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...
department. On clinical examination, the patient had no fever, was hemodynamically stable, normotensive, and normocar
dic. 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 cre-
tatinine 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 pre-
scribed. Further, ultrasonic examination showed a deep vein
thrombosis of the right leg for which the patient was pre-
scribed 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 rup-
ture with subcapsular hematoma of about 16x16 cm, haemo-
peritoneum, and signs of active arterial bleeding (Figure 1).
The patient was admitted to the intensive care unit and radi-
ological embolization of the main splenic artery was performed,
while systemic anticoagulation was suspended. Over time, the
respiratory status worsened with the patient requiring intuba-
tion 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 multifac-
torial in origin but aggravated by this abdominal mass effect
caused by the splenic rupture with subsequent massive abdomi-
nal hemorrhaging, a splenectomy was performed. This had an
immediate positive effect on mechanical ventilation, at least
temporary. Histological analysis showed subcapsular 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 de-
developed severe ARDS requiring prone positioning to optimize
oxygenation and musculat blocking agents in order to secure
lung-protective ventilation with permissive hypercapnia.

In the light of the histopathological picture of splenic ar-
teritis, vasculitis was suspected. With orchitis present as a
prominent feature in this patient, polyarteritis nodosa (PAN)
was considered, but when biomarkers returned highly posi-
tive 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 show-
ing right lateral segmental and subsegmental pulmonary
embolism with discreet ground-glass infiltration without
nodules (Figure 4A-C). Therapeutic heparinisation was re-
introduced, and the patient was transferred to a tertiary care
academic center for evaluation of veno-venous extracorpo-
real membrane oxygenation (ECMO) (Figure 2).

On admission to the tertiary care center, the patient’s oxy-
genation was severely compromised (P/F-ratio 72 on 100%
oxygen). Transesophageal echocardiography was unremark-
able 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 explain-
ing this patients’ severe hypoxemia (Video S1-S3). Intensive
supportive therapy including a lung-protective ventilation strat-
egy (Vt max. 6 mL/kg PBW, Pplat <= 30 cm H₂O) with per-
missive hypercapnia, regularly assessing individual pulmonary
mechanics (measuring quasi-static compliance and applying
PEEP at highest Compliance (or adequate saturation)), pron-
ing, aggressive negative fluid balance, and emergency immu-
nosuppressive therapy (pulse methylprednisolone 1 g) lead to
partial stabilization with successful weaning of the supplement-
al O2 to 50% within 12 hours after admission to our ICU.

An emergency veno-venous ECMO therapy could there-
fore 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 nega-
tive. Urinalysis showed un specific and moderate microscopic
hematuria, of a presumed glomerular origin.
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. Nevertheless, autopsy studies show a high percentage of splenic lesions suggesting frequent asymptomatic splenic involvement. A recent report suggests that splenic lesions, that is, mainly vascular infarctions, are common in ANCA-associated vasculitis (AAV), particularly in GPA, and may not always be visible on contrast-enhanced abdominal CT scans. 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.
Alveolar hemorrhage is a common feature in severe GPA which may require ECMO\(^\text{[10]}\) 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%.\(^\text{[11]}\) 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.\(^\text{[12]}\) Diffuse ground-glass opacity and consolidation are noted in up to 50% of patients with GPA.\(^\text{[13]}\) In the case presented here, despite severe hypoxemic respiratory failure fulfilling the BERLIN criteria for ARDS,\(^\text{[14]}\) 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.

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**CONFLICT OF INTEREST**

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

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