CASE REPORT
Acute Bullous Disease in Polymyalgia Rheumatica

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Abstract: Polymyalgia rheumatica (PMR) is a common inflammatory condition affecting elderly patients, often presenting with non-specific symptoms that complicate diagnosis. We report the case of a 75-year-old female with a history of PMR and multiple comorbidities, admitted for dysphagia and vesiculobullous skin and mucosal lesions. Despite inconclusive histopathological findings and limited access to specific autoantibody testing, the clinical presentation raised suspicion of a bullous autoimmune dermatosis, possibly drug-induced. The patient responded favorably to immunosuppressive and antimicrobial therapy. This case highlights the diagnostic challenges in overlapping autoimmune syndromes and underscores the importance of interdisciplinary management in complex immunomodulated patients.

Keywors: *polymyalgia rheumatica, bullous dermatoses, autoimmune skin disease, pemphigoid, immunosuppression.*

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INTRODUCTION

Polymyalgia rheumatica is the most common inflammatory rheumatic condition. It affects individuals over the age of 50 and is 2 to 3 times more prevalent among women. The most frequent symptoms include pain and morning stiffness in the shoulder and pelvic girdles, with onset that may be either acute or develop gradually over several days or weeks. The underlying pathophysiological mechanisms involve periarticular and synovial inflammatory processes, as well as muscular vasculopathies [1].

Currently, there is no established gold standard for the diagnosis of this condition, a fact underscored by the non-specific nature of its clinical manifestations, laboratory findings, and serological tests. Nevertheless, in current clinical practice, the diagnosis of polymyalgia rheumatica can be supported by the combination of morning stiffness and pain localized to the shoulder and pelvic girdles in a patient over the age of 50 years, who also presents markers of systemic inflammation. Furthermore, a rapid clinical response to glucocorticoid therapy and the exclusion of other potential causes of the presenting symptoms are additional elements that support the suspicion of polymyalgia rheumatica [2].

In 2012, both the American College of Rheumatology (ACR) and the European Alliance of Associations for Rheumatology (EULAR) established a joint set of provisional classification criteria. These were designed to improve the understanding of the disease and to facilitate the proper inclusion of research cohorts in future studies. The mandatory criteria continue to include age over 50 years, bilateral shoulder girdle pain, and elevated levels of C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR) [3,4].

Table 1. Provisional EULAR-ACR Classification Criteria for Polymyalgia Rheumatica [4].

Mandatory criteria: age over 50 years, bilateral shoulder girdle pain, and elevated C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR).		
	Without ultrasound	**With ultrasound**
Morning stiffness lasting more than 45 minutes	2	2
Morning stiffness lasting more than 45 minutes	1	1
Absence of rheumatoid factor and anti-cyclic citrullinated peptide (anti-CCP) antibodies	2	2
Absence of other joint involvement	1	1
Ultrasound: at least one shoulder with subdeltoid bursitis and/or biceps tenosynovitis and/or glenohumeral synovitis, and at least one hip with synovitis and/or trochanteric bursitis.	-	1
Ultrasound: subdeltoid bursitis and/or bicipital tenosynovitis and/or glenohumeral synovitis in both shoulders.	-	1
Without ultrasound: a score ≥ 4 is indicative of polymyalgia rheumatica, with a sensitivity of 68% and a specificity of 78%. **With ultrasound:** a score ≥ 5 is indicative of polymyalgia rheumatica, with a sensitivity of 66% and a specificity of 81%.		

CASE PRESENTATION

We present the case of a 75-year-old female patient with a known medical history of polymyalgia rheumatica, type 2 diabetes mellitus (managed with oral antidiabetic agents), permanent atrial fibrillation, and grade II obesity. She was admitted to the Department of Internal Medicine III at Colentina Clinical Hospital, Bucharest, Romania, approximately one month after her most recent medical evaluation, presenting with high dysphagia and odynophagia that had begun about ten days prior.

