Skin Metastases as the Initial Presentation of Pancreatic Carcinoma

Metástasis cutánea por carcinoma pancreático como primera manifestación clínica

To the Editor:

Cancer of the pancreas is the fourth most common cause of cancer-related death in the United States.[1] In Spain, its incidence is around 7 cases per 100 000 population and there has been a considerable increase in recent decades.[2] The most important skin manifestations related to cancer of the pancreas are jaundice and pruritus caused by biliary tract obstruction. In some cases there may be an associated pancreatic panniculitis[3] and superficial thrombophlebitis migrans. Skin metastases are rare and, when they occur, they tend to appear in the umbilical region.[4] We present a case of skin metastasis due to adenocarcinoma of the head of the pancreas; a tumor on the scalp was the first manifestation of the disease.

A 53-year-old woman with no past personal or family history of interest was seen for a tumor on the scalp, which had appeared approximately 2 months earlier and had grown progressively. On examination of the skin, a round, erythematous-violaceous nodule of 2.5 cm diameter was observed in the left frontoparietal region. The nodule was ulcerated, of rubbery consistency, adherent to the deep planes, and was not tender (Figure 1). In addition, the patient presented marked jaundice that had developed 4 days earlier and that had led to her referral and admission to the gastroenterology department for evaluation.

The most relevant findings in the blood tests were anemia (hemoglobin, 9.7 g/dL), leucocytosis (15 900/μL), thrombocytosis (513 000 platelets/μL), elevated total bilirubin (19.48 mg/dL [normal value, 0.1–0.2 mg/dL]) and direct bilirubin (17.66 mg/d [normal value, 0.05–0.25 mg/dL]), and increased levels of the following enzymes: amylase (304 U/L [normal value, 28–100 U/L]), lipase (1189 U/L [normal value, 17–60 U/L]), lactate dehydrogenase (841 U/L [normal value, 230–460 U/L]), alkaline phosphatase (863 U/L [normal value, 35–104 U/L]), aspartate aminotransferase (185 U/L [normal value, 1–31 U/L]), alanine aminotransferase (129 U/L [normal value, 1–31 U/L]), and γ-glutamyltransferase (983 U/L [normal value, 5–39 U/L]).

The chest radiograph was normal. Abdominal computed tomography revealed a mass in the head of the pancreas of 49×40×61 mm, with marked dilatation of the intrahepatic and extrahepatic biliary tract and of the gallbladder. There were also focal lesions in the liver, kidney, and bone characteristic of metastases, and multiple enlarged lymph nodes in the mesenteric and pancreatic regions.

Biopsies were taken of liver and of the skin tumor. A neoplastic epithelial growth with nests and tubular structures was observed in the liver biopsy. It was formed of a cylindric or cuboidal epithelium with irregular nuclei, prominent nucleoli, and marked mitotic activity. This growth was positive for cytokeratins 8 and 19 and for carcinoembryonic antigen in isolated cells, and was negative for chromogranin, synaptophysin, and enolase. The Ki67 index was high, at around 40%. The biopsy was reported as hepatic metastasis of pancreatic adenocarcinoma.

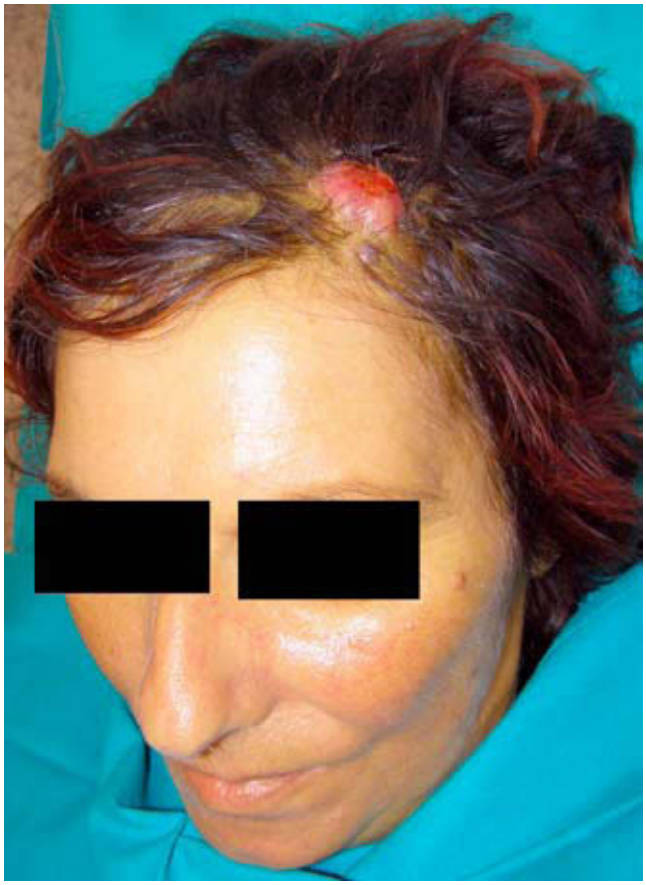

Figure 1 Ulcerated, erythematous-violaceous tumor situated in the left frontoparietal region.

