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Case Report

Vesiculo-bullous Darier disease late onset in association with polycythemia vera

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ABSTRACT

Vesiculo-bullous lesions as well as the late onset are extremely rare features of Darier disease (DD) making positive diagnosis more difficult. Its association with polycythemia vera prompts to look for signs suggestive of malignant hematological transformation. We report a case of a 62-year-old patient, followed in internal medicine since the age of 58 for polycythemia vera. She presented for pruriginous vesiculo-bullous dermatosis evolving for 4 years. On clinical examination, papulo-vesicular plaques were found involving all the folds: inguinal, axillary, inter-gluteal, neck and body with palmo-plantar blisters and pustules. Examination of the toe nails showed alternating red and white longitudinal bands. Abdominal examination showed moderate splenomegaly. Skin biopsy revealed focal acantholysis with supra-basal clefts, dyskeratosis with the presence of round bodies and grains compatible with Darier's disease. A paraneoplastic assessment was made including a thoraco-abdomino-pelvic CT scan, a breast ultrasound and mammography with cervico-vaginal smear, a CT scan of the cavum and a pancreatic MRI, which did not show any progressive malignant process. The patient was put on oral retinoids at a rate of 0.5 mg/kg per day and topical calcipotriol associated with bloodletting to reduce the hematocrit level. The evolution was marked by clinical improvement. The patient was followed in the hematology department and showed no acute leukemia or myelofibrosis or other neoplasms after a 2-year follow-up. We report a case of late DD in a woman followed for polycythemia vera, characterized by a rare vesiculo-bullous presentation and whose causal link remains to be determined.

Keywords: Vesiculo-bullous, Darier, Polycythemia vera, Leukemia

INTRODUCTION

Vesiculo-bullous lesions and late onset are extremely rare features of DD making positive diagnosis more difficult. Its association with polycythemia vera, is until now not described in literature, thus prompting us to look for signs suggestive of malignant hematological transformation.

CASE REPORT

We report a case of a 62-year-old patient, followed in internal medicine since the age of 58 for polycythemia vera under hydroxycarbamide with anarchic intake. She presented for pruriginous vesiculo-bullous dermatosis evolving for 4 years. There was no personal or family history of skin disorders. On clinical examination, papulo-vesicular plaques were found involving all the folds: inguinal, axillary, inter-gluteal, neck and body (Figure 1 A and B) with palmo-plantar blisters (Figure 2 A and B) and pustules at the axillary folds, the Nikolsky sign was negative. Examination of the toe nails showed alternating red and white longitudinal bands. Abdominal examination showed moderate splenomegaly. Skin biopsy revealed focal acantholysis with supra-basal

clefts, dyskeratosis with the presence of round bodies and grains compatible with DD (Figure 3). Direct immunofluorescence and anti-intercellular substance antibodies were negative. The hemoglobin was 16.5 gm/dl with a hematocrit level of 56% and normal reticulocytes, white blood cells and platelets as well as the blood smear were normal. The rest of the biological assessment, in particular renal, hepatic, lipid function, and HIV serology, were normal. Abdominal ultrasound confirmed homogeneous splenomegaly. Bone marrow biopsy was without abnormalities. A paraneoplastic assessment was made including a thoraco-abdomino-pelvic CT scan, a breast ultrasound and mammography with cervico-vaginal smear, a CT scan of the cavum and a pancreatic MRI, which did not show any progressive malignant process. The patient was put on oral retinoids at a rate of 0.5 mg/kg per day and topical calcipotriol associated with bloodletting to reduce the hematocrit level and then put back on hydroxycarbamide. The evolution was marked by clinical improvement (Figure 4) with a remarkable decrease in pruritus and reduction in hemoglobin and hematocrit levels. The patient was followed in the hematology department and showed no acute leukemia or myelofibrosis or other neoplasms after a 2-year follow-up.

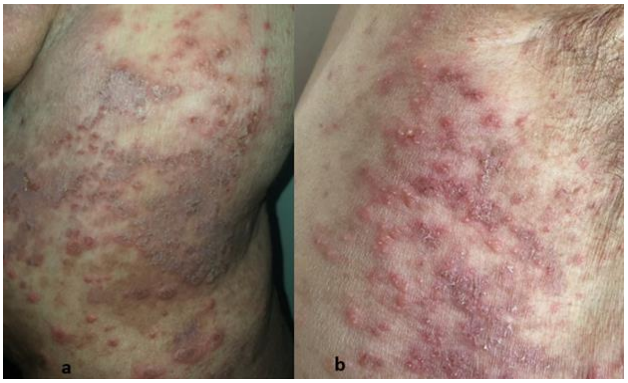

Figure 1 (A and B): Papulo-vesicular plaques affecting the trunk and abdomen. Pustules at the axillary fold.

Figure 2: Palmoplantar tense blisters.

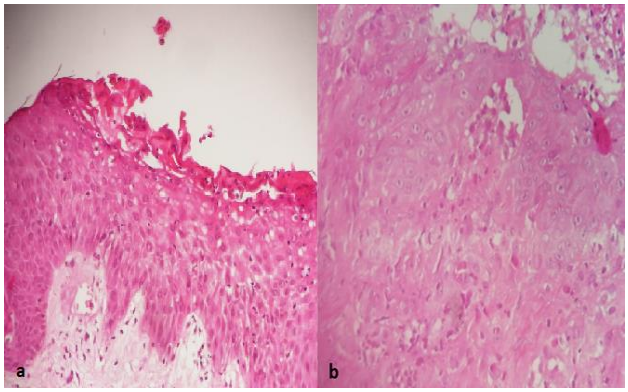

Figure 3 (A and B): Focal acantholysis with supra-basal clefts, dyskeratosis. Presence of round bodies and grains.

Figure 4: Complete healing of vesiculo-bullae.

DISCUSSION

DD is an autosomal dominant genodermatosis linked to intrinsic lesions of the inter-keratinocyte adhesion systems due to the mutation of the ATP2A2 gene. The elementary lesion is the "horny papule" which merges into brownish, papulo-keratotic and crusty layers, very pruritic predominating on the seborrhoeic areas associated with nail and mucosal lesions.[1] The vesiculobullous forms are rare and can lead to confusion with Hailey-Hailey disease, or even pemphigus or raise fears of viral superinfection.[2]

It usually appears in young adults with a familiar context of DD. Some acquired forms of late onset and sporadic character have been described. Late generalized forms are associated with a paraneoplastic syndrome; a literature search reveals three reported cases of acquired DD associated with malignancy; indeed some tumors can secrete factors such as transforming growth factor β which can interfere with the calcium homeostasis of keratinocytes involving or not the SERCA2 pump.[3] Generalized forms can be observed during HIV infection or occur after radiotherapy.[4] Late segmental zosteriform, linear, Blaschko linear or comedonal forms have been described in a few cases.[5,6] They are explained by a

genetic mosaicism induced by a mutation occurring during embryogenesis.

Polycythemia vera is an acquired myeloproliferative syndrome defined by an increase in the absolute mass of red blood cells. It is due to a somatic mutation in exon 14 of the JAK2 gene.[7] Aquagenic pruritus and skin and eyelid erythema are the dermatological manifestations observed during this pathology. DD during polycythemia vera can be part of a paraneoplastic syndrome announcing the evolution of the latter to acute leukemia. A second hypothesis suggested is an overactivation of the transforming growth factor pathway during myelofibrosis secondary to polycythemia vera.[8]

CONCLUSION

We report a case of late DD in a woman followed for polycythemia vera, characterized by a rather rare vesiculo-bullous presentation and whose causal link remains to be determined.

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