Our Dermatology Online

Case Report

Unexpected discovery of asymptomatic polycythemia vera in a patient with papulopustular rosacea caused by Demodex: A fortuitous association?

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ABSTRACT

Herein, we follow the case of a patient suffering from papulopustular rosacea caused by *Demodex* associated with polycythemia vera (PV), which was fortuitously diagnosed. Facial erythrosis must spark a suspicion of PV even if the case appears to be papulopustular rosacea caused by *Demodex*. This observation underlines the distinctive physiopathological processes of papulopustular rosacea caused by *Demodex* and that of PV; however, the dermatological clinical signs are similar. A skin biopsy does not allow us to differentiate the two pathological processes since only a blood sample analysis may exclude a diagnosis of PV. This case stresses the potential advantage of conducting systematic blood analyses for every patient presenting with clinical signs of rosacea, even of erythrodermic rosacea that does not respond to the classical therapeutics, to exclude the possibility of underlying asymptomatic PV. Dermatologists must be aware of the nonspecific dermal manifestations of this potentially fatal hematologic disorder.

Key words: Vaquez disease; polycythemia vera; papulopustular rosacea; erythrosis; *Demodex*

INTRODUCTION

Vaquez disease, or polycythemia vera (PV), is a chronic myeloproliferative neoplasm (NMP) with a prevalence of 1–3/100,000 persons. The median age of onset is sixty years, with a male-to-female ratio of 1:2 [1]. PV is a type of BCR-ABL-negative myeloproliferative syndrome similar to essential thrombocythemia, chronic myeloid leukemia, and myelofibrosis, which often originate from a genetic mutation affecting the normal activity of hematopoietic stem cells, resulting in clonal proliferation of mature yet abnormal cells [2].

PV is linked to the hyperproduction of erythrocytes through a mechanism independent of the rate of erythropoietin [3]. PV may remain asymptomatic for a long time, and a diagnosis may occur after a fortuitous discovery of polycythemia or after the manifestation of the nonspecific symptoms, such as fatigue, itching, and/or aquagenic pruritus and splenic enlargement [3,4]. The diagnosis is based on the WHO criteria [5]. Erythrosis is not a standard diagnostic criterion but may reveal the disease, as in our case.

CASE REPORT

A 59-year-old male consulted for persistent erythematous macules of the nose and cheeks with some erythrodermic papules (Fig. 1). The erythrosis had been present for two years but had been progressively worsening over the past several months. The patient had no remarkable medical history and did not express any specific complaints, except for moderated concomitant fatigue.

Clinical examination findings were normal. A biopsy was performed and favored granulomatous rosacea. Some follicular ostia were enlarged and keratotic, and contained *Demodex*. The upper dermis showed dilated vessels and a mostly lymphocytic infiltrate with periadnexal topography, infiltration of the epithelium,

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and sometimes small granulomas slightly separated from the follicles and made of epithelioid cells with some giant multinucleated cells (Figs. 2 and 3). Due to the complaint of fatigue, a routine blood test was performed. The results revealed hemoglobin at 23.6 g/dL (nle: 13–17), hematocrit at 75.9% (nle: 40–50), VGM at 78.7 μm^3 (nle: 80–99.8), MCH at 24.5 pg (nle: 27.5-34), a red blood cell count of 6,350,000/µL (nle: 4.30–6.1 million), hyperleukocytosis at 10300/µL (nle: 2100-7500), a platelet count of 485.10^3/µL (nle: 150–400), and a subnormal erythropoietin level.

A subsequent bone marrow biopsy showed hypercellularity, including prominent erythroid, granulocytic, and megakaryocytic proliferation. PCR molecular biology highlighted a mutation of exon 14 of V617F (71% of mutated alleles) and the absence of a mutation of exon 12 of the JAK2 gene. Abdominal echography revealed discrete splenomegaly without hepatomegaly. These results confirmed the diagnosis of a myeloproliferative syndrome with a PV type.

The treatment consisted of hydroxyurea 20 mg/kg/day and acetylsalicylic acid 80 mg, as well as bloodletting with the aim of obtaining a hematocrit under 45%. The demodicosis was treated locally with a cream containing 2% of benzyl benzoate with quick positive clinical results. One year later, the patient's erythrosis became more moderate.

DISCUSSION

PV is rarely mentioned in the differential diagnosis of papulopustular facial rosacea because of its low incidence and its atypical presentation. Rosacea is often mentioned as the first diagnostic hypothesis but has to be differentiated from other causes with vasomotor origin, related to medications or carcinoid tumors or mastocytosis. More frequently, rosacea has been differentiated from erythema pudicitae and menopausal hot flushes. Diabetes may also lead to the occurrence of facial erythema.