The skin biopsy showed malignant neoplastic cells in the dermis that tended to form poorly defined glandular structures (Figure 2). These cells had little cytoplasm and large, irregular nuclei with occasional mitotic figures. A degree of desmoplasia and fibrous proliferation of the surrounding tissue could be seen. Immunohistochemical analysis was positive for cancer antigen 125 (in some cells) and cytokeratins 8 and 19, and was negative for chromogranin and synaptophysin. The dermatologic pathology diagnosis was of skin metastasis due to poorly differentiated adenocarcinoma.

The final diagnosis was of adenocarcinoma of pancreas with liver, renal, bone, and skin metastases. The patient was referred to oncology for palliative treatment and died a month later.

Skin metastases represent approximately 10% of all tumor metastases, and breast cancer and melanoma are the most common origins.[5] In a recent study in Taiwan by Chu-Sung Hu et al,[6] skin metastases were found in 124 cases of 12 146 cancer patients (1.02%); once again there was a predominance of carcinoma of the breast as the most common cause, followed by cancers of the lung and oral

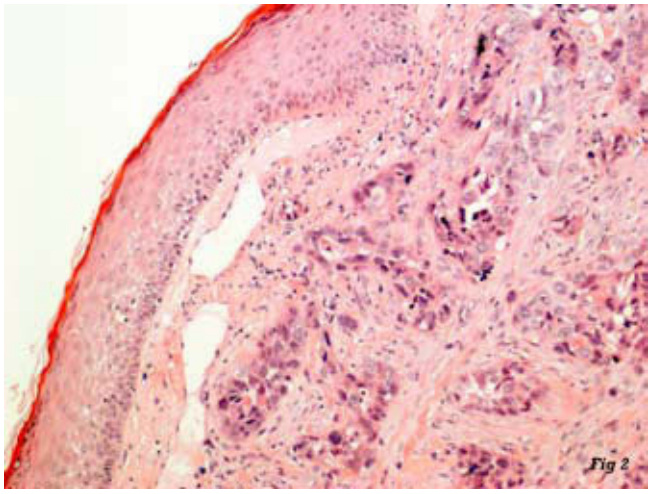

Figure 2 There was a proliferation of malignant neoplastic cells that tended to form poorly defined glandular structures (hematoxylin-eosin, ×100).

mucosa. Skin metastases tend to appear as late phenomena in the natural history of tumors, but they can occasionally be the presenting feature[7] or the first sign of recurrence.[8]

Skin metastases due to carcinoma of the pancreas are rare. Lookingbill et al[5] found 2 cases among 420 patients with skin metastases in a series of 4020 patients with metastatic disease.

The most common site of skin metastases due to carcinoma of the pancreas is the umbilicus, in a form known as Sister Mary Joseph nodule.[4] Yendluri et al[9] reviewed the English and Japanese language medical literature of the past 90 years and identified 57 cases of Sister Mary Joseph nodule from pancreatic tumors. In that review, it was significant that the majority of primary tumors (91%) were located in the body and tail of the pancreas, and not in the head as might be expected, given that between 70% and 80% of adenocarcinomas of the pancreas arise in the head.

The appearance of skin metastases at other sites not in the area of the umbilicus, as in the patient we report, is less common. Abdel-Hafez[10] published a new case of skin metastasis of pancreatic origin in the form of an indurated plaque in the neck and, to explore the subject in greater detail, carried out a review of the medical literature on skin metastases away from the umbilical region. He found 17 cases (15 men and 2 women) and the site varied, though there was a predominance on the skin of the head and neck.

Skin metastases can occasionally constitute the first sign for the diagnosis of pancreatic cancer. Miyahara et al[4] published 5 cases of skin metastases derived from cancer of the pancreas and reviewed a further 17. In 11 of those patients, the skin lesions were the first manifestation of the tumor, in 9 they were discovered during physical examination, and in 2 after the surgical intervention.

