

# Pancreatic panniculitis in systemic lupus erythematosus and Crohn's disease: rare event

## *Paniculite pancreática no lúpus eritematoso sistêmico e na doença de Crohn: raro evento*

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### ABSTRACT

Pancreatic panniculitis (PP) is a rare manifestation of pancreatic disease, involving subcutaneous adipose tissue. We report two cases of this entity: a 37-year-old female patient with systemic lupus erythematosus (SLE) and an elderly woman with Crohn's disease. These are two chronic autoimmune inflammatory diseases that can be uncommonly related to acute pancreatitis and that culminates in PP. We also provide a brief review of the treatment, diagnosis and morphology of the lesions, as well as the pathophysiology of the disease. The importance of histopathological analysis of lesion biopsies is highlighted as an important diagnostic tool.

**Key words:** fat necrosis; pancreatitis; Crohn disease; lupus erythematosus systemic.

### RESUMO

*A paniculite pancreática (PP) é uma manifestação rara de doença pancreática que acomete o tecido adiposo subcutâneo. Relatamos dois casos dessa entidade: uma paciente do sexo feminino, 37 anos, portadora de lúpus eritematoso sistêmico (LES) e uma idosa com doença de Crohn. Ambas manifestações são doenças inflamatórias crônicas autoimunes raramente relacionadas com o quadro de pancreatite aguda e que culminaram em PP. Também fizemos uma breve revisão sobre tratamento, diagnóstico e morfologia das lesões, bem como da fisiopatologia da doença. Destacamos a importância da imuno-histoquímica e da análise histopatológica de biópsias da lesão como ferramentas diagnósticas.*

**Unitermos:** necrose gordurosa; pancreatite; doença de Crohn; lúpus eritematoso sistêmico.

### RESUMEN

*La paniculitis pancreática (PP) es una manifestación rara de enfermedad pancreática que afecta el tejido graso subcutáneo. Reportamos dos casos de esa entidad: una paciente del sexo femenino, 37 años, con lupus eritematoso sistémico (LES), y una anciana con enfermedad de Crohn. Ambas manifestaciones son enfermedades crónicas autoinmunes raramente relacionadas con el cuadro de pancreatitis aguda y que culminaron en PP. También hicimos una breve revisión acerca de tratamiento, diagnóstico y morfología de las lesiones, así como fisiopatología de la enfermedad. Se resalta la importancia de la inmunohistoquímica y del análisis histopatológico de biopsias de la lesión como herramientas diagnósticas.*

**Palabras clave:** necrosis grasa; pancreatitis; enfermedad de Crohn; lupus eritematoso sistémico.

## INTRODUCTION

Pancreatic panniculitis (PP), described by Chiari, in 1883, consists of a rare cutaneous manifestation that, as the name indicates, is an inflammatory process of the subcutaneous tissue<sup>(1-3)</sup>. This cutaneous disorder is generally associated with benign pancreatic diseases, present in just 2%-3% of the cases, principally the acute and the chronic pancreatitis, although it is also found in malignant pancreatic neoplasms<sup>(1, 3-5)</sup>. According to Zundler *et al.* (2017), PP is diagnosed in elderly patients, with mean age of 60 years; however, it can appear at any age due to the different etiologies of the disease, such as pancreatitis, neoplasms, graft rejection, fistulas, trauma, etc. Regarding gender, most cases of PP affect male individuals, perhaps for the highest incidence of chronic pancreatitis in men<sup>(6,7)</sup>.

Although its pathophysiology is still uncertain, it is believed that: 1. the increase in levels of circulating pancreatic enzymes (trypsin, amylase, elastase I and lipase), which triggers subcutaneous fat secondary saponification, is the probable mechanism; 2. in the earliest stages of PP, the endothelial damage provoked by pancreatic enzymes permits their migration to the subcutaneous tissue<sup>(1, 3, 8, 9)</sup>; 3. trypsin plays a role in the increase of endothelial permeability and, therefore, would enable the movement of lipase from the intravascular space towards the interstitium<sup>(1)</sup>.

PP histology reveals a typical pattern of foci of liquefactive necrosis of the fat lobules, without presence of vasculitis, with anucleate adipocytes and cytoplasm with granular basophil material corresponding to calcium deposits ("ghost adipocytes"), resulting from saponification reactions. These dead adipocytes are grouped in the most central portion of the subcutaneous nodules, whereas in the periphery there is a polymorphonuclear infiltrate<sup>(5)</sup>.

PP treatment is almost always based on the correction of pancreatitis, allowing reduction in the levels of pancreatic lipolytic enzymes in the bloodstream. Thus, a surgery is commonly required to correct the pancreatic anomaly for an efficient treatment, with the consequent disappearance of symptoms<sup>(2, 5, 10)</sup>.