It is noteworthy that, prior to admission, the patient had self-administered antibiotic therapy consisting of one tablet of Amoxicillin-Clavulanic Acid 875/125 mg daily for 7 days. During this period, the clinical picture did not improve; instead, it worsened, with the appearance of erythematous skin lesions on the nasal and zygomatic areas, which evolved into vesiculobullous eruptions (Fig. 1). At the time of admission, these lesions contained serous-citrinous fluid deposits.

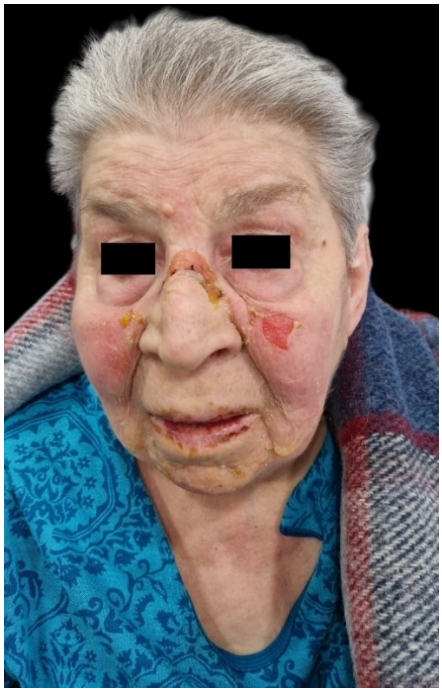


Figure 1. Erythematous vesiculobullous skin lesions at the time of presentation.

Additionally, due to pronounced dysphagia, the patient reported an unintentional weight loss of approximately 10 kg over the course of one month. She had no history of drug allergies, is a non-smoker, does not consume alcohol, and reports no occupational exposure to harmful substances.

The patient's outpatient medication regimen included: Prednisone 10 mg/day, Rivaroxaban 20 mg/day, Carvedilol 50 mg/day, Candesartan 32 mg/day, Lercanidipine 20 mg/day, Atorvastatin 40 mg/day, Esomeprazole 20 mg/day, Dulaglutide 1.5 mg subcutaneous injection once weekly, Dapagliflozin 10 mg/day, Alfacalcidol 0.5 mcg/day, Cinnarizine–Dimenhydrinate 20/40 mg/day, Vinpocetine 10 mg/day, and dietary supplements containing Citicoline–Bacopa monnieri 500/100 mg/day, as well as a combination of Ashwagandha–Bacopa monnieri–Nardostachys jatamansi 100/30/15 mg/day.

On physical examination, the patient appeared in poor general condition, with a body mass index (BMI) of 28.02 kg/m² and a suffering facial expression. She presented with erythematous, bullous facial skin lesions containing fluid, some covered with hemorrhagic crusts, along with xerotic skin and submammary intertrigo. The nasal, oral, and oropharyngeal mucosae were markedly congested, exhibiting multiple ulcerative lesions and gingival hypertrophy, as well as multiple whitish deposits on the tongue. Global muscle strength was decreased. Postural abnormalities included right-convex lumbar scoliosis and rounded thoracic kyphosis.

Peripheral oxygen saturation (SpO_2) was 95% on room air at rest, respiratory rate was 17 breaths per minute. Bilateral basal fine and subcrepitant crackles were noted. Blood pressure was low (90/60 mmHg in both arms, in the supine position), with a heart rate of 105 bpm, irregular, and a soft systolic ejection murmur was heard over the mitral and aortic areas. Varicose veins were present in the lower limbs. The abdomen was distended due to adipose panniculus, tympanic on percussion, and non-tender to palpation or spontaneously. The remainder of the physical examination was within normal limits.

