Inflammatory myofibroblastic tumor presenting as paraneoplastic pemphigus in a 7-year-old girl

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INTRODUCTION

Paraneoplastic pemphigus is an autoimmune disease associated with an underlying tumor. Several cases have been reported as unusual pemphigus vulgaris, erythema multiforme, or paraneoplastic bullous disease,[1] but the incidence of the condition is unknown.[2] Response to treatment is generally poor, with significant morbidity and mortality.

This condition is clinically characterized by severe mucositis and polymorphic blistering skin eruptions, and histologically by acantholysis, keratinocyte necrosis, and interface dermatitis.[3] Immunoprecipitation and immunoblot testing detect autoantibodies against desmosomal polypeptides.[4] We describe a case of paraneoplastic pemphigus associated with an abdominal inflammatory myofibroblastic tumor in a 7-year-old girl.

CASE REPORT

A previously healthy 7-year-old girl from the city of Valledupar, Colombia, presented to a different Institution in March 2009, with a 2-month history of severe depression, oral ulcers, denuded lips, and progressive bullae involving the face, extremities, and lower back and affecting 40% of her body surface (Figs 1 and 2). She had pemphigus vulgaris diagnosed by skin biopsy (Fig 3) and direct immunofluorescence and received treatment with oral prednisone, thalidomide, and azathioprine, with minimal improvement.

In June of 2009, she was admitted to our hospital and received multidisciplinary treatment

Fig 1. **A**, Back. **B**, Lips.

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Fig 2. **A**, Finger. **B**, Soles.

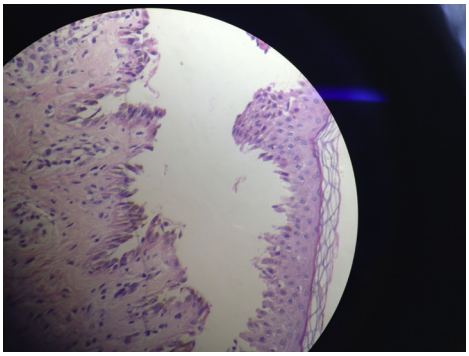

Fig 3. Skin biopsy taken before treatment initiation shows acantholytic intraepidermal vesicular dermatitis suggestive of vulgaris pemphigus.

by pediatrics, pediatric dermatology, infectious disease, psychiatry, and endocrinology. Initial management included intravenous immunoglobulin, methylprednisolone, azathioprine, oxacillin, rituximab (4 doses), and psychotherapy. After

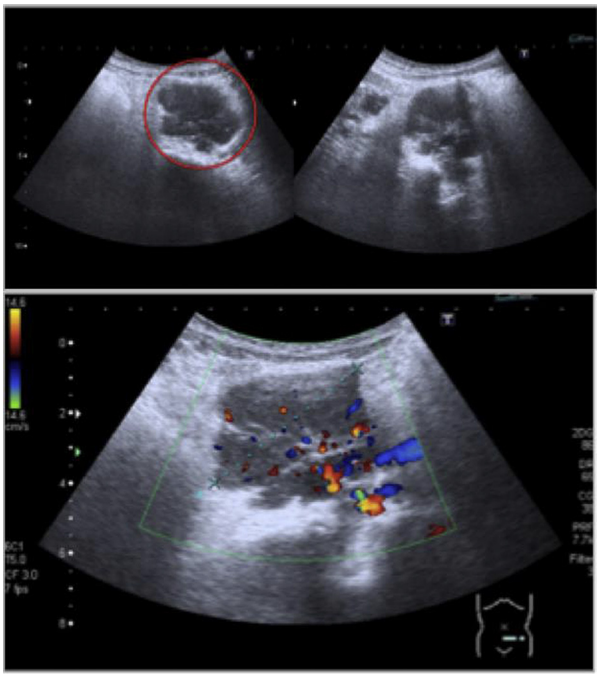

Fig 4. Abdominal ultrasound scan shows a 55-mm, hypoechoic, solid mass with low resistance.

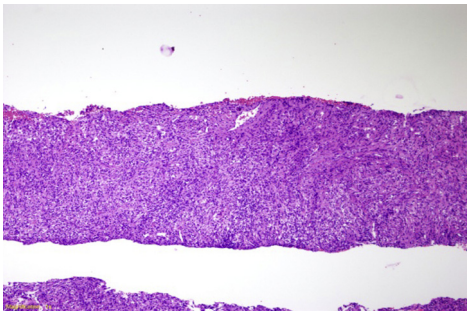

Fig 5. Biopsy of the abdominal mass found a fusocellular lesion associated with a mononuclear inflammatory infiltrate. A histologic diagnosis of an inflammatory myofibroblastic tumor was made.

