Received: 7 February 2021 | Revised: 8 May 2021 | Accepted: 11 May 2021

DOI: 10.1002/ccr3.4369

CASE REPORT

Clinical Case Reports Open Access WILEY

# Granulomatosis with polyangiitis (Wegener's) complicated by splenic rupture and severe acute respiratory distress syndrome: A case report

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**Abstract**

Even in the absence of disease-specific radiological signs of granulomatosis with polyangiitis (GPA), severe intrapulmonary GPA may be present. Rapidly establishing the diagnosis with a confirmatory biopsy is key to initiate lifesaving therapy.

**KEYWORDS**

ARDS, ECMO, granulomatosis with polyangiitis, GPA, Wegener's

## 1 | INTRODUCTION

Granulomatosis with polyangiitis (GPA), formerly termed Wegener's granulomatosis, is an antibody-mediated vasculitis that mainly affects the upper respiratory tract, the lungs, and the kidneys, with an annual worldwide incidence of about 10-20 cases per million.[1,2] GPA can affect all organs; however, the number of affected organs is reported highly variable. According to the 2012 International Chapel Hill Consensus Conference,[3] GPA is a small-to-medium vessel necrotizing vasculitis leading to necrotizing granulomatous inflammation. While its onset is usually subacute, splenic involvement in GPA is reported in the literature, but life-threatening nontraumatic splenic rupture is rarely documented as primary manifestation. Furthermore, GPA rarely causes severe acute respiratory distress syndrome (ARDS) without radiologic evidence of pulmonary bleeding and/or granulomatosis. Here, we report a case of GPA with nontraumatic splenic rupture as primary manifestation followed by ARDS lacking prominent disease-specific findings on chest computed tomography (CT).

## 2 | CASE HISTORY

A 32-year-old, obese Caucasian (height 192 cm, weight 128 kg) with a past medical history of former intravenous drug abuse, moderate arterial hypertension, and minor ischemic stroke presented with diffuse myalgia of four weeks duration with profuse diaphoresis and weight loss of about five kilograms over two months. Initially suffering from odynophagia and myalgia for which he went to his family doctor and was started on amoxicillin and clavulanic acid for presumed pharyngitis plus prednisone for seven days. Ten days later, the patient developed suprapubic pain, dysuria, and alguria and was treated as an outpatient with ciprofloxacin for presumed urinary tract infection for seven days. Serological markers supporting an underlying viral infection with a compromised immune system returned negative for HIV, HCV, and HBV. Anti-HBs was 283 IE/l, indicating an immunocompetent response to a previous vaccination.

Persistent worsening myalgia and testicular pain finally lead to self-admission of the patient to a rural emergency

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department. On clinical examination, the patient had no fever, was hemodynamically stable, normotensive, and normocardic. The only abnormal clinical features were bilateral diffuse testicular tenderness with pain, and a slightly swollen lower limb showing a positive Homan's sign. Initial laboratory studies were as follows: white blood cell count 12.6 G/l, 74% banded neutrophils, C-reactive protein 119 mg/l, serum creatinine 56 μmol/l, and creatinine kinase 29 U/L. The patient was admitted to the medical ward. Urine analysis showed proteinuria (0.78 g/24 hours) with normal urine and serum protein electrophoresis. Blood and urine cultures returned negative. Ultrasound showed bilateral epididymitis with a predominantly right-sided orchitis and ceftriaxone was prescribed. Further, ultrasonic examination showed a deep vein thrombosis of the right leg for which the patient was prescribed a therapeutic dose of enoxaparin. A cervico-thoraco-abdominal CT scan returned normal.

Five days later, the patient complained about a painful left upper flank and a progressive hemoglobin decrease was noted. Abdominal contrast-enhanced CT scan revealed splenic rupture with subcapsular hematoma of about 16x16 cm, haemoperitoneum, and signs of active arterial bleeding (Figure 1). The patient was admitted to the intensive care unit and radiological embolization of the main splenic artery was performed, while systemic anticoagulation was suspended. Over time, the respiratory status worsened with the patient requiring intubation and mechanical ventilation for hypoxic respiratory failure (Figure 2). Follow-up thoracic CT showed predominant left-sided atelectasis, marginal pleural effusions without signs for pulmonary embolism, and no structural lung parenchymal abnormalities. Due to constant need for blood transfusions, progressive pulmonary deterioration—most likely multifactorial in origin but aggravated by this abdominal mass effect caused by the splenic rupture with subsequent massive abdominal hemorrhaging, a splenectomy was performed. This had an immediate positive effect on mechanical ventilation, at least temporary. Histological analysis showed subcapsulary necrosis and hematoma with central acute focal inflammation of small to larger arteries in the proximity of focal splenic necrosis (Figure 3). While waiting histological results, the patient developed severe ARDS requiring prone positioning to optimize oxygenation and muscular blocking agents in order to secure lung-protective ventilation with permissive hypercapnia.

