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(CASE REPORT)

A rare clinical course of seronegative of diffuse alveolar hemorrhage coexisting with extra-capillary glomerular

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Abstract

Some disorders can cause concomitant kidney dysfunction with lung involvement. The diagnosis of diffuse alveolar hemorrhage (DAH) is considered in patients who develop progressive dyspnea with alveolar opacities on chest imaging and acute renal failure with proteinuria and hematuria occurs due to rapidly progressive glomerulonephritis (RPGN). These syndromes are caused by variable disorders the most frequent are ANCA associated vascularitis or goodpasture syndrome. DAH diagnosed by the presence of blood on bronchoscopic alveolar lavage, and RPGN by the presence of specific glomerular lesions on the renal biospy. Treatment should target the underlying disorder. Here, we describe in detail the clinical manifestations, diagnostic approach, and treatment of DHA in a 39-year-old male who presented an alveolar hemorrhage, with acute renal failure. Treatment involved the use of high-dose corticosteroids to suppress the autoimmune response. Finally, we discuss the striking response to corticosteroid treatment and emphasize the importance of early initiation of treatment.

Keywords: Corticosteroides; Thoracic Radiology; Diffuse Alveolar Hemorrhage; Diffuse Interstitial Lung Disease; Groundglass Opacity; Extracapillary Glomerular

1. Introduction

Pulmonary-renal syndrome (PRS) is a rare clinical condition defined by rapidly progressive glomerulonephritis (RPGN) and diffuse alveolar hemorrhage (DAH). Its etiology is mainly autoimmune and can be categorized by serological findings (ANCA; anti-GBM antibodies) and renal or pulmonary biopsy. In over 90% of the cases autoantibodies (ANCA, anti-GBM) can be detected, making unclassified PRS a diagnostically challenging entity to the clinician. Although the disease might proceed to cause serious consequences, it has could affect respiratory tracts. In over 80% of cases, renal problems such as glomerulonephritis develop. Glucocorticoids such as prednisone are used in combination with other medications that suppress the immune system to control inflammation. This case report presents an unusual clinical manifestation of PRS in a 39-year-old male presenting with alveolar hemorrhage with renal involvement.

2. Case Presentation

Here, we present the case of a 39-year-old male patient, with arterial hypertension treated by amlodipine 5mg 1 tablet by mouth each day. The patient was admitted to the Emergency department for etiological assessment of diffuse interstitial lung disease, associated with chronic anemia and acute renal failure in the context of altered general condition. Initially, the patient was hospitalized in nephrology for hemodialysis and treated with antibiotic therapy (C3G + levofloxacin) combined with short-term corticosteroid therapy without improvement and then we were consulted for an etiologic assessment of his diffuse interstitial lung disease. The patient has not traveled recently. He had worked as

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a farmer, and to his knowledge, had not taken care of any patients with a known infectious disease. He had no history of autoimmune disease. He did not use tobacco, did not do any recreational drugs and exposed to poultry. The patient reported stage II dyspnea and medium-grade hemoptysis for 20 days. Initial vital signs on admission revealed a conscious patient, with pale skin and mucous membranes, discolored conjunctiva, blood pressure, 161/78 mmHg, tachycardia at 120 beats/minute, and saturation at 94% AA. No skin lesions or peripheral neuropathy were noted. Ear, nose, and throat (ENT), pleuropulmonary, and cardiac examinations were normal. A frontal chest X-ray revealed an interstitial syndrome with bilateral infiltrative opacities (Figure 1).