In Spain, Ruiz de Erenchun Lasa et al[11] published 2 cases of skin metastases from adenocarcinoma of the pancreas. In the first of those cases, the skin metastases were situated on the face and were the first sign of the tumor, whereas in the second case, the lesions were situated in the umbilical region and constituted an additional clinical finding in a patient with obstructive jaundice.

Skin metastases due to carcinoma of the pancreas are an indicator of poor prognosis. In the review by Miyahara et al,[4] the mean survival was 5.8 months, with a range of 1 to 22 months, and Schoenlaud et al[12] found a mean survival of 3.3 months in 2 cases of skin metastases due to cancer of the pancreas drawn from a series of 200 patients with skin metastases.

We report a new case of skin metastasis on the scalp due to adenocarcinoma of the pancreas. This case has the peculiarity that the skin metastasis was the first visible sign of the tumor. We would like to draw attention to the importance of evaluation of the skin in the examination of patients with a suspected malignant tumor. Rapid visualization of skin lesions and the easy access for histological study can guide and speed up the request process for further additional tests.

References

1. Postier RG. The challenge of pancreatic cancer. Am J Surg. 2003; 186:579-82.
2. Hidalgo Pascual M, Ferrero Herrero E, Castillo Fé MJ, Guadarrama González FJ, Peláez Torres P, Botella Ballesteros F. Cáncer de páncreas. Epidemiología y diagnóstico. Rev Esp Enferm Dig. 2004; 96:714-22.
3. Segurado Rodríguez A, Guerra Tapia A, Jaén Olasolo P, Cuevas Santos J. Paniculitis pancreática: estudio de 12 casos y valoración comparativa de sus caracteres epidemiológicos, clínicos, histopatológicos y terapéuticos. Actas Dermosifiliogr. 1999; 90:227-34.
4. Miyahara M, Hamanaka Y, Kawabata A, Sato Y, Tanaka A, Yamamoto A, et-al. Cutaneous metastases from pancreatic cancer. Int J Pancreatol. 1996; 20:127-30.
5. Lookingbill DP, Spangler N, Helm KF. Cutaneous metastases in patients with metastatic carcinoma: A retrospective study of 4020 patients. J Am Acad Dermatol. 1993; 29:228-36.
6. Chu-Sung Hu S, Chen GS, Wu CS, Chai CY, Chen WT, Lan CC. Rates of cutaneous metastases from different internal malignancies: Experience from a Taiwanese medical center. J Am Acad Dermatol. 2009; 60:379-87.
7. Nicolas-Sánchez FJ, Garreta-Messegue J, Fernández-Cabrera L, Sarrat-Nuevo RM, Nicolás-Sanchez ME, Cabau-Rubies J. Metástasis cutáneas generalizadas como forma de presentación de un adenocarcinoma gástrico. Actas Dermosifiliogr. 2007; 98:215-6.
8. Marcoval J, Gallego MI, Moreno A. Metástasis cutánea inflamatoria como primer signo de recidiva de carcinoma escamoso de pulmón. Actas Dermosifiliogr. 2008; 99:157-9.
9. Yendluri V, Centeno B, Springett GM. Pancreatic cancer presenting as sister Mary Joseph's nodule. Case report and update of the literature. Pancreas. 2007; 34:161-4.
10. Abdel-Hafez HZ. Cutaneous pancreatic metastasis: A case report and review of literature. Dermatol Surg. 2008; 34:1580-3.
11. Ruiz de Erenchum Lasa F, Vázquez Doval FJ, Sola Casas MA, De Alava E, Quintanilla Gutierrez E. Metástasis cutáneas de adenocarcinoma de páncreas. Estudio de dos casos. Actas Dermosifliliogr. 1991; 82:455-8.
12. Schoenlaub P, Sarraux A, Grosshans E, Heid E, Cribier B. Survie après métastases cutanées: étude de 200 cas. Ann Dermatol Venereol. 2001; 128:1310-5.

S. Gómez-Diez,[a,*] B. García-García,[a]
M.S. Fernández-García,[b] and N. Pérez-Oliva[a]

[a]*Servicio de Dermatología, Hospital Universitario Central de Asturias, Facultad de Medicina, Oviedo, Spain*

[b]*Servicio de Anatomía Patológica, Hospital Universitario Central de Asturias, Facultad de Medicina, Oviedo, Spain*

*Corresponding author.
E-mail address: sangodi@telefonica.net
(S. Gómez-Diez).