In the light of the histopathological picture of splenic arteritis, vasculitis was suspected. With orchitis present as a prominent feature in this patient, polyarteritis nodosa (PAN) was considered, but when biomarkers returned highly positive for PR-3 antineutrophil cytoplasmic antibodies (ANCA), an ANCA-associated vasculitides was favored, suggesting GPA (298.8 IU/mL). Methylprednisolone was prescribed at 5mg/kg. In the light of persistent severe hypoxemia, a contrast-enhanced pulmonary CT scan was performed showing right lateral segmental and subsegmental pulmonary

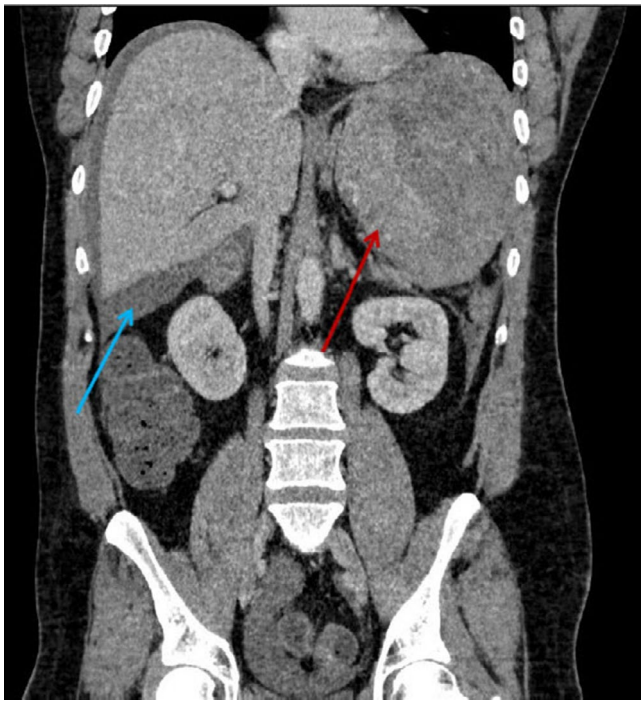

**FIGURE 1** Abdominal contrast-enhanced computed tomography (CT) showing splenic rupture, subcapsular hematoma, and active arterial bleeding (red arrow). Peri-hepatic hemoperitoneum is present (blue arrow)

embolism with discreet ground-glass infiltration without nodules (Figure 4A-C). Therapeutic heparinisation was reintroduced, and the patient was transferred to a tertiary care academic center for evaluation of veno-venous extracorporeal membrane oxygenation (ECMO) (Figure 2).

On admission to the tertiary care center, the patient's oxygenation was severely compromised (P/F-ratio 72 on 100% oxygen). Transesophageal echocardiography was unremarkable showing normal left and right ventricular dimensions and function with competent valves, no wall motion abnormalities and only a small patent foramen ovale, in summary not explaining this patients' severe hypoxemia (Video S1-S3). Intensive supportive therapy including a lung-protective ventilation strategy (Vt max. 6 mL/kg PBW, $P_{plat}$ <= 30 cm $H_2O$) with permissive hypercapnia, regularly assessing individual pulmonary mechanics (measuring quasi-static compliance and applying PEEP at highest Compliance (or adequate saturation)), proning, aggressive negative fluid balance, and emergency immunosuppressive therapy (pulse methylprednisolone 1 g) lead to partial stabilization with successful weaning of the supplemental O2 to 50% within 12 hours after admission to our ICU.

An emergency veno-venous ECMO therapy could therefore be avoided. Having averted the immediate life-threatening problem, drug-induced vasculitis (ie, cocaine) was considered, given the patient's history of former drug abuse. This was abandoned when repeat toxicological results came back negative. Urinalysis showed unspecific and moderate microscopic hematuria, of a presumed glomerular origin.

