Case report

Localized Segmental facial pemphigus foliaceus: a rare and atypical presentation

.

ABSTRACT

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| **Background:** Pemphigus foliaceus (PF) is a rare autoimmune blistering disorder caused by IgG4 autoantibodies targeting desmoglein 1, leading to superficial intraepidermal acantholysis. While typically presenting with widespread lesions, localized forms are exceptionally rare.  **Objective:** To describe a unique case of localized pemphigus foliaceus confined to the left hemiface in a 70-year-old woman, highlighting its diagnostic challenges and successful therapeutic approach.  **Case Presentation:**  A 70-year-old woman with no significant past medical history, present a one year history of eroded, erythematous, crusted lesions on the left side of her face. The lesions had been treated unsuccessfully with topical antifungals, topical corticosteroids, antibiotics, and oral antibiotics with no amelioration. Upon clinical examination, a non-pruritic, non-painful, scaly erythematous plaque was observed, localized to the left hemiface, involving the cheek and left periorbital region. There were no other lesions on the rest of her skin, mucous membranes, or hair. Histopathology and direct immunofluorescence confirmed the diagnosis of PF. The patient was treated with high-dose systemic corticosteroids (1.5 mg/kg/day prednisone) and rituximab, resulting in complete lesion resolution. No progression to generalized disease was observed.  **Conclusion:** This case underscores the exceptional rarity of localized pemphigus foliaceus, particularly when confined to a single hemiface. Its atypical presentation can mimic other dermatological conditions, posing diagnostic challenges |

*Keywords: Acantholysis, Autoimmune, Desmoglein, Pemphigus, Rituximab*

1. INTRODUCTION

Pemphigus foliaceus (PF) is a superficial autoimmune blistering disorder characterized by the production of IgG4 autoantibodies against desmoglein 1, a desmosomal cadherin essential for epidermal adhesion [1]. The resulting acantholysis leads to fragile, superficial blisters that rupture easily, leaving erosions rather than intact bullae [1,2]. Clinically, PF presents as well-demarcated, scaly, crusted erosions, predominantly involving seborrheic areas such as the face, scalp, and trunk [2]. Localized forms of PF are exceedingly rare, often presenting a diagnostic challenge due to their ability to mimic other dermatoses such as seborrheic dermatitis, eczema, or impetigo [3,4]. Various triggers, including environmental factors and topical agents, have been implicated in the localized manifestation of PF [5]. The disease typically affects individuals between the fifth and sixth decades of life but can occur outside this age range [6,7]. Herein, we report a rare case of localized unilateral facial PF in an elderly woman, emphasizing the clinical, histopathological, and therapeutic considerations.

2. Case presentation

The patient was a 70-year-old woman who presented to our hospital with a 1year history of eroded, erythematous, crusted lesions on the left side of her face. The lesions had been treated unsuccessfully with topical antifungals, topical corticosteroids, antibiotics, and oral antibiotics for a presumed diagnosis of leishmaniasis or impetigo. The patient had no significant past medical history.

Upon clinical examination, a non-pruritic, non-painful, scaly erythematous plaque was observed, localized to the left hemiface, involving the cheek and left periorbital region. There were no other lesions on the rest of her skin, mucous membranes, or hair. (Figure 1)

A skin biopsy revealed a mildly acanthotic epidermis with superficial intraepidermal cleavage and acantholytic cells within the cleavage zone, suggesting a superficial pemphigus pattern. (Figure 2). Direct immunofluorescence exhibited a "grilled" appearance with C3, IgA, and IgM deposits, supporting a diagnosis of pemphigus. Indirect immunofluorescence demonstrated a positive anti-intercellular substance antibody titer of 40, and a desmoglein 1 level of 280, confirming the diagnosis.

Paraclinical tests showed no abnormalities and tests for antinuclear antibodies and anti-double-stranded DNA were negative. The skin culture and PCR came back negative.

Based on the clinical findings and paraclinical investigations, a diagnosis of pemphigus foliaceus was established. The patient was treated with systemic corticosteroid therapy, specifically prednisone at a dosage of 1.5 mg/kg/day, with a gradual taper, in addition to rituximab. The patient responded well to treatment, and all lesions healed completely.