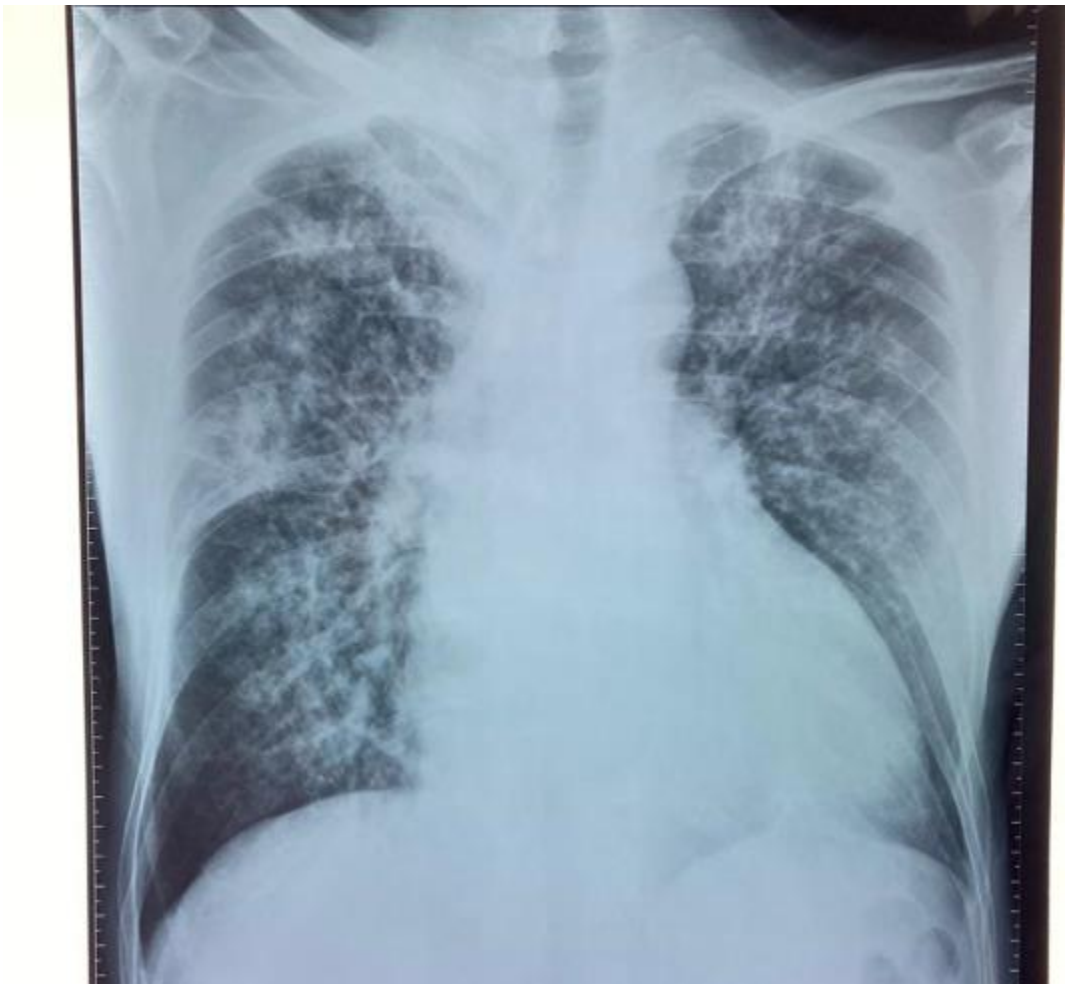

Figure 1 Posteroanterior chest radiograph demonstrating bilateral interstitial syndrome

The image shows diffuse bilateral infiltrative opacities predominantly in the middle and lower regions.

A biological workup showed normochromic normocytic regenerative anemia, negative C-reactive protein, normal white blood count, elevated D-dimers, negative 24-hour proteinuria, and elevated blood urea (Table 1).

Table 1 Laboratory Results

	RESULTING LABORATORY VALUE
COMPLETE BLOOD COUNT	
WHITE BLOOD CELLS	6740
HEMOGLOBIN	7.1
MEAN CORPUSCULAR VOLUME	84.1
MEAN CORPUSCULAR HEMOGLOBIN	34.3
PLAQUETTE	139000

BLOOD UREA NITROGEN	2.16
CREATININE	68.32
PROTEIN URINALYSIS	0.72
Anti-ANA	negative
Anti-DNA	negative
c-ANCA	negative
p-ANCA	negative

