Pemphigus Mimicking Common Skin Diseases – Atypical Presentation Delaying Correct Diagnosis: Case Series of Five Patients

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Pemphigus, a rare skin disorder, encompasses a class of mucocutaneous autoimmune blistering diseases characterized by loss of cell-cell adhesion (acantholysis) mediated by autoantibodies to epidermal cell surface proteins [1]. The presence of flaccid non-inflammatory blisters and erosions that arise on normal-appearing skin and variable involvement of the mucous membranes characterize its three major variants: pemphigus vulgaris, pemphigus foliaceus, and paraneoplastic pemphigus. The diagnosis of pemphigus is based on three key elements: a) the presence of typical clinical lesions, b) demonstration of acantholysis on skin biopsy, and c) the finding of anti-desmoglein autoantibodies in tissue, whether present in the patients' serum or not.

Table 1. Clinical summary of five patients treated in our department for pemphigus

Patient #	Age (yrs) Gender	Initial diagnosis	Initial treatment	Time to diagnosis of pemphigus	Current status
1 (index case)	50 M	Psoriasis	Topical steroids, acitretin	5 months	Remission
2	82 F	Burn	Sulfadiazine silver	2 months	Remission, maintained with prednisone 30 mg/day
3	69 M	Generalized herpes zoster	Acyclovir (per os)	10 days	Partial remission, maintained with triamcinolone 8 mg/day
4	74 M	Squamous cell carcinoma	Cryotherapy	4 months	Partial remission, maintained with prednisone 10 mg/day
5	53 M	Solar keratoses	Cryotherapy	3 months	Prednisone initiated

Generally, if the disease is not treated definitively and promptly, as may occur in cases of incorrect diagnosis, the condition usually deteriorates, and delay in instituting appropriate therapy may cause later difficulties in disease management. It is well known that even if the initial presentation is limited, if systemic treatment is not given the disease will eventually generalize. In the absence of the characteristic lesions of flaccid bullae and erosions, pemphigus may not be included in the differential diagnosis. In this report we present five patients whose atypical presentations were initially diagnosed as other skin disorders. They were referred to our department due to lack of response to initial therapy and were subsequently diagnosed and successfully treated for pemphigus in our department.

Patient Description

A 50 year old Caucasian male (index case) presented to a dermatologist with a 5 month history of widespread pruritic eruption. Based on the clinical appearance and histological findings in lesional skin, he was diagnosed with psoriasis. The eruption did not improve with 3 months of topical steroids or 2 months of acitretin (Neotigason®, Roche, Israel) at a daily dose of 25 mg per os. At presentation to our department, physical examination revealed a symmetric eruption composed of circumscribed erythematous scaling plaques involving the scalp, face and trunk. Our clinical impression was of atypical psoriasis, and treatment with acitretin was continued in combination with phototherapy. However, on repeated examinations we noted a number of plaques with crusts rather than scale. These discrepancies from the classic clinical appearance of psoriasis, combined with resistance to treatment, prompted additional evaluation. Direct immunofluorescence analysis of fresh tissue demonstrated intercellular deposition of immunoglobulin G and C3, and the diagnosis of pemphigus foliaceus was established. Systemic steroids were initiated with excellent clinical response.

Table 1 presents a summary of clinical findings of this and four additional patients who were initially diagnosed with other disorders and were subsequently diagnosed with pemphigus vulgaris in our department. The five cases represent diverse clinical presentations and initial diagnoses, but have in common the findings of discrete lesions with superficial epidermal changes as well as resistance to conventional therapy. In all five cases, the resistance to treatment prompted additional evaluation, including biopsy and direct immunofluorescence, which led to the correct diagnosis.

Comment

Prompt diagnosis of relatively rare skin diseases may be challenging even for skilled dermatologists. In this case series we present five patients who were initially diagnosed with more common

skin disorders by the treating dermatologist. They were admitted to our department because of non-responsiveness to treatment for the initial diagnosis.

The average time from initial presentation to diagnosis of pemphigus ranges from 3 to 6 months. In our series, the average time was 2.9 months. Presentation with the characteristic lesions of flaccid bullae and superficial skin erosions facilitates the diagnosis of pemphigus and allows rapid initiation of appropriate therapy. However, the initial lesions of pemphigus may exhibit markedly atypical morphology or distribution, even – although rarely – as foot ulcers [2] or paronychia [3]. In addition, the oral lesions of pemphigus vulgaris, which may prompt consideration of the diagnosis, may sometimes be misleading and prolong the time to correct diagnosis.

Since the clinical presentation of pemphigus may vary significantly from the classic lesions [4], especially in the initial phase of disease, a high index of suspicion is required. Resistance of common skin disease to well-established therapy, as exemplified in our five patients, should raise concern for an alternative diagnosis of autoimmune blistering disorders and prompt additional diagnostic steps, including biopsy and direct immunofluorescence.

References

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