3. discussion

Localized pemphigus foliaceus is an exceptionally rare variant of the disease, with only 26 cases reported in the literature to date (Table1). Interestingly, some of these cases, initially presenting as localized lesions, later progressed to more widespread disease. This highlights the dynamic nature of PF, where localized forms can potentially evolve into more generalized manifestations, complicating the clinical course and management [3].

Moreover, certain topical medications, such as imiquimod and nonsteroidal anti-inflammatory drugs (NSAIDs), have been implicated in the development of localized PF. The exact mechanisms by which these agents trigger or exacerbate the disease are not fully understood, but their role in modifying local immune responses may contribute to the pathogenesis[4]. This association underscores the need for careful consideration of topical treatments in patients with localized PF, as these medications might influence disease progression [5].

The case presented here is particularly notable for its localized and unilateral manifestation, our patient denied application of any topical medications. Typically, pemphigus presents with widespread, generalized blistering; however, in this patient, the disease was confined to the left hemiface, a presentation that is atypical and can easily be mistaken for other dermatologic conditions such as eczema, seborrheic dermatitis, or even cutaneous malignancies.

Histologically, localized PF displays the classical features of superficial intraepidermal acantholysis, and direct immunofluorescence typically reveals intercellular deposits of IgG and C3 within the epidermis [1,2]. Detection of anti-desmoglein 1 antibodies in the serum further supports the diagnosis [1].

The therapeutic approach in this case involved systemic corticosteroid therapy combined with rituximab, a B-cell depleting agent [6]. Prednisone at a dosage of 1.5 mg/kg/day was selected as the initial treatment, reflecting the need for high-dose steroids in managing extensive disease activity. The addition of rituximab, which targets CD20-positive B cells, is increasingly recognized as an effective treatment for pemphigus, particularly in refractory cases or those requiring steroid-sparing strategies. The patient’s favorable response, with complete healing of the lesions, aligns with existing evidence supporting the efficacy of this combined therapeutic approach.

