Disseminated superficial porokeratosis in a patient with cholangiocarcinoma: a paraneoplastic manifestation?*

Poroceratose superficial disseminada num doente com colangiocarcinoma: manifestação paraneoplásica?

Tiago Torres [1]
Glória Cunha Velho [2]
Manuela Selores [3]

Abstract: Porokeratosis refers to a group of hereditary or acquired disorders of epidermal keratinization and is characterized histologically by the presence of a cornoid lamella. The clinical variant referred to as disseminated superficial porokeratosis has been described in the literature in association with immunosuppressive conditions that include organ transplant, infections and immunosuppressive treatments. The association of disseminated superficial porokeratosis with solid organ malignancies has seldom been described, only 5 such cases having been published. The present report refers to a patient with lesions of disseminated superficial porokeratosis of sudden onset shortly before diagnosis of a cholangiocarcinoma.
Keywords: Cholangiocarcinoma; Genes p53; Porokeratosis

Resumo: As poroceratoses compreendem um grupo de doenças da queratinização epidérmica, hereditárias ou adquiridas, caracterizadas histologicamente pela presença de lamela cornoide. A variante clínica designada por poroceratose superficial disseminada tem sido descrita na literatura, associada a estados de imunossupressão, como transplantação de órgãos, terapêuticas imunossupressoras e infecções. A sua associação a neoplasias sólidas foi raramente descrita na literatura, estando publicados apenas 5 casos. Descrevemos o caso clínico de um paciente que desenvolveu, subitamente, lesões de poroceratose superficial disseminada, concomitantemente ao diagnóstico de um colangiocarcinoma.
Palavras-chave: Colangiocarcinoma, Genes p53; Poroceratose

INTRODUCTION

Porokeratoses refer to a group of hereditary or acquired diseases characterized by abnormal epidermal keratinization. They present clinically as annular lesions with hyperkeratinized borders and an atrophic center; histologically, they are characterized by the presence of a cornoid lamella.

Six clinical variants have been described[1]: classic porokeratosis of Mibelli; 2) disseminated superficial porokeratosis; 3) disseminated superficial actinic porokeratosis; 4) porokeratosis palmaris et plantaris disseminata; 5) linear porokeratosis; and 6) punctate porokeratosis.

Disseminated superficial porokeratosis (DSP) has been described in association with immunosuppressive states such as organ transplant, immunosuppressive treatments, infections and hematopoietic malignancies. [2,3] Nevertheless, the association of this condition with solid organ tumors is rare. To the best of our knowledge, only five such cases have been described to this date in the literature. [4-6]

This report describes a patient who suddenly developed lesions of disseminated superficial porokeratosis shortly before being diagnosed with a cholangiocarcinoma. The authors speculate that this may represent a paraneoplastic manifestation.

Received on March 3th, 2009.
Approved by the Peer Review Board and accepted for publication on March 3th, 2009.
* Study carried out at the Dermatology Clinic, Centro Hospitalar do Porto, Santo Antonio Hospital, Porto, Portugal.
Conflict of interest: None / *Conflito de interesse: Nenhum*
Financial funding: None / *Suporte financeiro: Nenhum*

[1] Medical Intern in Dermatovenereology, Dermatology Clinic, Centro Hospitalar do Porto, Santo Antonio Hospital, Porto, Portugal.
[2] Associate Professor of Dermatology, School of Biomedicine, Porto University; Assistant Physician; Dermatology Clinic, Centro Hospitalar do Porto, Santo Antonio Hospital, Porto, Portugal.
[3] Professor of Dermatology, Department Head, School of Biomedicine, Porto University; Director, Dermatology Clinic, Centro Hospitalar do Porto, Santo Antonio Hospital, Porto, Portugal.

CASE REPORT

A male patient, 80 years of age, with a history of ischemic cardiopathy and essential hypertension, was hospitalized due to an advanced stage cholangiocarcinoma, diagnosed two weeks previously, at which time the patient developed abdominal pain and jaundice.

During hospitalization, he was referred to the Dermatology Department for evaluation of mildly pruriginous skin lesions disseminated all over his body, which had appeared abruptly, approximately one month prior to the appearance of the signs and symptoms related to the tumor.

At physical examination, multiple papules were found, in addition to round, well-defined brownish erythematous plaques with slightly raised, hyperkeratotic borders and atrophic centers, involving sun-exposed and non-sun-exposed areas of the skin (Figure 1).

