

## Case report

# Pancreatic panniculitis: a paraneoplastic syndrome preceding diagnosis of pancreatic acinar cell carcinoma

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Pancreatic panniculitis is a rare form of panniculitis which is associated with pancreatic disorders with acinar cell carcinoma which is in the first rank of all neoplastic causes. It presents with tender subcutaneous nodules, frequently on the legs, which are not specific and thus histopathological evaluation is mandatory for a definitive diagnosis. We report the case of a female patient who suffered from persistent multiple painful bumps on both legs which had been histologically diagnosed as pancreatic panniculitis. Later, further investigation revealed hidden pancreatic acinar cell carcinoma. This case illustrates that refractory cutaneous manifestations in the elderly may be a warning sign of a concealed serious condition. **Chiang Mai Medical Journal 2021;60(4):795-800. doi: 10.12982/CMUMEDJ.2021.65**

**Keywords:** Panniculitis; pancreatic panniculitis; pancreatic disorders; acinar cell carcinoma; diagnosis

## Introduction

Pancreatic panniculitis is a rare form of panniculitis which occurs in 0.3 to 3 percent of patients with pancreatic disorders (1). It is generally described as being associated with benign pancreatic diseases, e.g., acute or chronic pancreatitis, and less commonly with pancreatic pseudocyst, post-traumatic pancreatitis, pancreas divisum, pancreatic vascular fistulas as well as pancreatic carcinoma (1-7). Among the various types of pancreatic neoplasm, acinar cell carcinoma is a rare tumor but is highly associated with pancreatic panniculitis. Here, we report on a female patient who presented with pancreatic panniculitis which later resulted in a further diagnosis of pancreatic acinar cell carcinoma.

## Case report

An 82-year-old woman with a history of ische-

mic stroke, Alzheimer's disease, and squamous cell carcinoma on the chin, presented at our dermatology clinic with a 2-week history of multiple painful bumps on both legs. She was afebrile and in good general condition, without any associated complaints. She also denied any joint pain or swollen joints. Physical examination showed multiple discrete ill-defined erythematous subcutaneous nodules with moderate tenderness, varying in size from 2 to 5 centimeters, on both legs (Figure 1). The remainder of the physical examination results were unremarkable and arthritis was not observed. Initially, erythema nodosum was suspected and 1.2 milligrams per day of oral colchicine was administered for 2 weeks but her lesions persisted. As there was no clinical response to this treatment, a skin biopsy was performed. The histopathological examination found mixed

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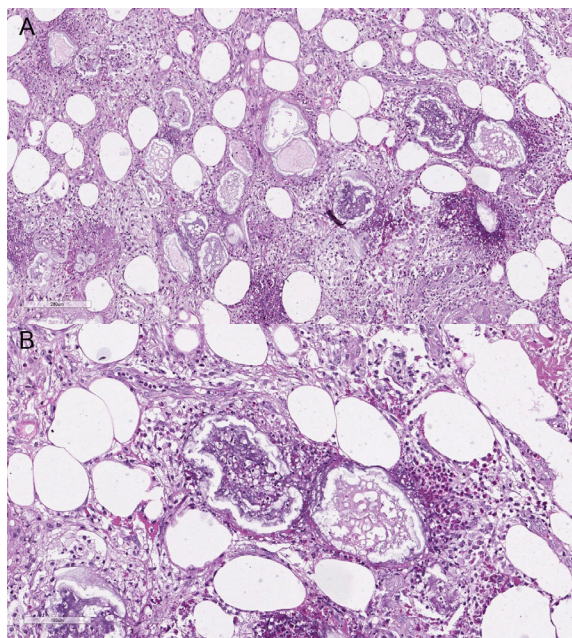
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**Figure 1.** Multiple discrete ill-defined erythematous subcutaneous nodules varying in size from 2 to 5 centimeters on both legs

septal and lobular panniculitis with infiltration of neutrophils and eosinophils. Focal fat necrosis, including ghost-like adipocytes with basophilic material deposits, was also observed (Figure 2). These findings are consistent with pancreatic panniculitis. Further investigation revealed normal serum amylase [68 U/L (normal range: 28-100 U/L)] but high serum lipase [10599 U/L (normal range: 13-60 U/L)]. A complete blood count showed mild eosinophilia (605 cells/cu.mm.) and a liver function test was unremarkable. Computed tomography of the whole abdomen showed an exophytic lobulated heterogenous enhancing mass arising from the tail of the pancreas, a condition which is compatible with pancreatic acinar cell carcinoma. The tumors also extended to the left adrenal gland, the left kidney, and the left ureter, causing obstructive uropathy of the left kidney. Thrombosis of the proximal left splenic vein extending to the main portal vein was also detected. Additionally, bilateral ovarian and multiple liver metastases were also revealed (Figure 3). The patient was referred to a gastroenterolo-



**Figure 2.** (A) Histopathology of the skin biopsy revealed mixed septal and lobular panniculitis with infiltration of neutrophils and eosinophils and focal fat necrosis, including ghost-like adipocytes with basophilic material deposits. (Original magnification x100). (B) Original magnification x200.

gist for evaluation and management. The extent and severity of the disease, however, rendered her unsuitable for definitive treatment. Following discussions with the patient and family, they opted for supportive end of life care.