From a laboratory standpoint, upon admission, the patient presented with a biological inflammatory syndrome characterized by leukocytosis (13,120/mm³) and neutrophilia (9,210/mm³), LDH = 221 U/L, ESR = 57 mm/h, fibrinogen = 621 mg/dL, C-reactive protein (CRP) = 208.15 mg/L, and procalcitonin = 1.79 ng/mL. Serum protein electrophoresis revealed elevated alpha-2 (13.10%) and alpha-1 (6.90%) globulin fractions. Cardiac enzymes were altered, with NT-proBNP = 2,077 pg/mL and high-sensitivity troponin T (hs-Troponin T) = 65.60 pg/mL. Laboratory findings also indicated a nitrogen retention syndrome, with serum creatinine = 2.53 mg/dL and serum urea = 97.30 mg/dL. The tumor marker CA-125 was also elevated at 59.50 U/mL.

A dermatological consultation was requested, raising the suspicion of either drug-induced pemphigus vulgaris or a post-medication reaction. As such, Tzanck cytodiagnosis, skin biopsy, and histopathological examination were recommended, along with topical treatment using emollient- and glycerin-based ointments. Both the Tzanck smear and skin biopsy with cytological analysis revealed non-specific acute inflammation. The skin punch biopsy identified an extensive area of epidermal necrosis, associated with a moderate lymphocytic inflammatory infiltrate, with perivascular and diffuse interstitial distribution of neutrophils.

Additionally, direct immunofluorescence testing yielded negative results for IgG, IgA, IgM, and complement component C3. Finally, paraffin-embedded histopathological examination concluded the presence of a non-specific chronic ulcerated dermatitis.

Regarding dysphagia and odynophagia, the ENT specialist identified the presence of

pseudomembranes on the buccal mucosa, hypopharynx, and soft palate, and recommended the initiation of topical anti-inflammatory treatment and avoidance of mucosal trauma.

The infectious component of the case was also investigated by collecting samples from the nasal, pharyngeal, lingual, and cutaneous sites for colonization screening; all results were negative. Given the persistent inflammatory profile, the infectious disease specialist raised the suspicion of possible facial cellulitis and recommended initiating broad-spectrum antimicrobial therapy with Meropenem 1 g/24 h and Fluconazole 200 mg/24 h.

Chest radiography showed no changes compared to the previous imaging performed during the patient's last hospitalization (January 15, 2024). The electrocardiogram revealed atrial fibrillation with a rapid ventricular response (135 bpm), signs of left ventricular hypertrophy (LVH), and ST segment depression in leads I, III, and aVL.

Topical treatment was initiated, along with systemic antibiotic therapy as per the infectious disease specialist's recommendation, consisting of a carbapenem (meropenem) and a triazole antifungal agent (fluconazole). The clinical course was favorable, with improvement observed both in the cutaneous lesions (Figure 2 and 3) and in inflammatory markers (Figure 4).