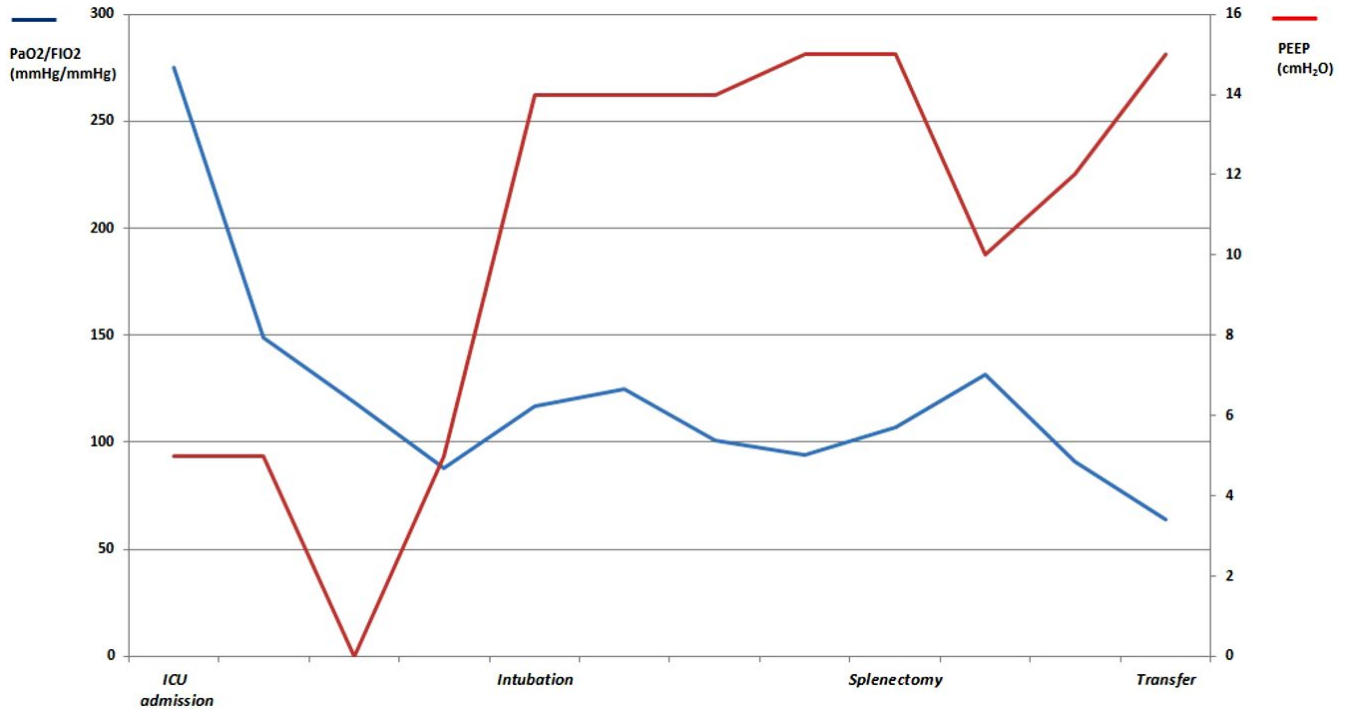


**FIGURE 2** (x) patient's time course; (y) oxygenation (blue, left y-axis) and applied PEEP (red, right y-axis)

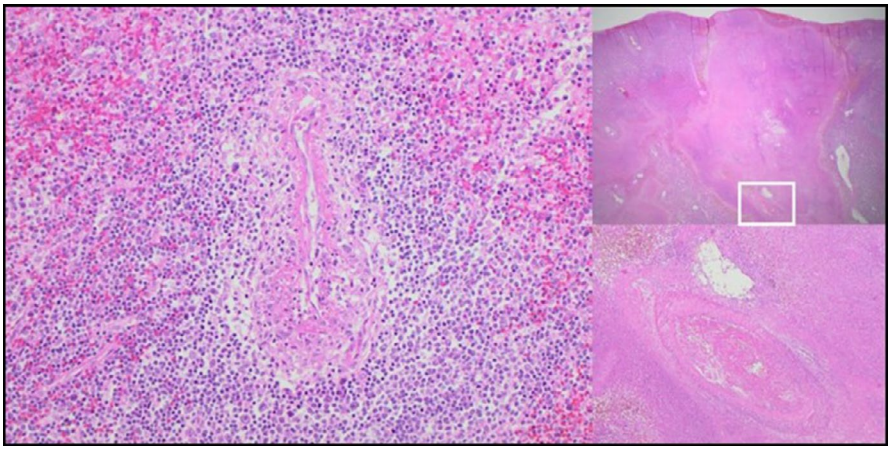

**FIGURE 3** Histology of the spleen showing subcapsulary necrosis and hematoma with central acute focal inflammation of a medium-sized artery in the proximity of focal splenic necrosis (hematoxylin/eosin)

On the subsequent day, emergency renal biopsy results confirmed necrotizing, pauci-immune crescentic glomerulonephritis (Figure 5). Total plasma exchange (TPE) was started followed by cyclophosphamide bolus (1g) iv with continued pulse methylprednisolone (1g per day for 3 days followed by 1mg/kg of body weight). Following immunosuppressive therapy, the patients' clinical evolution was rapidly favorable, and subsequent transfer to a community ICU for weaning from mechanical ventilation and treatment of intensive care unit acquired weakness was performed.

