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Pancreatic disease, panniculitis, polyarthrtitis syndrome successfully treated with total pancreatectomy: Case report and literature review

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ABSTRACT

INTRODUCTION: Pancreatic disease can be complicated by extrabdominal manifestations such as panniculitis and polyarthritis. The symptomatic triad comprising pancreatic disease, panniculitis and polyarthritis is also known as PPP syndrome and is characterized by severe chronic sequels and high mortality rate. We describe a case of PPP syndrome successfully treated with spleen preserving total pancreatectomy; in addition we performed a literature review.

PRESENTATION OF CASE: A 67 years old male presented panniculitis and polyarthritis without clinical abdominal symptoms. Clinical presentation, laboratory values and radiological findings demonstrated an acute pancreatitis and a pancreatic cancer was suspected; failure of conservatory treatments and high suspicious of malignancy led to perform a spleen preserving total pancreatectomy. Finally histological examination excluded a pancreatic cancer and confirmed a chronic pancreatitis. Patient was discharged with complete resolution of the extrabdominal disease.

DISCUSSION: In literature only 64 cases of PPP syndrome have been reported. Abdominal symptoms do not often appear at presentation and diagnosis may be delayed. Panniculitis develope in any part of the body but especially on the distal parts of the lower extremities, around the ankles and pretibial regions of the legs. Between osteo-articular manifestations polyarthritis is the most common one, although oligoarthritis, and monoarthritis in have been reported.

CONCLUSION: PPP syndrome is a rare disease with a high mortality rate. A timely diagnosis and an aggressive treatment may improve the prognosis of this condition.

1. Introduction

The association between pancreatic disease, panniculitis and polyarthritis was described for the first time by Boswell et al. in 1973 [1]. In the so called PPP (pancreatic disease, panniculitis and polyarthritis) syndrome extrabdominal manifestation can predate or coincide with pancreatic disease and a prolonged misdiagnosis is frequent [2]. Pancreatitis and pancreatic cancer are the main causes of PPP syndrome [3], although other pancreatic diseases have been reported such as pancreatic disease [4], abdominal trauma, [5] and pancreas divisum [6]. Mortality rate is 24% when PPP syndrome is caused by pancreatitis and 74% when associated with pancreatic cancer [3].

We present a case of PPP-syndrome in a patient with recurrent chronic pancreatitis and a suspected pancreatic head cancer, describing clinical and diagnostic characteristics. In addition we performed a literature search (PubMed database, National Library of Medicine, Bethesda, MD) using MEDLINE subheadings and key words “pancreatic carcinoma” or “pancreatitis” or “ pancreatic disease” or “panniculitis” or “subcutaneous fat necrosis” and “arthritis.” Only English; Spanish and French language reports were selected.

2. Case report

A 67-year-old male was admitted presenting multiple painful tender subcutaneous nodules on trunk, arms and legs. He referred

Abbreviation: PPP syndrome, Pancreatic disease, panniculitis and polyarthritis.

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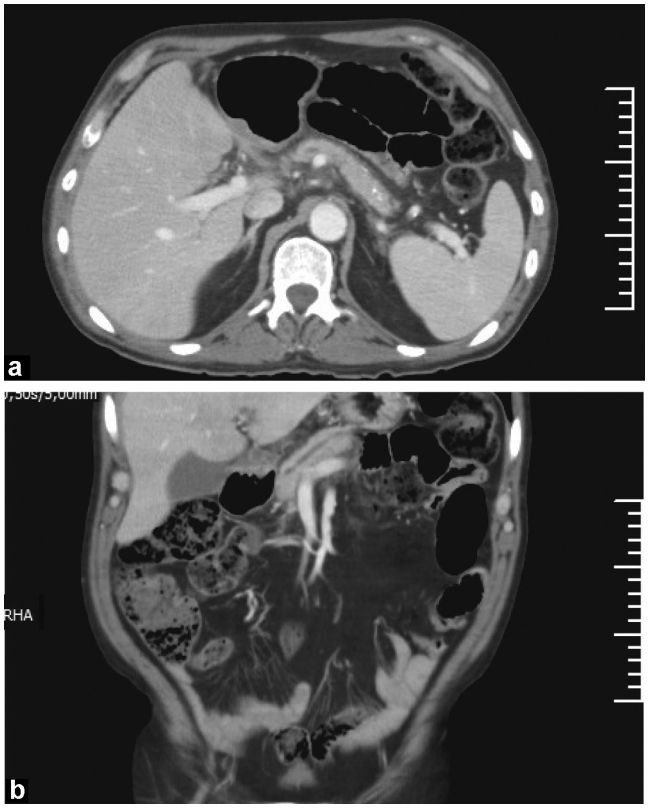

Fig. 1.