**Table.1A: Summary of publications on localized pemphigus foliaceus-1**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Author | | | Age | Location of lesions | | | Pathology findings | | | DIF, IIF, and/or ELISA | | | Traitment | | |
| Newton | | | 27 | Left side of nose | | | Subcorneal bulla acantholysis | | | * *DIF*: intercellular IgG and | | | topical steroids | | |
| and al. | | |  |  | | |  | | | C3 | | |  | | |
|  | | |  |  | | |  | | | * *IIF*: positive | | |  | | |
|  | | | 62 | Nose | | | Acantholysis in granular | | | * *DIF*: intercellular C3 | | | cyclophosphamide | | |
|  | | |  |  | | | layer | | | * *IIF*: positive | | |  | | |
|  | | |  |  | | |  | | |  | | |  | | |
|  | | | 43 | Nose | | | N/A | | | N/A | | | Oral prednisone 5---15 mg/d | | |
|  | | |  |  | | |  | | |  | | |  | | |
| Paramsoty | | | 34 | Tip of nose, | | | Subcorneal blister with acantholytic cells | | | * *DIF*: IgG between | | | Prednisolone 30 mg/day | | |
| and al. | | |  | external nares and | | |  | | | epidermal cells | | |  | | |
|  | | |  | nasolabial fold | | |  | | | * *IIF*: positive at a titre of | | |  | | |
|  | | |  |  | | |  | | | 1:40 | | |  | | |
|  | | | 65 | Nose and behind | | | Intraepidermal bulla acantholysis | | | * *DIF*: IgG between | | | clobetasol propionate | | |
|  | | |  | left ear | | |  | | | epidermal cells and granular | | |  | | |
|  | | |  |  | | |  | | | IgM in basement membrane | | |  | | |
|  | | |  |  | | |  | | | * *IIF*: negative | | |  | | |
| Yamamoto | | | 81 | Right cheek | | | Intraepidermal cleft in | | | * *DIF*: IgG in intercellular | | | minocycline 100 mg | | |
| and al. | | |  |  | | | granular layer and | | | spaces of upper cell layers | | | nicotinamide 9.0 g daily and | | |
|  | | |  |  | | | acantholytic cells within | | | * *IIF*: negative | | | betamethasone valerate 2.0 g | | |
|  | | |  |  | | | the cleft | | |  | | |  | | |
| Termeer | | | 83 | Scalp | | | Split in upper granular | | | * *DIF*: IgG in upper | | | tacrolimus 0.1% | | |
| and al. | | |  |  | | | layer of epidermis and | | | epidermal layers | | |  | | |
|  | | |  |  | | | superficial bulla filled | | |  | | |  | | |
|  | | |  |  | | | with acantholytic | | |  | | |  | | |
|  | | |  |  | | | keratinocytes and fibrin | | |  | | |  | | |
| Lin and al. | | | 53 | Left side of face | | | Superficial acantholytic | | | * *DIF*: IgG at keratinocyte | | | IM 0.1% TAC and topical clobetasol | | |
|  | | |  |  | | | vesicular dermatitis | | | cell surface in granular | | | propionate | | |
|  | | |  |  | | |  | | | layer | | | and oral prednisone | | |
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|  | | |  |  | | |  | |  | | |  | | |
| Author | Age | | | Location of lesions |  | | Pathology findings | | | DIF, IIF, and/or ELISA | | | Traitment  **Table.1B: Summary of publications on localized pemphigus foliaceus-2** | | |
| Kishibe | 63 | | | Tip of nose | Subcorneal acantholysis | | | | | * *DIF*: IgG deposition | | | oral prednisolone | | |
| and al. |  | | |  |  | | | | | * *IIF*: negative | | | 40 mg daily | | |
|  |  | | |  |  | | | | | *ELISA*: negative for | | |  | | |
|  |  | | |  |  | | | | | anti-desmogleins 1 and 3 | | |  | | |
|  |  | | |  |  | | | | | antibodies | | |  | | |
| Zaraa | 42 | | | Scalp | Acantholytic cells | | | | | * *DIF*: positive | | | Topical clobetasol propionate and | | |
| and al. |  | | |  |  | | | | | * *IIF*: positive | | | infiltration of triamcinolone | | |
|  |  | | |  |  | | | | | *ELISA*: positive for | | | acetonide | | |
|  |  | | |  |  | | | | | anti-desmoglein 1 | | |  | | |
|  |  | | |  |  | | | | | antibodies | | |  | | |
|  | 34 | | | Right cheek | Acantholytic cells | | | | | * *DIF*: positive | | | oral prednisone and | | |
|  |  | | |  |  | | | | | * *IIF*: positive | | | cyclophosphamide | | |
| Ohata | 68 | | | Right cheek | Dyskeratotic | | | | | * *ELISA*: positive for | | | prednisolone | | |
| and al. |  | | |  | acantholytic cells in | | | | | anti-desmoglein 1 antibody | | | 30 mg/d | | |
|  |  | | |  | infundibulum of hair | | | | |  | | |  | | |
|  |  | | |  | follicle | | | | |  | | |  | | |
| Maderal and al. | 19 | | | Right cheek and | Intercellular staining | | | | | * *DIF*: positive | | | clobetasol | | |
|  |  | | | temple | with IgG and C3 | | | | | * *ELISA*: negative for | | | prednisone 60 mg with gradual taper | | |
|  |  | | |  |  | | | | | desmogleins 1 and 3 | | |  | | |
| Ramzi and al[8] | 62 | | | Trunk and limbs | ND | | | | | ND | | | Intralesional Rituximab | | |
|  |  | | |  |  | | | | |  | | |  | | |
| Lapointe and al [9] | 81 | | | Right temple cheek and nose | parakeratosis,  acanthosis,and spongiosis of the epidermis | | | | | *DIF*: intercellular deposition of IgG and C3 in the epidermis | | | Doxycycline 100mg twice daily | | |
| Espadas and al [10] | 38 | | | Cheeks and nose | orthokeratosis, focal parakeratosis, intraepidermal blisters with acantholytic and dyskeratotic cells | | | | | ND | | | topical betamethasone valerate 1% cream twice daily | | |
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**Table.1C: Summary of publications on localized pemphigus foliaceus-3**