## 3 | DISCUSSION

Splenic involvement in GPA is rare and reported in only few patients.[4-6] Nevertheless, autopsy studies show a high percentage of splenic lesions suggesting frequent asymptomatic splenic involvement.[7] A recent report suggests that splenic lesions, that is, mainly vascular infarctions, are common in ANCA-associated vasculitis (AAV), particularly in GPA,[8] and may not always be visible on contrast-enhanced abdominal CT scans.[8,9] Splenic rupture is rarely described as a life-threatening condition, especially in the early stages of GPA. In the case presented here, splenic involvement was recognized early and finally pointed to the diagnosis of severe GPA (PR-3 ANCA titers). Interestingly, the reported unspecific symptoms including presumed urogenital tract infection and deep vein thrombosis were likely unspecific but presumably associated presentations of GPA. Anticoagulation might have supported intrasplenic bleeding in the presence of vasculitis. Thus, indication and anticoagulation management should trigger caution in severe GPA.

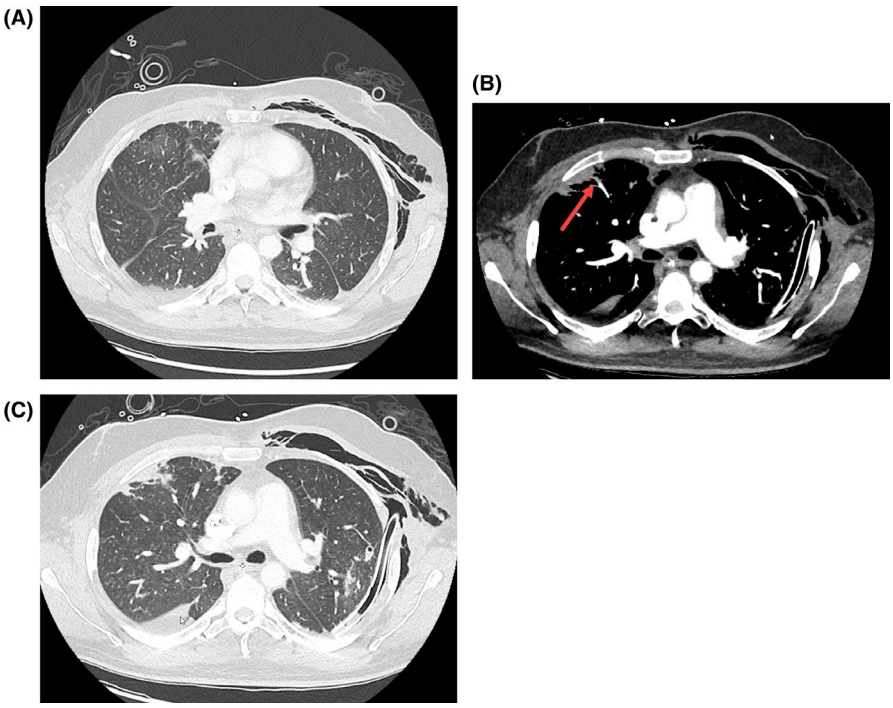


**FIGURE 4** (A) Pulmonary contrast-enhanced computed tomography (CT) showing minimal alterations of lung parenchyma and right-sided small pleural effusion. A left chest tube was placed during splenectomy with subcutaneous emphysema. (B) Pulmonary contrast-enhanced computed tomography (CT) showing segmental and subsegmental contrast agent filling defects indicating pulmonary embolism. (C) Pulmonary contrast-enhanced computed tomography (CT) showing discrete signs of bilateral pulmonary infiltrates