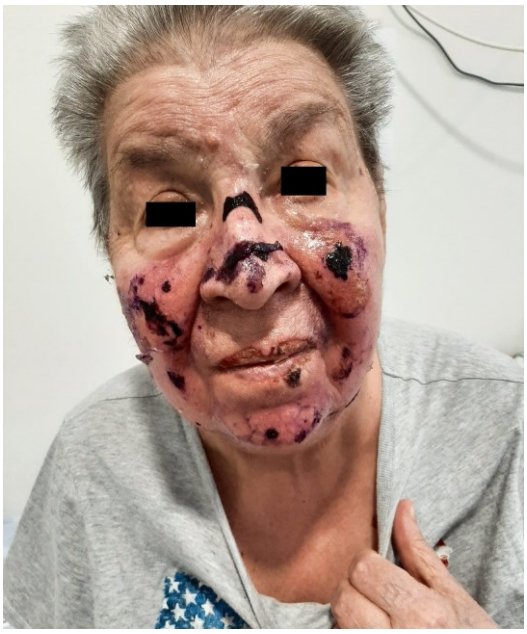


Figure 2. Clinical status of the patient 10 days after admission

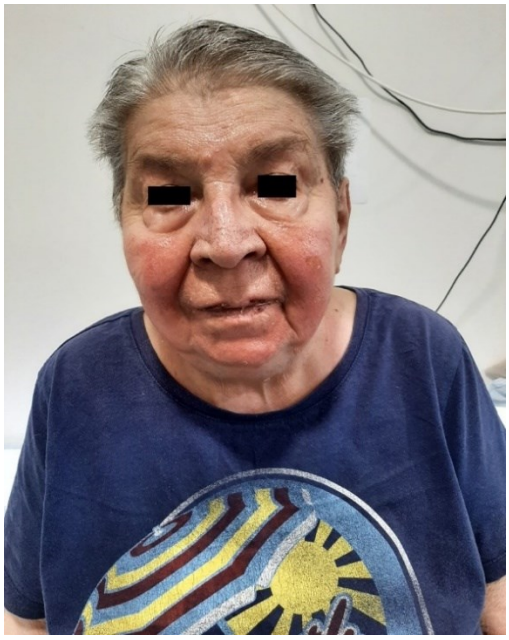
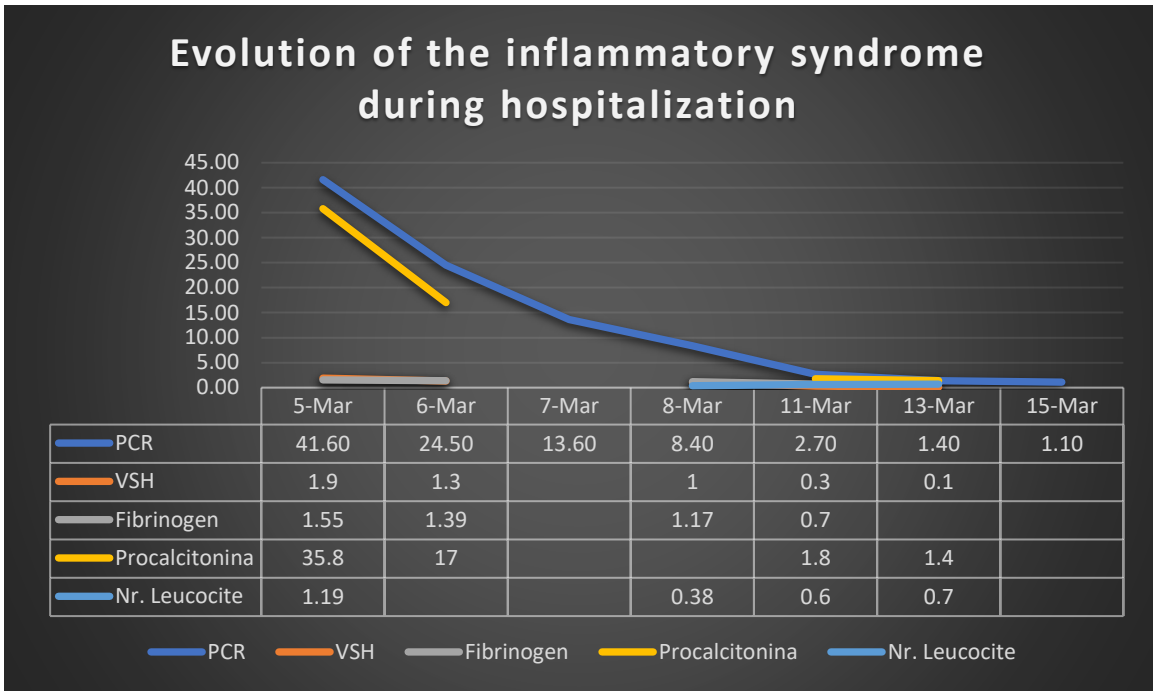


Figure 3. Clinical status of the patient 13 days after admission



	5-Mar	6-Mar	7-Mar	8-Mar	11-Mar	13-Mar	15-Mar
PCR	41.60	24.50	13.60	8.40	2.70	1.40	1.10
VSH	1.9	1.3		1	0.3	0.1	
Fibrinogen	1.55	1.39		1.17	0.7		
Procalcitonina	35.8	17			1.8	1.4	
Nr. Leucocite	1.19			0.38	0.6	0.7	

Figure 4. Dynamics of inflammatory markers throughout the hospital stay

Throughout the hospitalization, the patient continued immunosuppressive therapy with moderate-to-high-dose corticosteroids (methylprednisolone). A maximum dose could not be administered due to underlying cardiovascular comorbidities and fluid retention decompensation, which necessitated continuous diuretic depletion.