Melanomas and Basal Cell Carcinomas in a Patient With Parkinson Disease

Melanomas y carcinomas basocelulares en un paciente con enfermedad de parkinson

to the Editor:

Recent studies have detected an increased risk of melanoma in patients with Parkinson disease. The majority of these studies agree that there is a 2-fold increase in the risk of melanoma in patients with idiopathic Parkinson disease, and found a 20% increase in the risk of nonmelanoma skin cancer,[1,2] even in patients who had still not developed the disease, that is, they found a positive association between Parkinson disease and melanoma.[3] A common etiological factor could exist that leads to the destruction of the substantia nigra and the malignant transformation of skin melanocytes.

It is believed that the genetic determinants of idiopathic Parkinson disease increase susceptibility of the skin to UV radiation.[1]

Based on the existence of a common metabolic pathway for the synthesis of melanin and dopamine, it has been suggested in the medical literature that treatment with levodopa in patients with Parkinson disease increases the risk of melanoma and nonmelanoma skin cancer.[1-7]

Levodopa is an amino acid that is not usually present in cell proteins. However, in vitro studies have shown that it is incorporated into cell lines derived from different melanomas.[3]

We present the case of a 42-year-old man, with a 10-year history of Parkinson disease treated with levodopa. In May 2005, he underwent excision of a melanoma on the left flank (Figure 1); histologically the tumor was Clark level II and had a Breslow depth of 0.5 mm, with no ulceration and no areas of regression. The study of extension was negative. The patient received no coadjuvant treatment.

In February 2008, the patient was referred from the oncology department for the recent appearance of multiple squamous erythematous plaques with pearly borders on the back and on the extensor surfaces of both arms (Figure 2). On physical examination, the patient also presented an atypical pigmented lesion on the right flank. Histological study of the lesions on the back confirmed that they were superficial basal cell carcinomas. The pigmented lesion was reported as melanoma, Clark level V and with a Breslow depth of 3.8 mm.

The second melanoma was surgically excised. The study of extension was negative. Photodynamic therapy was given for the basal cell carcinomas, with a good outcome.

The suspicion that levodopa could increase the risk of melanoma has been suggested in a number of clinical trials

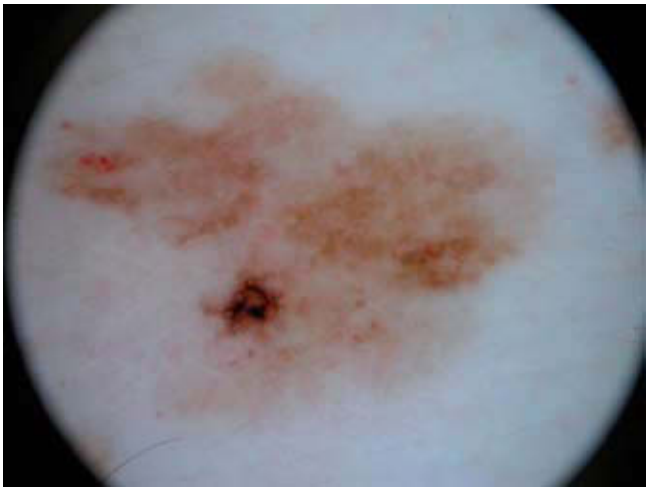

Figure 1 Dermoscopic image of the first melanoma.

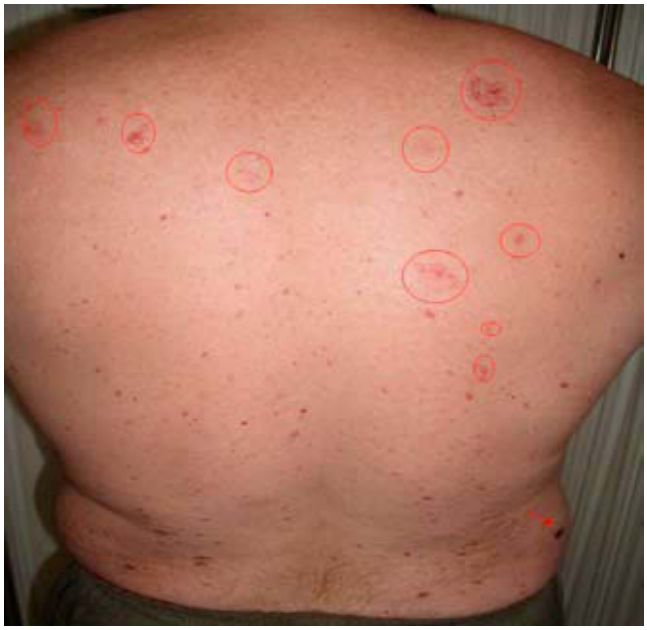

Figure 2 Multiple basal cell carcinomas on the back (circles). Melanoma on the right flank (arrow).