Histopathology of the keratotic border of the lesion showed the presence of a cornoid lamella and dyskeratotic keratinocytes, compatible with a diagnosis of porokeratosis (Figure 2).

Due to the advanced stage of the neoplasia, only palliative treatment was given, consisting of percutaneous transhepatic biliary drainage. The dermatosis was observed to progress over the following two months until the patient's death.

DISCUSSION

The development of porokeratosis lesions is believed to depend on the interaction between genetic and exogenous factors, resulting in peripheral expansion of a mutant clone of keratinocytes.

Disseminated superficial porokeratosis has been described in association with immunosuppressive states such as organ transplant, immunosuppressive therapies, infections and hematopoietic malignancies [2,3] that appear to function as triggering factors in genetically susceptible patients.

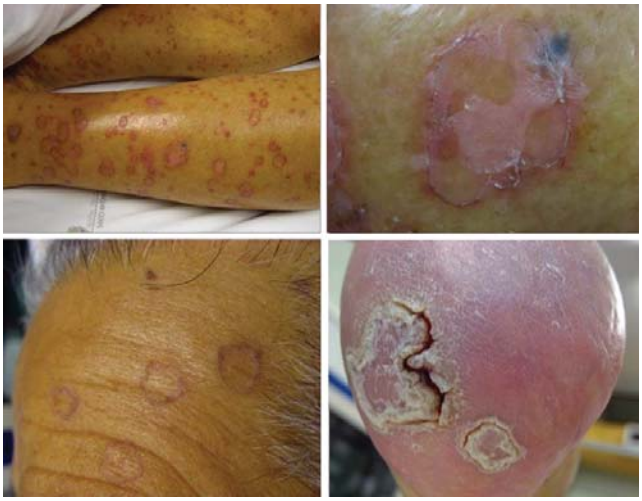

Figure 1: Lesions of disseminated superficial porokeratosis

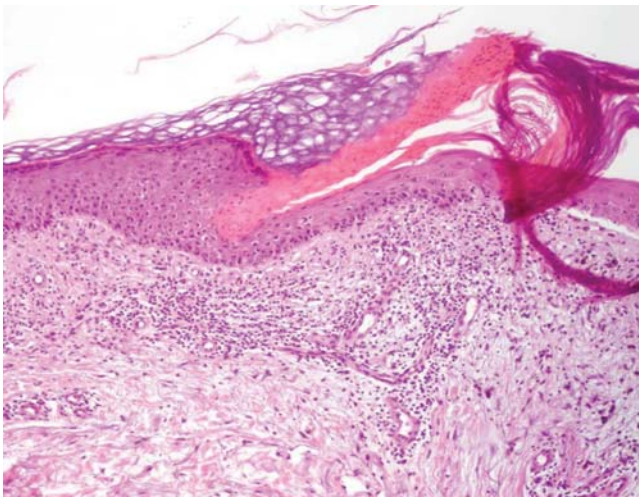

Figure 2: Histopathology (hematoxylin and eosin; magnification 10x): cornoid lamella and dyskeratotic keratinocytes

The sudden onset of DSP lesions during the development of solid organ malignancies is rare. To the best of our knowledge, only five such cases have been reported: three in patients with hepatocellular carcinomas, [4] one in a patient with a cholangiocarcinoma [5] and another in a patient with an ovarian adenocarcinoma. [6] In the latter case, the course of the DSP was found to run parallel to that of the tumor, resolution of the skin lesions occurring after surgical treatment of the subjacent tumor. In the other cases, the dermatosis progressed in parallel with the cancer.

The p53 gene, principally its overexpression, has been implicated in the pathogenesis of various solid organ tumors. [7,8] Recent studies have highlighted the importance of this gene in the oncogenesis of hepatocellular carcinoma, cholangiocarcinoma and ovarian adenocarcinoma. [9-11] Overexpression of the p53 gene in keratinocytes above and adjacent to the cornoid lamella in porokeratosis lesions has also been demonstrated, resulting in early apoptosis and abnormal differentiation of these cells. This finding suggests its involvement in the pathogenesis of these lesions. [12-14]

Therefore, the immunological abnormalities and cytotoxic alterations induced by the tumor are believed to affect the biology of keratinocytes, leading to the development and proliferation of a mutant clone and giving rise to porokeratosis lesions in genetically susceptible patients.