DISCUSSION

Autoimmune bullous diseases represent a group of disorders resulting from an autoimmune response directed against intercellular adhesion molecules or components of the basement membrane of the skin and mucous membranes. These conditions are frequently associated with significant morbidity and occasional mortality. They exhibit a marked female predominance and may occur at any age, though they are most commonly diagnosed between the ages of 40 and 60.

Autoimmune bullous diseases include both the pemphigus group—comprising pemphigus vulgaris and pemphigus foliaceus—and the pemphigoid group, which encompasses bullous pemphigoid, dermatitis herpetiformis, and acquired epidermolysis bullosa [5,6]. Both groups are characterized by the interaction between IgG-type autoantibodies and structural desmosomal proteins. In pemphigus vulgaris/foliaceus, these autoantibodies are directed against desmoglein-1, desmoglein-3, and other cadherin-like intercellular adhesion molecules[7-11]. In the pemphigoid group, the autoantibodies target hemidesmosomal proteins such as BP180, BP230, laminin 332, integrin α6β4, and type VII collagen [5,12]. Among the rare and atypical forms are IgA pemphigus, IgG/IgA pemphigus, and paraneoplastic pemphigus [6].

In the scientific literature, the term *autoimmune diathesis* is already used to emphasize the association between multiple immunologically mediated disorders [5]. In this context, numerous studies have investigated the relationship between bullous diseases and other immune-mediated pathologies.

A notable example is the interrelationship between bullous pemphigoid and psoriasis. A retrospective cohort study conducted in 2020, which included 3,924 patients with bullous

pemphigoid and 19,280 control subjects, found that patients with bullous pemphigoid were 2.6 times more likely to develop psoriasis compared to the control group. Moreover, the prevalence of pre-existing psoriasis was higher among patients with bullous pemphigoid. The same study also highlighted that a personal history of psoriasis was associated with a 50% increased risk of developing bullous pemphigoid [13].

A second example of disease association is the link between bullous pemphigoid and neurological disorders. This association has been highlighted by findings showing that patients with bullous pemphigoid are five times more likely to develop stroke, Alzheimer's disease, Parkinson's disease, or epilepsy [14,15]. Other reported associations include those between bullous pemphigoid and autoimmune thyroid disorders such as Hashimoto's thyroiditis and Graves' disease [16–18]. Moreover, a higher prevalence of anti-thyroid peroxidase antibodies has been observed in patients diagnosed with bullous pemphigoid [19].

At the same time, it is important to note that, to date, very few cases have been reported in the literature describing an association between pemphigus or pemphigoid and polymyalgia rheumatica. In this regard, we highlight a case reported in 1980 of a female patient who, over the course of four years, successively developed bullous pemphigoid, polymyalgia rheumatica, and hyperthyroidism [20].

Another distinctive feature of this case lies in the diagnostic challenge posed by the cutaneous and mucosal changes, given the discrepancy between the suggestive clinical signs and symptoms and the non-specific histopathological findings. This occurred in the context of the logistical unavailability of serological testing for pemphigus–pemphigoid-specific autoantibodies, such as anti-desmoglein-1, anti-desmoglein-3, BP180, and BP230.

CONCLUSIONS

In conclusion, this case further emphasizes the importance of investigating the associations between immune-mediated disorders, recognizing the risks involved in managing immunomodulated patients, and ensuring effective, interdisciplinary collaboration aimed at improving quality of life for affected individuals.

Author contributions:
A.B.D, D.N. and R.A.I. conceived the original draft preparation. V.A.I, G.G., I.A.B., A.B., and C.D. were responsible for the data acquisition, collection and assembly of the articles. A.B.D, D.N. and R.A.I. were responsible for the conception and design. D.N. and R.A.I. were responsible with the supervision of the manuscript.

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