40 days of hospitalization, skin lesions partially improved. After discharge, prolonged courses of prednisone and continuous azathioprine temporarily controlled her disease. Cushing's syndrome, a small cataract, skin infections, and myopathy developed as side effects of therapy.

Between April 2010 and July 2011, she required multiple hospitalizations for relapses and skin infections. In August 2011, she was seen in the emergency room for severe abdominal pain and fever. Salmonellosis was documented, and an abdominal ultrasound scan found a 55-mm vascularized mass in the right flank (Fig 4); biopsy of the mass showed an inflammatory myofibroblastic tumor (Fig 5).

Table I. Original diagnostic criteria for paraneoplastic pemphigus (Anhalt et al[1])

1. Painful mucosal ulcerations and blisters and a polymorphous skin eruption in the context of an occult or known neoplasm
2. Intraepidermal acantholysis, keratinocyte necrosis, and vacuolar interface changes in histopathology
3. Deposition of IgG and complement C3 in intercellular epidermal and basement membrane zones seen on direct immunofluorescence
4. Detection of serum autoantibodies to stratified squamous epithelia, columnar, and transitional epithelia by indirect immunofluorescence
5. Serum immunoprecipitation of a characteristic complex of four proteins (250, 230, 210, and 190 kDa) from keratinocytes of transitional epithelia by indirect immunofluorescence

Table II. Camisa and Helm criteria for the diagnosis of paraneoplastic pemphigus[11]

Major Criteria
1. Polymorphous mucocutaneous eruption
2. Concurrent internal neoplasia
3. Characteristic serum immunoprecipitation findings

Minor Criteria
1. Positive cytoplasmic staining of rat bladder by immunofluorescence
2. Intercellular and basement membrane zone immunoreactants on direct immunofluorescence of perilesional tissue
3. Acantholysis in biopsy specimen from at least one anatomic site of involvement

Surgical removal of 95% of the lesion was possible, with the remaining 5% adhered to the internal iliac vein. After surgery, the skin lesions began to improve and disappeared. At 4 years of follow-up, the residual tumor remains stable, and she remains asymptomatic without medications.

DISCUSSION

Paraneoplastic pemphigus is a neoplasia-associated autoimmune disease, first described by Anhalt et al,[5] characterized by the production of autoantibodies against a complex of desmosomal proteins (desmoplakin I and II, bullous pemphigoid antigen 1, envoplakin, periplakin and desmoglein).[6,7]

Paraneoplastic pemphigus is mainly associated with lymphoproliferative disorders such as non-Hodgkin lymphoma, chronic lymphocytic leukemia, and Castleman's disease. Nonlymphoid malignant neoplasms, such as benign thymomas,[8,9] poorly differentiated sarcomas, and carcinomas of the lung, colon, pancreas,[10] and cervix[11] are rarely associated.[12,13]

Stomatitis is a cardinal feature and often the earliest presenting sign and is extremely resistant to therapy. Patients can present with vesicles, bullae, erosions, crusting, pruritic skin eruption resembling bullous pemphigoid,[14] and erythematous papules with central vesiculation resembling erythema multiforme. Nikolsky sign can occasionally be seen.[15] Blisters and lichenoid lesions on the palms and soles, and pseudomembranous conjunctivitis, as in our patient's case, help to differentiate the condition from pemphigus vulgaris.[16] The most commonly affected areas are the trunk, proximal extremities, head, and neck.[17]

In 1990, Anhalt et al[5] proposed diagnostic criteria (Table I), which Camisa and Helm[18] modified in 1993 (Table II).

The course of Paraneoplastic pemphigus does not necessarily parallel the course of the underlying neoplasm. This condition can be associated with pulmonary disease including bronchiolitis obliterans and IgG deposits in respiratory epithelium, which in some cases may lead to respiratory failure accounting for the mortality cause in these patients.[19,20]

Inflammatory myofibroblastic tumors are rare neoplastic lesions that occur primarily in children and young adults.[21] They may present in any organ, most often seen in soft tissues, lungs, and abdomen.[22] These tumors were considered to have a benign clinical course, but now it is recognized that they can have an aggressive behavior and occasionally an unfavorable prognosis.[23] Few cases of paraneoplastic pemphigus associated with inflammatory myofibroblastic tumors have been reported,[24] none in children.

The tumor can be locally recurrent and rarely metastasizes. In most cases, complete surgical resection of the lesion is curative.

Although paraneoplastic pemphigus is rare in childhood and adolescence, it should be included in the differential diagnosis of periorificial erosive dermatitis. Lesions that are refractory to therapy should prompt an aggressive search for a possible occult neoplasm with imaging of the chest, abdomen, and pelvis.

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