Table 1 : Test Observed Hemoglobin 7.1 g/dL 12-16 g/dL Mean corpuscular volume 79.9 fL 80-100 fL Average corpuscular hemoglobin content 24.1 pg 27-32 pg D-dimers 3,019.33 ng/mL p-ANCA Negative , ANA , Anti-DNA 24 UI/mL TABLE 1: Laboratory investigations WBC, white blood count; c-ANCA, antineutrophil cytoplasmic antibodies; p-ANCA, perinuclear anti-neutrophil cytoplasmic antibodies; ANA, antinuclear antibodies; anti-DNA, anti-double-stranded antibodies; FEIA, fluorescent enzyme immunoassay

Sputum tests for mycobacteria were negative. An immunological workup revealed the absence of ANCA with cytoplasmic fluorescence, and p-ANCA was negative. The rest of the immunological workup, particularly antinuclear antibodies (ANA), was negative also anti-DNA antibodies were negative. Chest computed tomography (CT) showed diffuse bilateral ground glass associated with septal and non-septal thickening, giving a crazy paving appearance, more marked in the upper lobes with sparing of the subpleural region, suggestive of alveolar hemorrhage (Figure 2).

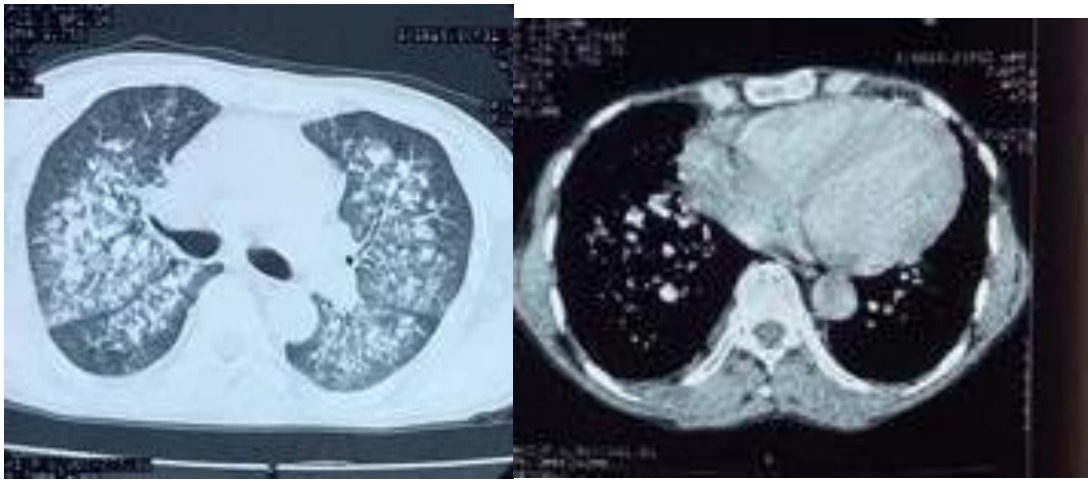

Figure 2 Chest computed tomography scan in the parenchymal window showing alveolar hemorrhage Chest computed tomography scan showing bilateral diffuse ground glass, giving a crazy paving appearance, more marked in the upper lobes with sparing of the subpleural region, suggesting alveolar hemorrhage. Associated with left sided cardiomegaly with RV:LV ratio <1

In spite of high CRP levels (62 mg/L) we suspected a relapse of a pulmonary-renal syndrome with pulmonary hemorrhage rather than an infection because of low PCT levels and a drop of hemoglobin from 10.6 to 7.1 g/dL within 5 days due to alveolar bleeding. Moreover, the patient showed no clinical improvement under long-lasting broad antibiotic treatment. Despite repeatedly negative results in laboratory testing for anti-ANA and ANCA a therapy with methylprednisolone (1 g/d) was started, continued for three days. After pulmonary stabilization a bronchoscopy with bronchoalveolar lavage (BAL) and Perls' staining revealed predominantly histiocytic macrophagic alveolitis with hemosiderosis.

A renal biopsy was performed and revealed extracapillary glomerular nephropathy and necrotic vasculitis lesions

The diagnosis of RPGN histologically established immunosuppressive continued by prednisolone 60 mg per day. .

