

Tocilizumab treatment for high-altitude antisynthetase syndrome-associated interstitial lung disease complicated by rectus sheath hematoma: A case report

Li Yang

Lhasa People's Hospital

Zhuoga Ci

Lhasa People's Hospital

Dandan Shi

Lhasa People's Hospital

Jiaxin Yang

Lhasa People's Hospital

Xingya Shi

Lhasa People's Hospital

Yuntao Zhang

412814726@qq.com

Lhasa People's Hospital

Case Report

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Abstract

Introduction:

Anti-Jo-1 antibody-positive antisynthetase syndrome (ASS) is frequently complicated by interstitial lung disease (ILD), and some patients respond poorly to glucocorticoids. The impact of chronic high-altitude hypoxia on the progression of ASS-ILD remains poorly documented. Tocilizumab (TCZ) has shown efficacy in refractory ASS-ILD; however, TCZ-induced hypofibrinogenemia when combined with anticoagulation may increase bleeding risk. Moreover, persistent elevation of creatine kinase (CK) after treatment is often attributed to ongoing myositis activity, but local tissue injury can also cause marked CK elevation and may influence therapeutic decisions. To the best of our knowledge, this is the first report of TCZ treatment for ASS-ILD in a patient residing at high altitude, documenting a life-threatening rectus sheath hematoma associated with TCZ-induced hypofibrinogenemia during concurrent anticoagulation.

Case presentation:

A 54-year-old Tibetan woman living at high altitude(3,650m) presented with a 7-day history of dry cough, dyspnea, and fatigue. Initial methylprednisolone treatment was effective; however, after discontinuation, she rapidly developed acute respiratory distress syndrome requiring endotracheal intubation. Anti-Jo-1 antibody positivity confirmed the diagnosis of ASS-ILD. Re-administration of methylprednisolone was ineffective. After a single intravenous dose of TCZ, pulmonary lesions improved markedly, but fibrinogen levels continued to decline. Due to deep vein thrombosis, anticoagulation therapy was initiated, and 6 days later, she developed large bilateral rectus sheath hematomas. Following intensive treatment, her condition stabilized. Although interleukin-6 and C-reactive protein levels normalized, CK remained persistently elevated. Subsequent surgery revealed rectus sheath necrosis as the cause of CK elevation, and CK levels decreased significantly after surgery.

Conclusion

TCZ may effectively treat glucocorticoid-refractory ASS-ILD at high altitudes; however, TCZ-associated hypofibrinogenemia may contribute to severe bleeding complications, particularly when combined with anticoagulation. During TCZ therapy, regular monitoring of fibrinogen levels and individualized anticoagulation management are essential. The potential influence of high-altitude hypoxia on ASS-ILD progression requires further investigation. In addition, elevated CK levels in patients with ASS should be carefully evaluated to distinguish active myositis from other causes, as this may directly affect treatment decisions.

Background

Antisynthetase syndrome (ASS) is a distinct subtype of idiopathic inflammatory myopathy characterized by the presence of anti-aminoacyl-tRNA synthetase antibodies. Approximately 70% of patients develop interstitial lung disease (ILD), and 20%–40% may present with rapidly progressive ILD (RP-ILD) [1, 2]. Chronic hypoxia at high altitude may upregulate hypoxia-inducible factor-1 α (HIF-1 α) expression and promote the production of inflammatory cytokines, including interleukin-6 (IL-6), which may contribute to more aggressive ASS-ILD progression [3, 4]. Although glucocorticoids remain the mainstay of treatment, their efficacy is limited in some refractory patients. Tocilizumab (TCZ), an IL-6 receptor inhibitor, has shown potential efficacy in refractory ASS-ILD [5, 6]. However, TCZ may reduce hepatic fibrinogen synthesis through inhibition of IL-6 signaling, thereby increasing bleeding risk [7]. Furthermore, elevated creatine kinase (CK) levels in patients with ASS require careful evaluation to distinguish active myositis from non-myositis causes. Here, we report a case illustrating the balance between efficacy and safety of TCZ in high-altitude ASS, highlighting the risk of unusual-site bleeding associated with TCZ-related hypofibrinogenemia during anticoagulation and emphasizing the importance of identifying the cause of CK elevation in ASS patients.

Case presentation

A 54-year-old Tibetan woman, a long-term resident of Lhasa (3,650 m), with no smoking history and untreated chronic hepatitis B, presented in March 2026 with a 7-day history of dry cough, dyspnea on exertion, and fatigue. She denied rash, myalgia, Raynaud's phenomenon, or muscle weakness. On admission, her respiratory rate was 26 breaths/min, and oxygen saturation on room air was 86%. Lung auscultation revealed coarse breath sounds without crackles or wheezes. Chest computed tomography (CT) showed multiple patchy and nodular opacities in both lungs (Fig. 1a). C-reactive protein (CRP) was 57.65 mg/L, and myoglobin was mildly elevated. A presumptive diagnosis of viral pneumonia was made, and empirical therapy with antiviral agents, broad-spectrum antibiotics, and methylprednisolone 40 mg/day was initiated. On day 7, repeat CT showed partial resolution of pulmonary lesions (Fig. 1b), and methylprednisolone was discontinued.

