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Single Case

Sneddon-Wilkinson Disease and Monoclonal Gammopathy of Undetermined Significance in the Elderly: Case Report

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Keywords

Sneddon-Wilkinson disease · Subcorneal pustular dermatosis · Monoclonal gammopathy of undetermined significance · Corticosteroids

Abstract

Sneddon-Wilkinson disease (SWD) or subcorneal pustular dermatosis is considered a rare pustular skin disease with chronic relapsing course. An association between SWD and other chronic conditions, such as IgA or IgG monoclonal gammopathy of undetermined significance (MGUS), IgA myeloma, pyoderma gangrenosum, thyroid gland disorders, and neoplastic diseases other than MGUS/myeloma, is known. We describe the case of a 92-year-old male patient with SWD and a concurrent IgG MGUS who had been treated with systemic betamethasone, topical mometasone furoate, and methylprednisolone aceponate, with a complete and durable resolution of symptoms and skin lesions without side effects. Systemic and topical steroids were very effective and well tolerated in our patient. This is the second case reported in the literature on the efficacy of a corticosteroid regimen in SWD in a fragile patient. This therapeutic approach (instead of dapsone therapy) has been used due to its relatively good safety profile.

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Introduction

Sneddon-Wilkinson disease (SWD) or subcorneal pustular dermatosis has been initially described in 1956 by Sneddon and Wilkinson and is now considered a rare idiopathic and benign disease, with a chronic-relapsing course [1].

A well-known correlation exists between SWD and IgA monoclonal gammopathy of undetermined significance (MGUS) in up to 40% of cases. The concomitant occurrence of SWD and IgG MGUS, myeloma, especially IgA myeloma, pyoderma gangrenosum, rheumatoid arthritis, lupus erythematosus, Sjögren syndrome, Crohn disease, SAPHO (synovitis, acne, pustulosis, hyperostosis, and osteitis) syndrome, multiple sclerosis, hyperthyroidism, hypothyroidism, and neoplastic diseases, including chronic lymphocytic leukemia, thymoma, apudoma, and lung squamous cell carcinoma, are reported in the literature [1–3]. Other rare associated conditions are respiratory infection with *Mycoplasma pneumoniae*, HIV infection, and medical ultrasound exposition [3, 4].

It is clear that treatment of an underlying disease, such as myeloma, can bring about a complete resolution of SWD in certain patients, with a strong correlation with the trend of the underlying disease, so SWD in some cases can be considered as a true paraneoplastic entity [2]. SWD characteristically starts with a relapsing symmetrical pustular eruption involving the trunk and intertriginous areas; it can also affect the flexor areas of the limbs. Presence of pustules on the palms and soles have also been reported, but the face and mucous areas are almost never affected. The typical lesion is described as a millimeter-sized pustule, arising on a normal or slightly erythematous skin surface [3]. The upper content of the lesions is classically described as clear, while the base content is purulent (an aspect known as "half-half" content) [1]. There is a tendency to coalescence, and annular or serpiginous lesions are observed after that. After rupture of the pustules, areas of superficial desquamation, crusting, and hyperpigmentation are reported [1]. A generally mild pruritus can be present [1]. On histology, subcorneal accumulation of neutrophils without spongiosis or acantholysis (in early lesions), with perivascular inflammatory infiltrate of neutrophils and occasional eosinophils can be easily observed. Acantholysis could be reported in older lesions [3]. SWD clinical appearance could resemble pustular psoriasis, a chronic inflammatory skin disease whose differential diagnosis is sometimes a challenge both for clinicians and pathologists [5–8].

Case Presentation

We report the case of a 92-year-old man admitted to our Dermatological Division for the presence of large erythematous macules symmetrically located on the limbs and upper chest and intertriginous disposition (Fig. 1, 2). The lesions had been appearing during the last 7–8 months and had slightly enlarged. He also reported mild pruritus and weight (approximately 10 kg in 6 months) and appetite loss. The patient had a personal history of total gastric resection for peptic ulcer, and benign prostatic adenoma. The skin lesions presented as large, erythematous macules and plaques with serpiginous and polycyclic borders; coalescing papules were also observed. No mucosal lesions were noted. The patient was apyrexial and had not been exposed to newly introduced drugs in the last months.

