Eruptive Disseminated Porokeratosis Associated With Internal Malignancies: A Case Report

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Porokeratosis is a chronic skin disorder characterized by the presence of patches with elevated, thick, keratotic borders histologically featuring cornoid lamella. While porokeratosis usually is clinically defined by a slow onset, an eruptive variant has been reported. We report a 77-year-old woman affected by pancreatic carcinoma with eruptive disseminated porokeratosis (EDP). We reviewed published cases of EDP developing suddenly or within a few months and found a total of 16 patients, 6 with internal malignancies of the liver or gastrointestinal tract. These findings suggest that patients with EDP should be investigated for the presence of internal malignancies.

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Porokeratosis is a clonal disorder of keratinocytes characterized by atrophic plaques surrounded by ridgelike borders with the histologic feature of cornoid lamella. Five clinical variants of porokeratosis have been described: Mibelli disease, disseminated superficial (actinic), porokeratosis palmaris et plantaris disseminata, linear, and punctate porokeratosis.[1] Squamous cell carcinoma may arise on porokeratosis lesions.[2,3] In some patients, disseminated porokeratosis is observed following immunosuppression,[4,5] particularly in patients who have had renal transplants.[6-10] Eruptive disseminated porokeratosis (EDP) is a more recently described form characterized by a sudden onset of numerous small monomorphic pruritic lesions on the trunk and extremities.[11-20] The development of EDP occurs in a time frame varying from a few days to a few months. It has been described in patients with cancer, particularly of the liver or digestive tract.[21-23] Sometimes skin lesions precede the diagnosis of cancer and spontaneously regress after cancer therapy, which implies that EDP may be a paraneoplastic syndrome.[21] We describe a case of EDP associated with pancreatic carcinoma in a hepatitis C virus (HCV) carrier and review the literature on other cases of EDP.

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Case Report

A 77-year-old woman presented with monomorphic, hyperpigmented, patch, round lesions with peripheral keratotic rings and atrophic centers of 2 weeks' duration. The lesions initially appeared on the abdomen and rapidly spread to the legs and arms (Figure 1), predominantly at the extensor surfaces, sparing the palms, soles, and face. Most of the lesions were asymptomatic and some were accompanied by pruritus or stinging. The patient had a 2-month history of pain radiating from the epigastrium to the back, weight loss, and asthenia. Her symptoms rapidly worsened with increasing pain and development of jaundice, as well as pruritus, ascites, and edema of the lower extremities. The patient was a chronic HCV carrier (diagnosed at the age of 52 years) with serum alanine aminotransferase levels persistently within reference range. There was no other noteworthy medical or surgical history. Her mother died of pancreatic carcinoma. Biopsy of a skin lesion showed mild hyperkeratosis with a flattened crest network in the center (Figure 2). At the periphery, typical cornoid lamella with dyskeratotic basal keratinocytes was found. A moderate lymphohistiocytic infiltrate was present in the dermis. Computed tomography of the abdomen and pelvis identified a tumor at the tail

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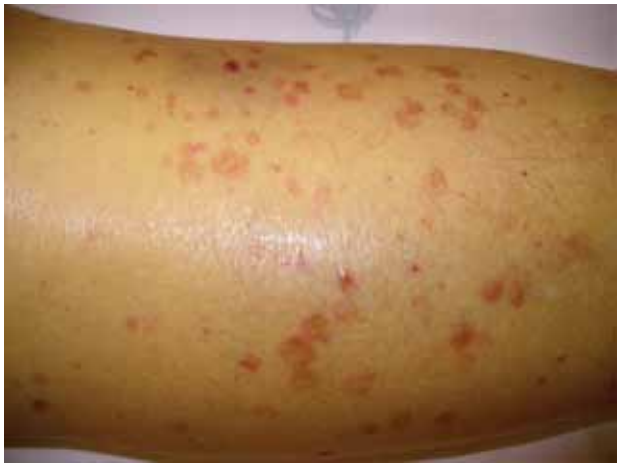

Figure 1. Eruptive disseminated porokeratotic lesions on the leg.

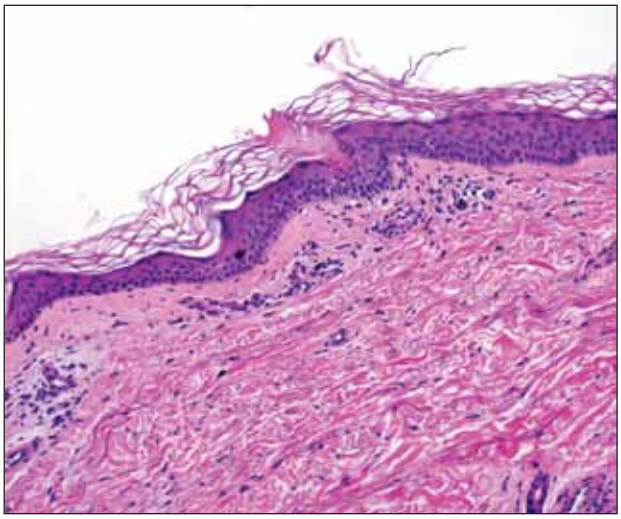

Figure 2. A biopsy specimen taken from the border of a porokeratotic lesion showed moderate epidermal atrophy in the center and the typical cornoid lamella with dyskeratotic basal keratinocytes at the periphery. A moderate lymphohistiocytic infiltrate was present in the dermis (H&E, original magnification ×100).

of the pancreas (4.8×2.3 cm). Concomitantly, many nodular metastases were visualized in the liver, along with portal vein thrombosis. Liver biopsy confirmed metastases from pancreatic carcinoma. The patient died 2 weeks later of hepatic failure.