After the definitive diagnosis of Pulmonary-renal syndrome with no detection of antibodies the treatment continued. No follow-up radiological examinations were conducted at the current time. The subsequent course was favorable, with good improvement in symptoms.

3. Discussion

The term pulmonary renal syndrome (PRS) is used to describe a combination of diffuse pulmonary hemorrhage and glomerulonephritis occurring as the presenting manifestation of multisystem autoimmune disease [1 The diagnosis of DAH is suspected in patients with hemoptysis, anemia, progressive dyspnea, and a pattern of focal or diffuse areas of ground glass opacities or consolidations on chest imaging [2-3]. The most common causes are systemic vasculitis, connective tissue disorders, immune-complex-mediated disorders, and post-transplant hemorrhages [2]. The occurrence of pulmonary renal syndrome, which is a rare and etiologically heterogeneous group of diseases, constitutes a medical emergency associated with a high risk of fatal outcome.

A bronchoscopy with bronchoalveolar lavage is the diagnostic gold standard for DAH, as the accumulation of blood can be seen in the alveolar spaces and infection can be more definitively ruled out [3]. Although, in the present patient, bronchoscopy was performed and the lavage specimens were obtained and revealed predominantly histiocytic macrophagic alveolitis with hemosiderosis.

Treatment consists of starting high-dose corticosteroids promptly to reduce inflammation and lung alveolar epithelial swelling [2]. When evaluating a patient with a possible pulmonary renal syndrome, ANCA and anti-GBM assays currently play a critical role in the diagnosis and classification of vasculitic syndrome. In 1982, antibodies directed against neutrophil cytoplasmic antigens were first described in patients with pauci-immune glomerulonephritis [4]. Studies suggest that over 90% of patients with PRS present with one or more antibodies (ANCA, anti-GBM) in the serum, making PRS with no detection of antibodies as in the above-mentioned case very rare [5–6], albeit there have been reports of seronegative relapses in anti-GBM disease after immunosuppressive therapy [7].

Although our patient was negative for ANCAs and anti-GBM antibody throughout hospitalization, Salama et al. reported that it is possible to prove the existence of low titer anti-GBM antibody using the Biosensor analysis (biomolecular interaction analysis system) for patients with anti-GBM disease [8].

In the renal biopsy, scarred crescents without linear deposition of IgG along the basement membrane emphasize the possibility of a seronegative ANCA-vasculitis with RPGN. A significant improvement of renal function as in our patient seems to make the diagnosis of an ANCA-associated vasculitis more probable.

The observation of almost complete convalescence of renal and pulmonary function despite delayed disease-specific treatment makes this case very interesting.

Clinical data concerning the course of patients with seronegative PRS is scarce and in most cases the disease leads to end-stage renal failure [5, 9, 10]. As in PRS with a detection of specific antibodies or typical findings in renal or pulmonary biopsy, treatment with corticoids and cyclophosphamide is the basis of any therapy for patients with a suspected seronegative PRS.

Glucocorticoid is the main therapy for the DAH syndrome associated with systemic vasculitis, connective tissue disease, and Goodpasture's syndrome. For the treatment of DAH, intravenous pulse methylprednisolone 500 to 2000 mg daily for up to five days was recommended in initial treatment, followed by gradual tapering depending on the response to therapy and then maintenance on an oral preparation [11]. In this patient, 1000 mg intravenous methylprednisolone daily for 3 days with a subsequent tapering dose of intravenous methylprednisolone and long-term oral prednisolone were administered.

In some cases plasma exchange has been described to have beneficial effects on patients with seronegative and therefore uncategorizable PRS [12].

4. Conclusions

Seronegative pulmonary-renal syndrome is a rare but potentially life-threatening clinical condition. As the diagnostic process is complicated by the absence of antibodies, end-stage renal disease and even death have been reported as a

common consequence of seronegative PRS. This case illustrates the rare instance of renal and pulmonary recovery after therapy with corticosteroids,

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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