A complete drug withdrawal and also a prolonged topical and systemic antifungal therapy had been attempted a few weeks before by the general practitioner, with no clinically relevant results. Cultures for bacteria and fungi were also negative. Peripheral blood cell counts showed a modest anemia (11.2 g/dL), with a slight alteration of creatinine (1.41 mg/dL).

Vitamin blood levels were in the normal range. Serum cancer markers were normal, with the exception of carcinoembryonic antigen (14 ng/mL), CA 19-9 (135 U/mL), and CYFRA 21.1 (8.3 ng/mL). Prostate-specific antigen was elevated (24.8 ng/mL). Serum chromogranin A and neuron-specific enolase were slightly elevated (129.8 and 9.8 ng/mL, respectively), while serum glucagon was normal. Serotonin metabolites in the 24-h urine collection were normal. Serum electrophoresis showed a minimal albumin decrease (3.3 g/dL), with a marked IgG decrease (417 mg/dL). Immunofixation also revealed the presence of a monoclonal IgGκ component, with an elevation of serum free κ light chain (22.7 mg/dL). Urinalysis and urinary electrophoresis were normal (Bence-Jones protein was negative), and urinary free light chain searching revealed a value at the upper standard limits.

In order to exclude a malignancy, a chest and abdomen CT scan was performed, with the detection of a right colonic wall thickening. At endoscopy, the only relevant lesion was a colon polyp; histology revealed a tubular adenoma with low-grade dysplasia that was completely removed. Transrectal prostate ultrasound confirmed the presence of an adenoma, and medical therapy with terazosin and dutasteride was continued. We requested also a skull CT and a rib and pelvis X-ray, which were all negative for bone resorption areas.

At this point, 3 cutaneous biopsies were performed on the left thigh, 2 in the lesional and 1 in the perilesional skin. In all biopsies, the epidermis showed multiple subcorneal pustular collections of neutrophils with minimal spongiosis and a moderate superficial lymphoid infiltrate in the papillary dermis. The PAS special stain revealed no fungal organisms. Direct immunofluorescence was negative in all specimens. At histology, multiple subcorneal pustules were present in all the specimens, with the presence of a neutrophil infiltrate (Fig. 3). We made the diagnosis of Sneddon-Wilkinson disease in a patient with IgGκ MGUS, and the patient started a hematological follow-up.

Discussion

To our knowledge, this is the second case reported of SWD in a nonagenarian, and with increasing population survival, rare diseases will be more frequent in a previously little studied population. A complete diagnostic procedure is always mandatory in order to exclude skin conditions in which immunosuppressive treatments are contraindicated and to find (and eventually treat) a potentially lethal associated disease.

The pathogenesis is unclear, although the condition is actually considered an abnormal response of inflammation cells (neutrophils) to chemotactic factors (TNF-α, interleukin-8, C5a) [9]. This hypothesis could also be supported by the clear response to anti-TNF drugs [10]. Differential diagnoses include pustular psoriasis, the subcorneal type of IgA pemphigus and pemphigus foliaceus, dermatitis herpetiformis, impetigo [3] and dermatophytosis [1], as well as AGEP (acute generalized exanthematous pustulosis).

It is important to note that pustular content is sterile, and also at microscopic evaluation, there is no evidence of pathogens (as confirmed in our case) [3]. There is also a still unclear correlation with the pustular or plaque form of psoriasis. It has been reported that also years after the diagnosis of SWD, the onset of one of these forms of psoriasis could be expected (some authors consider SWD a form of pustular psoriasis in some cases). In other cases, a differential diagnosis with subcorneal IgA pemphigus is difficult. Generally, immunofluorescence is helpful (with evidence of intercellular IgA deposits against desmocollin 1 only in pemphigus), but immunofluorescence could become positive only years after an initial diagnosis of SWD, and the relationship between this subgroup and classic SWD still remains unclear [3].

In our case, direct immunofluorescence was negative, and a decisive confirmation, in a chronic case, without the typical, better described, clinical features of the acute form, came from histology.

As regards therapy, dapsone is generally considered the first choice, but response is not homogeneous nor constant [2] and long-term treatment is difficult, often because of hematological complications (methemoglobinemia or hemolytic anemia) [3]. Acitretin and etretinate have been reported to be effective, in contrast to isotretinoin (with a dose of 0.5 mg/kg/day).