## CASE REPORTS

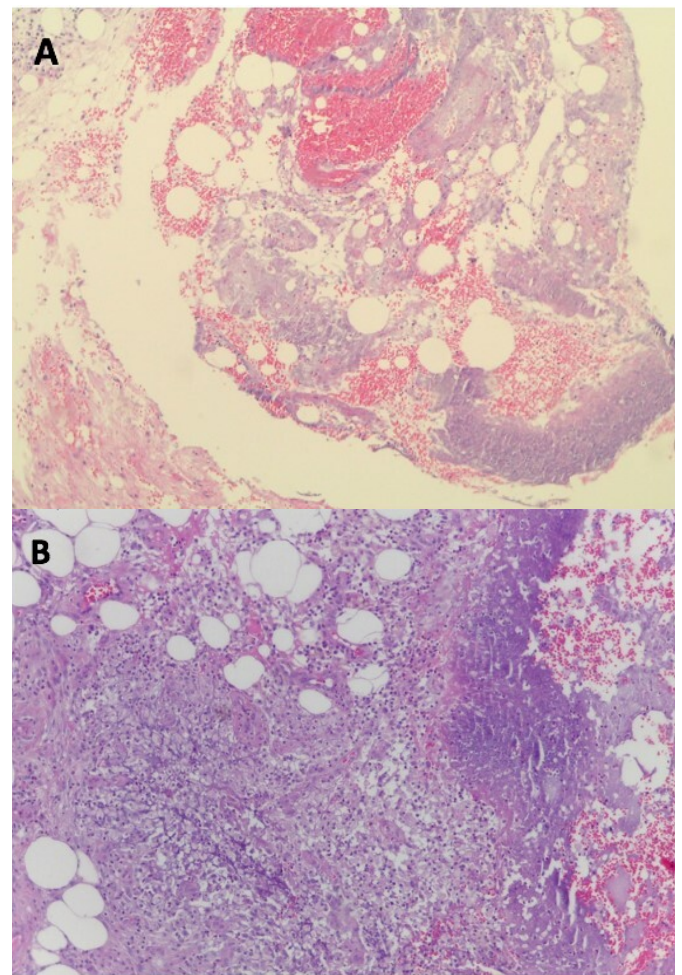
### Case 1

Brazilian female mixed-race 37-year-old patient, with a history of chronic kidney disease (CKD) for eight years, on peritoneal dialysis, was diagnosed with systemic lupus erythematosus (SLE) five years before. She denies tobacco use and alcohol consumption. Laboratory tests indicated a rise in amylase and lipase enzymes. The patient was hospitalized

with abdominal pain, nausea, vomiting, and multiple painful nodules, of approximately 1-2 cm, with mild erythema in trunk and upper and lower limbs. Biopsies were carried out on the lesions of right arm and thigh. The initial hypotheses were PP (with fat necrosis), lupus panniculitis, poststeroid panniculitis, indurated erythema/nodular vasculitis, erythema nodosum and type 2 leprosy reaction. The final diagnosis was PP triggered by lupus pancreatitis (LP) (**Figure 1**).

### Case 2

Brazilian 70-year-old female patient, with a 23-year history of Crohn's disease treated with methotrexate 12.5 mg/day, and CKD treated conservatively. She was hospitalized with complaints of abdominal pain, nausea, vomiting, fever, with asymptomatic nodular

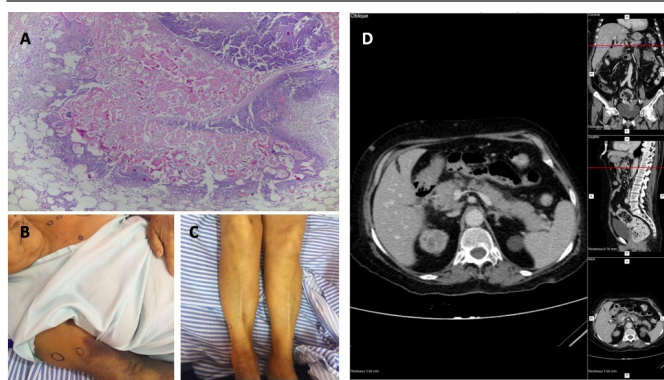


**FIGURE 1** – Lobular panniculitis compatible with PP

*A) enzymatic necrosis of adipocytes in the involved areas, ghost cells and hemorrhagic foci (HE, 40×); B) lobular panniculitis with inflammatory infiltrate composed of histiocytes and neutrophils; there are still necrotic areas, cell debris and saponification (HE, 100×).*

*PP: pancreatic panniculitis; HE: hematoxylin and eosin stain.*

lesions disseminated in the trunk and upper and lower limbs, but could not easily tell the time of onset. The lesions were biopsied, and the histopathological report described lobular panniculitis associated with areas of liquefactive necrosis and ghost adipocytes, compatible with PP. Computed tomography (CT) of abdomen and pelvis was performed and revealed jejunal and ileal loops, besides ascending colon with adjacent fat densification. Enlarged pancreas with parenchymal densification was compatible with acute pancreatitis. Subcutaneous nodules of soft-tissue density were also observed in areas of thorax and abdomen (**Figure 2**).