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| --- | --- | --- | --- | --- | --- | --- |
| Author | Age | Location of lesions |  | Pathology findings | DIF, IIF, and/or ELISA | Traitment |
| Kunadia and al. | 15  60  70    50      80 | Left face  Right face  Scalp and forehead    Back    Scrotum | subcorneal blister with suprabasal epidermal acantholysis and a mixed inflammatory infiltrate with neutrophils and eosinophils | | *DIF*: heavy IgG and C3 staining in the upper epidermis and negative staining of the basement membrane zone. | Topical clobetasol  Initial systemic prednisone 40 mg/day, dapsone 100 mg/day  Initial systemic prednisone 40 mg/day Dapsone 100 mg/day  Dapsone 25 mg/day (1 month) later increased to 100 mg/day  Topical betamethasone dipropionate cream daily  Pimecrolimus 1% topical cream twice/day  Halobetasol cream+tacrolimus 0.1% ointment  Dapsone 75 mg/day+topical desonide 0.05% cream for 1.5 years  Dapsone 50 mg/day for 3 years |
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| Chhabra and al. [11] | 57 | Face neck, upper trunk, and both upper limbs | subcorneal bullae with acantholytic cells | | * *DIF*: positive | dexamethasone cyclophosphamide pulse therapy |
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|  |  |  |  | |  |  |
| Sadafi and al. [12] | 75 | Nose | Acantholytic cells | | * *DIF*: positive * *ELISA*: positive for anti-desmoglein 3 | mycophenolate mofetil 1500 mg twice daily, dapsone 50 mg daily, and prednisone 17.5 mg daily. |
|  |  |  |  | |  |  |
| Milani-Nejad and al.[13] | 68 | Right lower extremity distal to the knee | ND | | * *DIF*: prominent intercellular immunoglobulin G and C3 deposition throughout the epidermis | Topical corticosteroids |
|  |  |  |  | |  |  |
|  |  |  |  | |  |  |
|  |  |  |  | |  |  |
| Ghoneim and al.[14] | 37 | Left ala of the nose | intergranular acantholysis and intradermal lymphocytic infiltration | | * *DIF*: intercellular anti-desmoglein antibodies (IgG) and complement component-C3 | Triamcinolone ointment and a onetime intralesional injection of triamcinolone 2.5 mg/mL. |
|  |  |  |  | |  |  |
| Walker and al. [15]  Loubaris and al | 51  70 | Right cheek  Left hamiface | prominent epidermal hyperplasia and lymphocytic dermal infiltrate and acantholytic cells  Acanthotic epidermis with superficial intraepidermal cleavage and acantholytic cells within the cleavage zone | | *DIF*: intercellular IgG and C3 deposition throughout the epidermis  *DIF*: Positive | Oral prednisone and mycophenolate mofetil  Oral prednisone at a dosage of 1.5 mg/kg/day, in addition to rituximab |
|  |  |  |  | |  |  |

**Figure 1: A 70-year-old female patient with an erythematous plaque with mild scaling on her left hemiface, showing a segmental distribution before treatment (a). After treatment, the lesion completely healed with no evidence of residual scarring (b).**

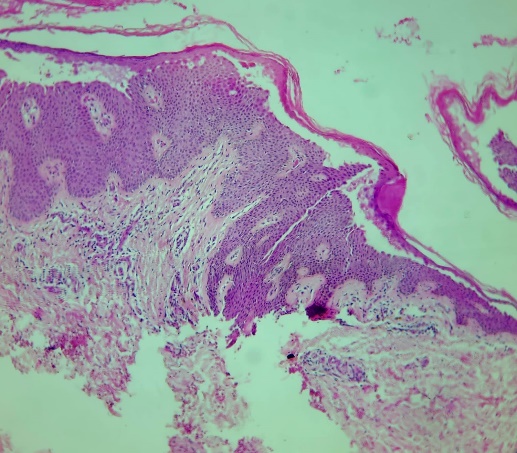
**** **Une image contenant Visage humain, personne, peau, joue

Le contenu généré par l’IA peut être incorrect.**

a

b

**Figure 2: Histopathology showing acanthotic epidermis, with superficial intraepidermal cleavage and acabntholytic cells ( 10 x).**

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4. Conclusion

This case emphasizes the importance of maintaining a high index of suspicion for pemphigus in patients with chronic, non-responsive facial plaques, even when the presentation is localized and atypical. Early biopsy and immunofluorescence studies are critical in establishing the diagnosis and guiding appropriate treatment. The successful management of this patient with systemic corticosteroids and rituximab demonstrates the efficacy of this therapeutic approach in achieving disease remission. This case contributes to the growing body of literature on the diverse clinical manifestations of pemphigus and underscores the need for individualized patient care in managing this complex autoimmune disorder.

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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