Psoralen ultraviolet and broadband or narrowband UVB alone or in combination with other treatments may be an effective choice. In some cases, there is a response to potent topical or systemic steroids. The use of topical tacalcitol, sulfapyridine and sulfamethoxypyridazine, ketoconazole, tetracycline, minocycline, vitamin E, cyclosporine, colchicines, mizoribine, and mebhydroline is anecdotal but in some cases effective. Anti-TNF drugs, like infliximab, can lead to a rapid control in severe cases (in line with the hypothetic role of TNF-α) not responsive to other drugs, but the response can be temporary [3]. Etanercept has also been reported to be an effective second-line therapy in refractory cases, and multiple-drug combination regimens are possible [10].

In our case, an intravenous therapy with 3 mg betamethasone once daily and topical mometasone furoate was started, with significant improvement after 1 week. After 2 weeks, betamethasone was tapered, and topical mometasone furoate was continued for 2 weeks and then replaced by a methylprednisolone aceponate topical emulsion and emollients therapy. After 5 months, all skin lesions had disappeared, and the patient was asymptomatic.

This is the second case report on the efficacy of a corticosteroid regimen in SWD in elderly patients. We chose this approach due to the low probability of side effects in a fragile patient [11].

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflicts of interest to disclose.

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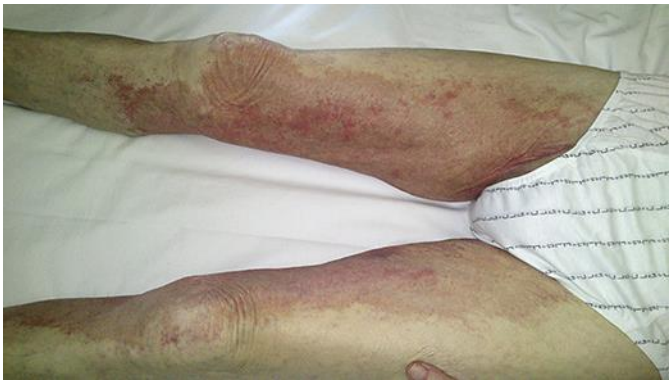

Fig. 1. Erythematous macules symmetrically located on intertriginous areas.

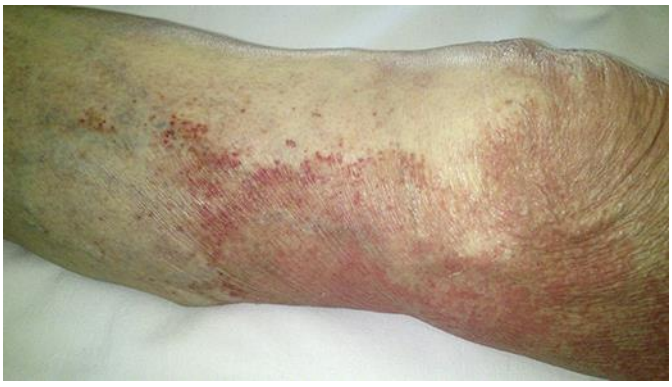

Fig. 2. Complete resolution of clinical manifestation following corticosteroids therapy.

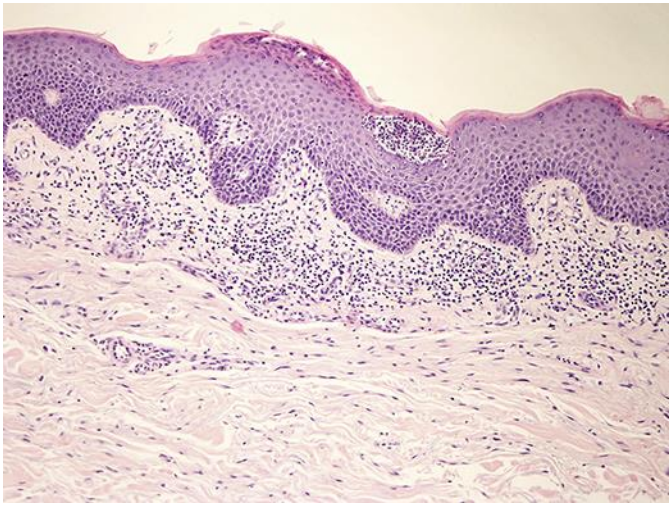

Fig. 3. Subcorneal pustular collections of neutrophils with minimal spongiosis and a moderate superficial lymphoid infiltrate in the papillary dermis (EE, ×20).