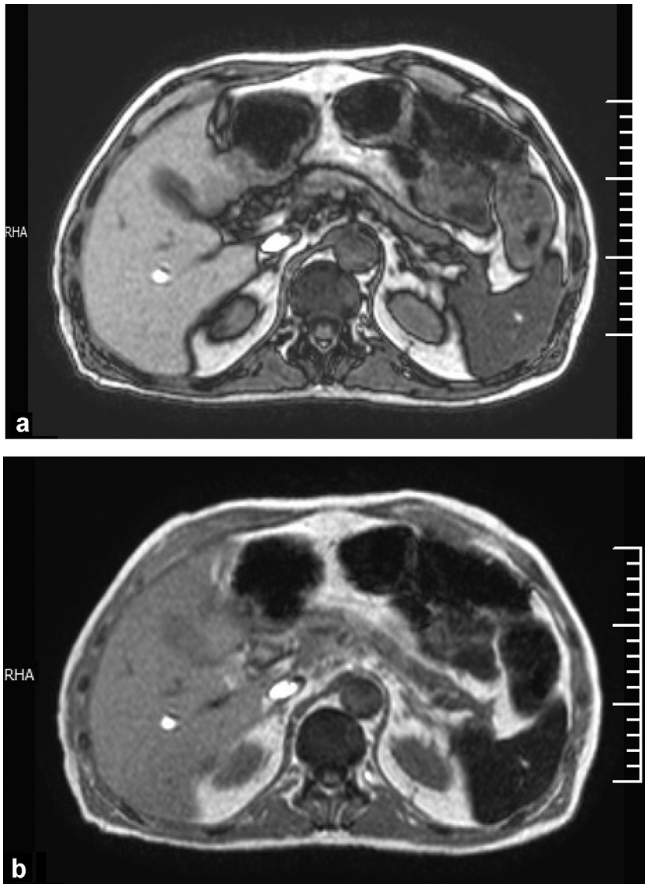

Fig. 2.

neither pain nor fever. In his medical history he reported an alcoholic abuse and an alcoholic chronic pancreatitis within 3 episodes of acute pancreatitis. Initial investigations revealed hemoglobin level of 12.2 g/dl, normal white blood cells and platelet count, an elevated C-reactive protein of 153 mg/L, serum level amylase of 4544 IU/mL and lipase level of 3885 IU/mL. A CT scan showed an acute pancreatitis with enlargement of pancreatic head in a context of chronic pancreatitis. Skin biopsy revealed a lobular panniculitis with extensive fat necrosis and areas of saponification. On standard culture an E. Coli was isolated. After 2 weeks of parenteral nutrition, octreotide infusion and antibiotic therapy a clinic improvement of skin lesions and a normalization of pancreatic enzyme levels were observed. The patient was discharged with a diagnosis of pancreatic panniculitis.

Patient was readmitted to the hospital 30 days after discharge for panniculitis recurrence and acute arthritis of hands and feets with complete functional impairment. During hospitalization also ankles, knees and right wrist presented signs of acute arthritis that require surgical drainage. MRI findings showed synovitis with thickening of synovium in the affected joints and intramedullary fat necrosis of adjacent bone segments. The synovial fluid analysis demonstrated a pancreatic necrosis with negative gram staining and serial cultures. No clinical improvement with FANS and corticoid treatment was observed after two week of treatment.

Abdominal CT scan demonstrated an acute pancreatitis complicating a chronic pancreatitic disease (Fig. 1). Pancreatic study was completed by an abdominal MRI that confirmed pancreatitis (Fig. 2). Additionally on ecoendoscopy EUS FNA was performed with inconclusive result. Therefore, due to the symptoms persistence and the worsening of the extraabominal disease despite the remission of pancreatitis a clinical suspicious of pancreatic cancer was planned and lead to performed a surgical resection.

Intraoperatively, a steatonecrosis aera in the epiploic retrocavity was found, extending from the posterior wall of the stomach to the ventral surface of the transverse colon: pancreatic gland was atrophic with diffuse peripancreatic inflammation reaction that caused difficult anatomic identification of vascular structures.

Splenic artery and vein are identified and dissected from the pancreatic tail and pancreas is mobilized until celiac trunk. Hepatic and left gastric artery are dissected. Finally mesenteric-portal axis is isolated and a spleen preserving total pancreatectomy performed. Histologic examination excluded a malign disease and confirmed a chronic pancreatitis.

The patient underwent rapid clinical improvement with resolution of cutaneous lesions. Before discharged MRI feet showed an improvement of widespread bone marrow signal abnormality and a partial resolution of bone fat necrosis. Clinically, osteo-articular manifestation persisted during 6 months.

He was discharged in good condition on the 16nd postoperative day; currently, at 4 years of follow up, the patient is asymptomatic with a complete resolution of panniculitis and an important improvement of the affected joints, with a residual chronic pain of right knee and wrist.