Comment

Porokeratosis lesions are believed to result from the peripheral expansion of an abnormal mutant clone of epidermal keratinocytes, which may be triggered by UV light, trauma, infection, or immunosuppression.[4,5] Therefore, porokeratosis has been observed in patients with organ transplants, cancer, and chronic inflammatory diseases treated with immunosuppressants. Eruptive disseminated porokeratosis is a unique variant of porokeratosis with disseminated lesions appearing within a few weeks. Some of the patients with EDP also have been affected by systemic diseases, and interestingly enough, by internal malignancies.[21-23] We present a case of EDP in a patient affected by pancreatic carcinoma.

The Table presents the characteristics of 16 patients with EDP as described in the literature. The mean age was 67 years and sex was almost equally distributed (7 females and 9 males); no familial cases of porokeratosis were reported. Twelve patients developed EDP in a rapidly spreading mode, ranging from a few days to 2 weeks. Less than one-third of patients had preexisting porokeratosis. Moreover, it is of great interest that 6 patients with EDP were affected by a liver or gastrointestinal tract malignancy. It is important to note that these 6 patients did not have preexisting porokeratosis. The diagnosis of porokeratosis preceded the cancer diagnosis by a few weeks in 3 of 6 patients. Therefore, the sudden onset of disseminated porokeratosis lesions should draw attention to the presence of an internal malignancy. Of 16 patients, 4 were HCV carriers and also had liver or pancreatic carcinoma.

A possible link between porokeratosis and tumors may be cancer-associated immunosuppression. Another possibility is the close relationship between HCV core protein and expression of the protein p53, which is among the more important tumor suppressor gene products. Hepatitis C virus is in fact involved in the induction of p53 mutations during the molecular pathogenesis of hepatocellular carcinoma.[24] The tumor suppressor protein p53 serves as an important gatekeeper and effector of the cell cycle. Its main functions include induction of cell cycle arrest and activation of apoptotic cell death.[25] Increased expression of the p53 tumor suppressor gene, abnormal DNA ploidy, and premature apoptosis in keratinocytes under or adjacent to cornoid lamella has been reported to be associated with the molecular pathogenesis of porokeratosis.[21,25-27] Gastrointestinal tract tumors frequently are associated with increased BCL2 expression, K-*ras* mutation, and impairment of the p53 pathway, resulting in the accumulation of protein p53 with apoptosis inhibition after a nonreparable genotoxic event and the survival of only mutated cells.[28]

Conclusion

Our case and other published cases suggest that a sudden onset of EDP should alert physicians to the possible presence of an internal malignancy. In these instances, patients should be subjected to the relevant

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Characteristics of Reported Cases of Eruptive Disseminated Porokeratosis

Patient No.	Age, y	Sex	Time of Onset	Preexisting Porokeratosis	Associated Malignancy	Other Diseases	Onset of Porokeratosis[a]	HCV	Reference
1	71	F	Sudden	+	–	–	N/A	–	Kanzaki et al[11]
2	60	F	2 wk	+	–	CVA	After	–	Kanzaki et al[11]
3	75	M	Sudden	+	–	–	After	–	Kanzaki et al[11]
4	69	M	Sudden	–	–	–	N/A	–	Stork and Kodetova[12]
5	70	M	2 wk	–	–	MDS	After	–	Levin and Heymann[20]
6	57	F	2 wk	–	–	Herpes simplex	Concomitant	–	Jang et al[13]
7	53	F	Sudden	–	–	Sore throat	After	–	Jang et al[13]
8	74	M	Sudden	+	–	Diabetes mellitus	After	–	Makino et al[14]
9	82	M	6 mo	+	–	–	N/A	–	Kanekura and Yoshii[15]
10	56	M	2 wk	–	–	Renal transplant	After	–	Knoell et al[9]
11	67	M	1 mo	–	Hepatic[b]	–	Before	+	Kono et al[21]
12	62	M	3 mo	–	Hepatic[b]	–	Before	+	Kono et al[21]
13	58	F	2 mo	–	Hepatic[b]	–	Before	+	Kono et al[21]
14	73	F	Sudden	–	Hepatic[c]	–	After	–	Lee et al[22]
15	73	M	Sudden	–	Colon[d]	Skin tumors	After	–	Takata et al[23]
16	77	F	2 wk	–	Pancreatic	–	After	+	Present case

Abbreviations: HCV, hepatitis C virus; F, female; +, positive; –, negative; N/A, not available; CVA, cerebrovascular accident; M, male; MDS, myelodysplastic syndrome.

[a]Onset of porokeratosis in relation to the cancer diagnosis.

[b]Hepatocellular carcinoma.

[c]Cholangiocarcinoma.

[d]Adenocarcinoma of the descending colon without adenomatous polyps.

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screening tests, particularly for gastrointestinal tract, liver, and pancreatic cancer.

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