pancreatic disease, with a time interval ranging from one to seven months, thereby serving as a significant diagnostic indicator [14].

The primary approach to treating PP involves addressing the underlying pancreatic disease [1, 2]. In cases associated with acute pancreatitis, resolution of skin lesions is typically seen with the normalization of pancreatic enzymes. Nevertheless, in cases associated with neoplasia, PP tends to exhibit a chronic and persistent nature [2]. The use of octreotide, a somatostatin analog, could potentially offer advantages in the treatment of individuals diagnosed with PP [15].

Symptomatic duodenal diverticula can be managed through operative or non-operative measures, with surgical intervention reserved for complicated cases [16]. In the presented case, symptomatic treatment led to initial regression of skin changes and a decrease in pancreatic enzyme levels.

Conclusion

This report emphasizes the uncommon occurrence of PP and its association with multiple diseases. Despite the absence of pancreatitis or other pancreatic abnormalities on imaging, the patient's history of acute pancreatitis and the presence of PD suggest a possible connection to the development of PP. The successful treatment with pancreatin further supports this hypothesis.

In conclusion, diagnosing PP involves assessing pancreatic enzyme levels and performing a skin biopsy. PP can be associated with various pancreatic disorders and other conditions, necessitating the exclusion of underlying diseases in order to manage effectively both the primary disease and cutaneous manifestations.

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