3. Discussion

The pathogenesis of PPP syndrome is not clear. Pancreatic diseases determinate an increased in the bloodstream of pancreatic enzymes that lead to saponification of fatty tissues such as subcutaneous fat or bone narrow. These enzymes may enter into the systemic circulation via the thoracic duct or portal circulation or via lymphatic channels [3]. Also individual susceptibility has been involved in the pathogenesis of this syndrome, in case of alpha-1 antitrypsin deficiency [7,8] or to a low levels of alpha-2 macroglobulin, that cause an increase of hematic trypsin

Table 1
Main characteristics of PPP syndrome.

	Pancreatitis	Pancreatic cancer
Number of patients	34	30
Average age	51.1	61.2
Male/Female	24/10	26/4
Alcolic abuse n(%)	16 (47)	–
Abdominal manifestation n(%)	13 (38)	12 (39)
Interosseous fat necrosis n(%)	16 (47)	10 (35)
Artritis n(%)		
mono	8 (23)	4 (13)
oli	4 (12)	6 (20)
poly	22 (65)	20 (67)

level [9,10]. Since pancreatic panniculitis resembling erythema nodosum, an immunologic process as cause of the subcutaneous fat, cannot be excluded [10]

In literature 64 cases of PPP syndrome are reported, 34 patients with pancreatitis [2,11–18], 30 patients with pancreatic cancer [3] (Table 1).

In almost 1/3 of patients abdominal symptoms such as abdominal pain, nausea, vomiting and fever, are absent or mild, which may lead to a delayed diagnosis [2] and can play a role in the hight mortality rate of this syndrome. Distinctive laboratory values include elevated serum amylase and lipase levels, leukocytosis and high levels of CPR. Eosinophilia can also be present.

Pancreatic panniculitis can precede, occur concurrently with or follow the pancreatic pathology. Clinically, panniculitis presents with erythematous, ill-defined, reddish-brown, painful or painless nodules. Skin lesions may appear on the legs but also on the abdomen, trunk, breast arms, and scalp. When associated with pancreatic cancer, pancreatic panniculitis is mostly localized in lower extremities and nodules are more persistent and often ulcerate [3]. Histologically features include panniculitis and lobular fat necrosis, without signs of vasculitis, with ghost-like cells within the cytoplasm, with an inflammatory infiltrate and focal calcification. Sterile or sovrainfected abscess formation may occur, as in our patient, breaking down to release thick, purulent material, rich in triglycerides [19].

Osteo-articular manifestations consist of polyarthritis, polyserositis and intramedullary fat necrosis. Arthritis manifestations usually present during the syndrome while in few patients symptoms appear before the diagnosis of pancreatic disease. Joint involvement is usually polyarticular, although oligoarticular or monoarticular patterns have also been reported; the most commonly affected joints are ankles, knees and wrists. Synovial aspiration shows a creamy high viscosity fluid with high lipid content. In most patients symptoms are transient, but an evolution to chronicity may occur in almost half of the patients [2,3]. MRI revealed characteristic radiologic findings such as thickening of the synovial membranes, soft-tissue swelling, osteolytic lesions and periostitis of the tubular bones of the extremities which correlate pathologically with areas of extensive intramedullary fat necrosis and trabecular bone destruction.

Conservatory treatment consists in supportive measure and management of secondary infection. Steroids, NSAIDs, and immunosuppressants for skin lesions or arthritis are usually ineffective [20]. Administration of octreotide may lead to an improvement of subcutaneous lesions. Surgery is the recommended in case of pancreatic cancer and galdbladder disease. Endoscopic procedures such as pancreatic stenting or pseudocyst drainage have also been described. In recent cases aggressive treatments have been reported, such as necrosectomy [11], pseudocyst endoscopic drainage [16], triple bypass surgery [18]. To our knowledge this is the first report of PPP syndrome succesfully treated with a total pancreatectomy.

4. Conclusion

PPP syndrome is a rare syndrome and can be caused by benign or malign pancreatic disease; in both cases cutaneous and ostearticular manifestations can precede or follow the pancreatic manifestations, and can lead to serious chronic sequele. When indicated endoscopic and surgical treatment may solve efficacy underlying pancreatic disease and associated cutaneous and osteoarticular manifestations with survival improvement.

Conflicts of interest

None.

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No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

Ethical approval

This study was approved by the Ethics Committee of the Sanchinarro Hospital, San Pablo University.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Emilio Vicente and Yolanda Quijano proposed the study.

Valentina Ferri and Benedetto Ielpo performed research and wrote the first draft.

Hipolito Duran, Eduardo Diaz, Isabel Fabra, Riccardo Caruso collected and analyzed the data.

Carlos Plaza and Silvia Rodriguez Participated substantially in search and analysis of articles in literature.

Lina Garcia and Virginia Perez Participated substantially in revision the manuscript.

All authors contributed to the design and interpretation of the study and to further drafts.

Guarantor

Valentina Ferri is the guarantor of the study.

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