**FIGURE 2** – A) lobular panniculitis with inflammatory infiltrate, extensive necrosis, cell debris and saponification with ghost adipocytes, compatible with PP (HE, 40×); B) and C) patient with asymptomatic nodular lesions, sometimes erythematous, disseminated over trunk and upper and lower limbs; D) CT presenting enlarged pancreas, with parenchyma densification and pancreatic fat. Nodules with soft-tissue density in the subcutaneous tissue  
PP: pancreatic panniculitis; HE: hematoxylin and eosin stain; CT: computed tomography.

## DISCUSSION

In case 1, we present a young patient who denies history of use of alcohol, tobacco and other recreational drugs; besides, the presence of choledocholithiasis was discarded, what excluded the two major causes of the disease acute manifestation (80%)<sup>(11)</sup>. Although the incidence of acute pancreatitis in individuals with CKD undergoing dialysis is higher than that in the general population, we concluded that the patient had a LP, a rare presentation of SLE, which, in its turn, is a chronic multisystemic autoimmune disease<sup>(11-13)</sup>.

LP in an uncommon association, with prevalence lower than 4.2% of the SLE cases<sup>(14, 15)</sup>. Although physiopathology is still uncertain, it is likely related to the immune complex deposition within the walls of pancreatic vessels, leading to vasculitis and, finally, pancreatitis<sup>(11, 13, 15)</sup>. It is characterized by abdominal pain (in more than 90% of the cases), nausea, vomiting (65%-75% of the cases) and fever (50%); however, the patient was not feverish<sup>(13, 16)</sup>.

The PL diagnosis is confirmed if the individual presents: elevated serum levels of pancreatic enzymes, evidence in imaging tests, exclusion of toxic metabolic causes and mechanical obstruction of the pancreatic duct<sup>(13, 16)</sup>. The patient met all the described criteria. It is worth highlighting that in case 1 the patient presented panniculitis associated with SLE, and not with LP. PP in patients with SLE is an extremely rare event, with less than 10 cases reported in the literature<sup>(17-19)</sup>.

In case 2, we have a patient without history of alcohol consumption or biliary lithiasis, but with Crohn's disease for more than 20 years. As well as SLE, Crohn's disease is an autoimmune inflammatory disease with severe intestinal damage, although it may also present extraintestinal manifestations, being a very uncommon cause of acute pancreatitis too<sup>(8, 14)</sup>. The leading causes of acute pancreatitis in patients with Crohn's disease are gallstones and certain medications used in the treatment of Crohn's disease<sup>(20)</sup>. Thus, we point towards a possible drug association, given that the presence of gallstones was excluded.

The PP lesions occur mainly in lower limbs, less frequently in abdomen, upper limbs, trunk, breasts, buttocks and scalp<sup>(1, 8)</sup>. These lesions present as tender plaques and edematous and erythematous nodules, which measure 1-2 cm in diameter<sup>(9)</sup>. In milder cases, the nodule can be single and resolve without the presence of ulcerations, as soon as the pancreatic inflammation recedes. Moreover, these nodules may evolve into necrotic abscesses with spontaneous ulceration, presence of exudate of an oily brown material due to liquefactive fat necrosis<sup>(5, 9)</sup>.

Panniculitis can be traditionally divided into septal, lobular and mixed (septal and lobular), what permits a better individual diagnosis of the disease. This classification, however, is only useful when panniculitis is histologically fully developed, as during its progression, it keeps altering itself. Studies propose that, despite PP is predominantly of the lobular type, it begins in a septal form, with a lymphoplasmatic infiltrate in the septa that involve fatty lobules and blood vessels<sup>(21, 22)</sup>. Consequently, as it evolves, the lesions, in a more advanced stage, take the lobular form, with predominantly granulomatous infiltrate, composed mainly of histiocytes, hemosiderin deposits and giant polynucleated cells. Later, this picture becomes a fibrosis<sup>(21, 23)</sup>. In both studied cases, there is evidence of "advanced" process, due to hemorrhage, infiltrate of histiocytes and neutrophils, associated with areas of enzymatic necrosis, and with ghost adipocytes.

## CONCLUSION

We presented unique and well-illustrated cases of PP, triggered by SLE and Crohn's disease. We highlight the importance of the histopathological correlation of cutaneous lesions with the clinical picture to confirm the diagnostic hypothesis.

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