## Discussion

The diagnosis of pancreatic panniculitis is both crucial and challenging since in 45 percent of cases of pancreatic panniculitis, the patient presents with cutaneous lesions before associated pancreatic disease is recognized.<sup>(1-2,6,8)</sup> In particular, pancreatic panniculitis is associated with pancreatic cancer and is usually the first sign of concealed malignancy. The tumor is usually advanced before cutaneous lesions appear.

Pancreatic panniculitis usually presents with ill-defined erythematous to red-brown edematous and tender nodules, arising singly or in crops frequently on the legs. These features do not clearly differentiate pancreatic panniculitis from other panniculitides, e.g., erythema nodosum



**Figure 3.** Acinar cell carcinoma of the pancreas with left adrenal gland, left kidney and left ureter involvement, and multiple liver metastasis

and erythema induratum. Nevertheless, lesional fluctuations and ulceration which discharge of an oily material may be present which are unique features of pancreatic panniculitis. Extracutaneous manifestations, including periarticular fat necrosis with concomitant arthritis and painful medullary fat necrosis in bone can also be observed (1,4,7).

In cases of non-specific clinical manifestations, a deep skin biopsy that includes subcutaneous tissue is mandatory for diagnosis. The lesion may begin as a septal panniculitis, but with progression, it takes on the appearance of a lobular or mixed septal/lobular process (8). Anucleate adipocytes with thickened, shadowy walls form the characteristic “ghost cells”. Saponification of fat by calcium salts results in deposition of granular or homogeneous basophilic materials (9). This “ghost cell” formation and saponification of fat distinguishes pancreatic panniculitis from other conditions (4,8).

Pancreatic acinar cell carcinoma, a rare tumor which represents only 1 percent of all pancreatic malignancies (2,6,10-11), is the most common cancer associated with pancreatic panniculitis

(2,3). The reason why acinar cell carcinoma frequently presents with this paraneoplastic phenomenon might be related to a high serum lipase level. The term “Lipase hypersecretion syndrome” has been coined for this condition which is characterized by subcutaneous fat necrosis and joint inflammation, and is often accompanied by eosinophilia. This infrequent condition occurs in up to 15 percent of cases of acinar cell carcinoma. The proposed pathogenesis is due to release of lipase into the blood stream by tumor cells, bringing on digestive action on distant non-digestive tissues: subcutaneous fat, bone, and joints. Most cases also have liver metastasis which may contain more enzymes, presumably due to the enzymes escaping the liver’s metabolism (the hepatic first pass phenomenon) (12).

In addition to the present case, we reviewed the literature of cases with pancreatic panniculitis associated with acinar cell carcinoma. In those reports, most of the patients were male in their 50s to 70s and nearly all had arthritis. Two-thirds of the cases presented with panniculitis preceding the diagnosis of malignancy, and the median serum lipase was 8168 IU/L (range, 810-327500). Eosinophilia, suggesting a poor prognosis, was declared in 5 of 6 patients, including our case. Unfortunately, when the diagnosis of pancreatic panniculitis was made, 12 of 15 patients also already had liver metastasis. The lesions were improved or resolved after cancer treatment in 6 cases, which supports the concept of pancreatic panniculitis as a paraneoplastic manifestation. As a result of the extent of the disease at presentation, nine cases were reported to have died from between a few months to 15 months following diagnosis. (Table 1)

## Conclusions

Based on the review of the literature and this case report, pancreatic panniculitis usually is the first sign of concealed acinar cell carcinoma, but it may also be a late manifestation as the majority of patients had already developed liver metastasis. Prognosis of these patients was poor. In cases of nonspecific cutaneous presentations, histopatho-