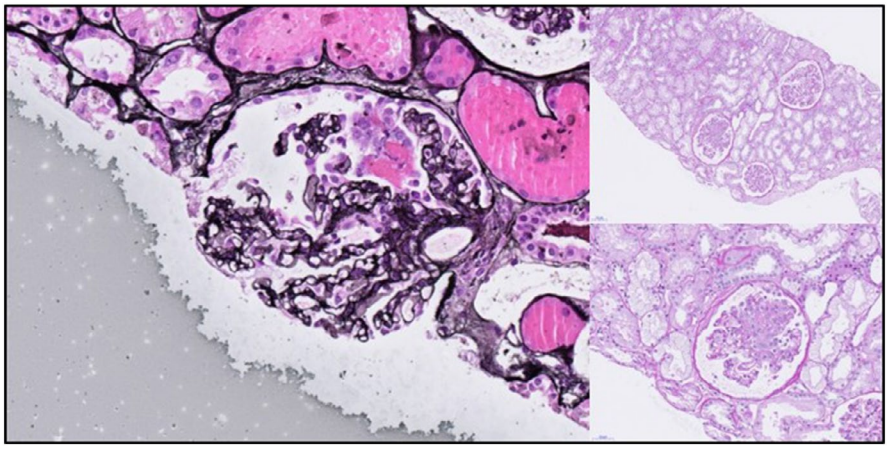

**FIGURE 5** Renal histology showing pauci-immune glomerulonephritis with partial (focal) necrosis (hematoxylin/eosin)

Alveolar hemorrhage is a common feature in severe GPA which may require ECMO[10] treatment in selected cases. However, the progression and the severity of pulmonary symptoms in our patient with oxygen-refractory respiratory failure leading to severe ARDS without distinct (ie, disease-specific) radiological findings were unusual. Chest CT patterns of lung parenchymal lesions related to arteritis typically include (besides alveolar bleeding) ground-glass opacities, reticular shadowing, interlobular septal thickening, consolidation/ granulomatosis, and honeycomb appearance. In severe GPA, the previously described consistency rate between radiological and lung histological findings on GPA patients was previously determined as 100%.[11] Pulmonary nodules and masses are the most common radiologic findings in GPA and are seen in up to 70% of patients either at presentation or during the course of the disease.[12] Diffuse ground-glass opacity and consolidation are noted in up to 50% of patients with GPA.[13] In the case presented here, despite severe hypoxemic respiratory failure fulfilling the BERLIN criteria for ARDS,[14] disease-specific radiological findings were lacking on repeat CT scans.

We thus conclude that even in the absence of disease-specific radiological signs of GPA, severe intrapulmonary GPA, likely induced by small- to medium-sized vasculitis may be present. This seems of prognostical importance and should institute guideline-based treatment including focused immunosuppressive therapy.

## ACKNOWLEDGMENTS

Published with written consent of the patient.

## CONFLICT OF INTEREST

JCS and PZ declare that the Department of Intensive Care Medicine, Inselspital, Bern, has received research or other

grants from (full departmental disclosure): Orion Pharma, Abbott Nutrition International, B. Braun Medical, CSEM, Edwards Lifesciences Services, Kenta Biotech, Maquet Critical Care, Omnicare Clinical Research, Nestle, Pierre Fabre Pharma, Pfizer, Bard Medica, Abbott, Anandic Medical Systems, Pan Gas Healthcare, Bracco, Hamilton Medical, Fresenius Kabi, Getinge Group Maquet, Dräger, Teleflex Medical, Glaxo Smith Kline, Merck Sharp and Dohme, Eli Lilly and Company, Baxter, Astellas, Astra Zeneca, CSL Behring, Novartis, Covidien, Hemotune, Phagenesis, and Nycomed outside the submitted work. The money was paid into departmental funds. No personal financial gain applies. All other authors declare no financial or nonfinancial conflict of interest.

## AUTHOR CONTRIBUTIONS

YA and GM: involved in acquisition of data, drafting of manuscript, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved final approval of the version to be published. HK: involved in contribution to the conception of the work, revising it critically for important intellectual content, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved final approval of the version to be published. JCS: involved in direct patient treatment, conception of the work, critical revision for important intellectual content, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved final approval of the version to be published. PZ: involved in direct patient treatment, acquisition of data, codrafting of manuscript, critical revision for important intellectual content, approval of the final version, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved final approval of the version to be published.

## ETHICAL APPROVAL

The patient has provided written consent.

## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

**How to cite this article:** Ahmad Y, Morawietz G, Ksouri H, Schefold JC, Zuercher P. Granulomatosis with polyangiitis (Wegener's) complicated by splenic rupture and severe acute respiratory distress syndrome: A case report. *Clin Case Rep*. 2021;9:e04369. https://doi.org/10.1002/ccr3.4369