The apparently temporal relationship between the onset of the DSP lesions and the development of the cholangiocarcinoma, as seen in this clinical case,

in addition to the known role of the p53 gene (particularly its overexpression) in the oncogenesis and pathogenesis of cholangiocarcinomas, the demonstration of p53 gene overexpression in keratinocytes of porokeratosis lesions and the absence of any other triggering factors, suggest that this skin disease may be paraneoplastic.

The authors would, therefore, recommend that, in a patient with DSP of sudden onset and in the absence of any other triggering factor, a subjacent solid organ tumor, namely carcinomas in which the p53 gene is pathogenically important, should be suspected. ❑

REFERENCES

1. O'Regan GM, Irvine AD. Porokeratosis. In: Wolff K, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffel DJ, editors. Fitzpatrick's Dermatology in General Medicine. New York: McGraw-Hill; 2008. p. 442-6.
2. Bencini PL, Tarantino A, Grimalt R, Ponticelli C, Caputo R. Porokeratosis and immunosuppression. Br J Dermatol. 1995;132:74-8.
3. Kanitakis J, Euvrard S, Faure M, Claudy A. Porokeratosis and immunosuppression. Eur J Dermatol. 1998;8:459-65.
4. Kono T, Kobayashi H, Ishii M, Nishiguchi S, Taniguchi S. Synchronous development of disseminated superficial porokeratosis and hepatitis C-virus related hepatocellular carcinoma. J Am Acad Dermatol. 2000;43:966-8.
5. Lee HW, Oh SH, Choi JC, Chang SE, Lee MW, Choi JH, et al. Disseminated superficial porokeratosis in a patient with cholangiocarcinoma. J Am Acad Dermatol. 2006;54:856-8.
6. Cannavó SP, Borgia F, Adamo B, Guarneri B. Simultaneous development and parallel course of disseminated superficial porokeratosis and ovarian cancer: Coincidental association or true paraneoplastic syndrome? J Am Acad Dermatol. 2008;58:657-60.
7. Diez M, Medrano MJ, Gutierrez A, Lopez A, Muguerza JM, Hernandez P, et al. P53 protein expression in gastric adenocarcinoma. Negative predictor of survival after postoperative adjuvant chemotherapy. Anticancer Res. 2000;20:3929-33.
8. de Roos MA, de Bock GH, de Vries J, van der Vegt B, Wesseling J. P53 overexpression is a predictor of local recurrence after treatment for both in situ and invasive ductal carcinoma of breast. J Surg Res. 2007;140:109-14.
9. Lu W, Lo SY, Chen M, Wu K, Fung YK, Ou JH. Activation of p53 tumor suppressor by hepatitis C virus core protein. Virology. 1999;264:134-41.
10. Okuda K, Nakanuma Y, Miyazaki M. Cholangiocarcinoma, recent progress, part 2: molecular pathology and treatment. J Gastroenterol Hepatol. 2002;17:1056-63.
11. Lancaster JM, Dressman HK, Clarkes JP, Sayer RA, Martino MA, Cragun JM, et al. Identification of genes associated with ovarian cancer metastasis using microarray expression analysis. Int J Gynecol Cancer. 2006;16:1733-45.
12. Magee JW, McCalmont TH, LeBoit PE. Overexpression of p53 tumor suppressor protein in porokeratosis. Arch Dermatol. 1994;130:187-90.
13. Arranz-Salas I, Sanz-Trelles A, Ojeda DB. p53 alterations in porokeratosis. J Cutan Pathol. 2003;30:455-8.
14. Shen CS, Tabata K, Matsuki M, Goto T, Yokochi T, Yamanishi K. Premature apoptosis of keratinocytes and the dysregulation of keratinization in porokeratosis. Br J Dermatol. 2002;147:498-502.

MAILING ADDRESS / ENDEREÇO PARA CORRESPONDÊNCIA:
Tiago Torres
Serviço de Dermatologia do Centro Hospitalar do Porto - Hospital de Santo António, EPE
Edifício das consultas externas, Ex CICAP,
Rua: D. Manuel II. 4100, Porto - Portugal.
Tel.fax: - 22 6097429 - 22 6097429
E-mail: tiagotorres2002@hotmail.com

How to cite this article/*Como citar este artigo*: Torres T, Machado S, Velho GC. Disseminated superficial porokeratosis in a patient with cholangiocarcinoma - a paraneoplastic manifestation? An Bras Dermatol. 2010;85(2):229-31.