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

Poroceratose superficial disseminada num doente com colangiocarcinoma: manifestação paraneoplásica?

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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 described1: 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. 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.

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.
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 that appear to function as triggering factors in genetically susceptible patients.

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, one in a patient with a cholangiocarcinoma and another in a patient with an ovarian adenocarcinoma. 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. Recent studies have highlighted the importance of this gene in the oncogenesis of hepatocellular carcinoma, cholangiocarcinoma and ovarian adenocarcinoma. 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.

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