The clinical difference between PV erythrosis and rosacea is not always clear. If erythrosis is accompanied by pustules, a diagnosis of rosacea or lupus is most likely. Rosacea is physiologically characterized by vasodilation of blood and lymphatic vessels, by the induction of angiogenesis, and by local inflammation, in which colonization by *Demodex* is more likely than in the general population [6]. Local immunosuppressive factors may enable the proliferation of *Demodex*. These processes contribute to maintaining and amplifying clinical symptoms by positive feedback, as *Demodex* participates in inflammation by maintaining vasodilation and hence erythrosis, and secrete local

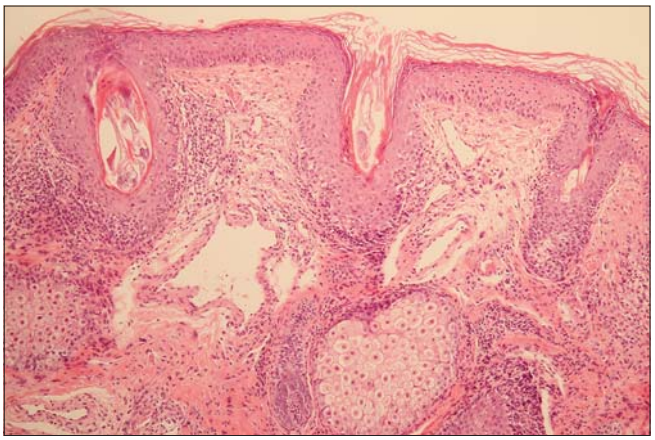

Figure 2: Superficial dermis with dilated vessels and periadnexal lymphoid cells (H&E, 50×).

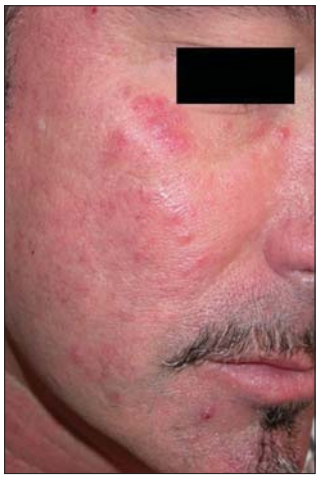

Figure 1: Persistent erythematous macules with erythrodermic papules of the cheek.

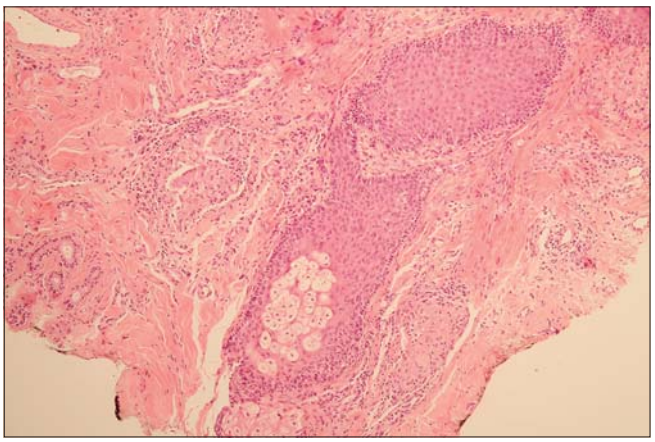

Figure 3: Lymphocytic infiltrate with mostly periadnexal topography, sometimes small granulomas constituted by epithelioid cells, with some giant multinucleated cells of the upper epidermis (H&E, 50×).

immunosuppressive factors favoring skin invasion by more *Demodex*, thus sustaining the inflammatory process [7].

The skin manifestations of PV, which may be clinically similar to those of rosacea, are secondary to polycythemia in the vascular flow. Because the blood vessels distend after reaching the large blood vessels of the internal organs, once the thickened blood reaches the skin capillaries, it may create a visible skin rash, which may be severe and deep, with or without telangiectasia. Some cases have been reported to have purpuric rashes, petechia, hemangioma, and an enlarged, thickened, red and cracked geographic tongue, cutaneous sarcoidosis, or granulomatous dermatitis [8-10].

Physiopathological parallelism may be drawn between these two entities: In both cases, erythema and telangiectasia may favor *Demodex* settlement in the skin, which contributes to the clinical symptomatology of rosacea [11]. It is impossible to differentiate these two pathologies only on the basis of a clinical examination and a skin biopsy. A hematological evaluation allows for a specific diagnosis of PV. The diagnosis of PV is important as, without adequate treatment, the survival period is estimated at merely 18 months, due to the high prevalence of thrombotic events. Venous or arterial thrombosis, hemorrhage, and transformation into myelofibrosis or myeloid leukemia are common complications of NMPs, such as PV.

CONCLUSION

In cases of suspected papulopustular rosacea or erythrosis rosacea, there is a need for differentiation from erythrosis linked to PV. A blood test allows for a specific diagnosis of PV. We postulate that vasodilation due to PV may promote the development of papulopustular rosacea in a sensitive patient. This case highlights the need for systematic blood testing in every patient presenting with clinical signs of rosacea, even of the erythrodermic kind, to exclude any underlying asymptomatic PV.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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