**Table 1.** Reported cases of pancreatic panniculitis associated with acinar cell carcinoma of the pancreas

| Year | First author            | Age at onset of pancreatic panniculitis/<br>Gender | Pancreatic panniculitis preceding the diagnosis of cancer/<br>Period preceding the diagnosis of cancer (months) | Arthritis | Eosinophilia | Serum lipase level (IU/L) | Distant metastasis at first diagnosis | Outcome                                                                                                  |
|------|-------------------------|----------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|-----------|--------------|---------------------------|---------------------------------------|----------------------------------------------------------------------------------------------------------|
| 1996 | Durden (13)             | 59/M                                               | No                                                                                                              | Yes       | No           | 54160                     | Liver                                 | Death                                                                                                    |
| 1999 | Heykarts (10)           | 61/F                                               | Yes/Several weeks                                                                                               | No        | N/A          | N/A                       | Liver                                 | Death 1 year after diagnosis                                                                             |
| 2004 | Beltraminelli (11)      | 60/M                                               | Yes/N/A                                                                                                         | Yes       | Yes          | 9276                      | Liver                                 | Death                                                                                                    |
| 2008 | Poelman (14)            | 74/M                                               | Yes/1                                                                                                           | No        | N/A          | 1840                      | No                                    | Death 2 months after diagnosis                                                                           |
| 2011 | Moro (15)               | 79/F                                               | No                                                                                                              | No        | N/A          | 1508                      | No                                    | Resolved after pancreatico-duodenectomy                                                                  |
| 2012 | Banfill (16)            | 69/M                                               | No                                                                                                              | Yes       | Yes          | N/A                       | Liver                                 | Resolved after metastasectomy                                                                            |
| 2014 | Arbeláez-Cortés (17)    | 68/M                                               | Yes/4                                                                                                           | Yes       | Yes          | 6951                      | Liver                                 | Death 4 months after diagnosis                                                                           |
| 2015 | Callata-Carhuapoma (18) | 36/F                                               | No                                                                                                              | Yes       | N/A          | 680                       | Liver, peritonuem                     | Initial improvement after chemotherapy but later disease progression and death 15 months after diagnosis |
| 2016 | Naeyaert (19)           | 59/M                                               | Yes/2                                                                                                           | Yes       | Yes          | 8168                      | Liver, right iliopsoas                | Resolved after chemotherapy                                                                              |
| 2017 | Yoshihiro (20)          | 50/M                                               | Yes/ N/A                                                                                                        | Yes       | N/A          | 327500                    | Liver, pelvis                         | Resolved after chemotherapy                                                                              |
| 2017 | Plier (21)              | 75/M                                               | No                                                                                                              | Yes       | N/A          | 16230                     | Liver                                 | Resolved after tumor radioembolization                                                                   |
| 2018 | Fernandez-Sartorio (4)  | 59/M                                               | Yes/4                                                                                                           | Yes       | N/A          | 7190                      | Liver                                 | Death 1 year after diagnosis                                                                             |
| 2018 | Rosa (22)               | 50/F                                               | Yes/1.5                                                                                                         | Yes       | N/A          | 24360                     | Liver                                 | Death a few months after diagnosis                                                                       |
| 2018 | Singh (23)              | 49/F                                               | No                                                                                                              | Yes       | N/A          | 810                       | Liver, pelvis                         | Cancer treatment ongoing                                                                                 |
| 2020 | Our case                | 82/F                                               | Yes/1                                                                                                           | No        | Yes          | 10599                     | Liver, ovary                          | Death 3 months after diagnosis                                                                           |

\*N/A: Not available

logic diagnosis is essential to making an early definitive diagnosis and to providing proper management, especially in elderly patients.

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## ชั้นไขมันใต้ผิวหนังอักเสบ: อาการแสดงที่เกิดขึ้นก่อนการวินิจฉัยโรคมะเร็งตับอ่อนชนิดอะซินาร์

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การอักเสบของชั้นไขมันที่เกี่ยวข้องกับโรคของตับอ่อนเป็นการอักเสบของชั้นไขมันที่พบน้อยโดยมะเร็งตับอ่อนชนิดอะซินาร์ เป็นสาเหตุที่พบได้บ่อยที่สุดในกลุ่มสาเหตุที่เกิดจากเนื้องอก รอยโรคมีลักษณะเป็นก้อนได้หนึ่ง พบได้บ่อยบริเวณขาซึ่ง รอยโรคไม่ได้จำเพาะต่อโรค จึงต้องอาศัยการตรวจทางพยาธิวิทยาเพื่อการวินิจฉัยโรค รายงานนี้แสดงผู้ป่วยหญิงที่มีการอักเสบของชั้นไขมันที่ขาและผลการตรวจเข้าได้กับการอักเสบของชั้นไขมันที่เกี่ยวข้องกับโรคของตับอ่อน ซึ่งนำไปสู่การ สืบค้นและวินิจฉัยมะเร็งตับอ่อนชนิดอะซินาร์ รายงานผู้ป่วยรายนี้แสดงให้เห็นถึงความสำคัญของอาการทางระบบผิวหนัง ในผู้สูงอายุว่าอาจเป็นสัญญาณเตือนของภาวะหรือโรคที่รุนแรงที่ซ่อนอยู่ **เชียงใหม่เวชสาร 2564;60(4):795-800.**

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