After steroid withdrawal, dyspnea gradually worsened. By day 13, the respiratory rate increased to 34 breaths/min, and oxygen saturation decreased to 65% despite face mask oxygen at 8 L/min (PaO₂/FiO₂ ratio: 142) (Table 1). Repeat CT showed increased diffuse ground-glass opacities (Fig. 1c). She was transferred to the respiratory intensive care unit (RICU) and underwent endotracheal intubation and mechanical ventilation (pressure-controlled assist-control mode [P-AC], positive end-expiratory pressure [PEEP] 12 cmH₂O, pressure support [PS] 16 cmH₂O, and fraction of inspired oxygen [FiO₂] 70%) because of severe respiratory failure. Treatment included meropenem, moxifloxacin hydrochloride, methylprednisolone (80 mg/day), mucolytics, and nutritional support. Bronchoscopy showed mucosal hyperemia and a small amount of bloody secretions. Metagenomic next-generation sequencing of bronchoalveolar lavage fluid detected *Candida albicans* (44,531 sequence reads), and fluconazole was added. Immunofluorescence testing for myositis-specific antibodies revealed anti-Jo-1 antibody positivity (1:320, ++), while all other antibodies were negative. Based on the clinical features and imaging findings, a diagnosis of anti-Jo-1-positive ASS-associated rapidly progressive ILD was established.

Table 1
Clinical course and key parameters from admission to recovery

Time point	Event	Key clinical parameters	Subsequent changes
Day 1 (admission)	Presented with 7-day history of dry cough, dyspnea, and fatigue	SpO ₂ 86% (room air); chest CT showed bilateral patchy nodular opacities; CRP 57.65 mg/L	Started on methylprednisolone 40 mg/day
Day 7	Follow-up CT showed partial absorption; methylprednisolone discontinued	CT lesions partially resolved	Clinical improvement
Day 13	Relapse after discontinuation; transferred to RICU	Oxygenation index 142; chest CT showed increased diffuse ground-glass opacities; elevated IL-6 and CRP	Intubated; methylprednisolone increased to 80 mg/day; antibiotics initiated
Day 15	Right upper-extremity deep vein thrombosis detected	—	Enoxaparin started (4000 IU q12h → 5000 IU q12h)
Day 17	Single dose of tocilizumab (TCZ) 8 mg/kg IV; IVIG + inhaled nitric oxide for 3 days	Rapid decline in CRP and IL-6; CK 621 U/L; oxygenation index improved from 120 to 220 mmHg; PEEP reduced from 12 to 6 cmH ₂ Oa	Fibrinogen decreased from 2.7 to 1.07 g/L
Day 21	Bilateral rectus sheath hematomas developed	Hb dropped from 110 to 68 g/L; abdominal CT showed ~ 1100 mL hematoma; hemorrhagic shock occurred	Anticoagulation stopped; hemostatic therapy, blood transfusion, fibrinogen and cryoprecipitate supplementation
Day 24	Successful extubation	Oxygenation index recovered	Significant improvement in pulmonary imaging
Day 29	Persistent CK elevation; mycophenolate mofetil (MMF) added (0.75 g bid)	CK 945 U/L	Lungs improved but myositis markers remained high
Day 33	Surgical evacuation of hematoma	Intraoperative findings: local necrosis of rectus sheath	—
Day 36	Post-operative recovery	CK decreased to 510 U/L (reduction > 46%)	Follow-up: CRP, IL-6, and fibrinogen normalized; good respiratory function

Time point	Event	Key clinical parameters	Subsequent changes
	Abbreviations: SpO ₂ , peripheral oxygen saturation; CRP, C-reactive protein; CT, computed tomography; RICU, respiratory intensive care unit; IL-6, interleukin-6; TCZ, tocilizumab; IVIG, intravenous immunoglobulin; CK, creatine kinase; PEEP, positive end-expiratory pressure; Hb, hemoglobin; MMF, mycophenolate mofetil.		
	a Methylprednisolone was administered as a daily intravenous dose.		
	b Enoxaparin was given subcutaneously.		
	c The oxygenation index was calculated as PaO ₂ /FiO ₂ .		
	d TCZ was administered as a single infusion of 8 mg/kg body weight.		
	e MMF was started at 0.75 g twice daily.		
	f Surgical evacuation was performed on day 33.		
	g Follow-up assessments after day 36 showed normalization of inflammatory markers and good functional recovery.		

Despite high-dose methylprednisolone therapy, oxygenation did not improve, and CRP, IL-6, and myoglobin levels continued to increase, suggesting glucocorticoid-refractory disease. Given the markedly elevated IL-6 levels and previous reports suggesting a role of IL-6 in ASS-ILD, a multidisciplinary team (MDT) discussion was conducted. After obtaining informed consent from the family, a single intravenous dose of TCZ (8 mg/kg) was administered on day 17, together with intravenous immunoglobulin and inhaled nitric oxide for 3 days. CRP and IL-6 levels declined rapidly, oxygenation improved from 120 to 220 mmHg, and PEEP was reduced from 12 to 6 cmH₂O. However, following TCZ administration, fibrinogen levels decreased markedly from 2.7 g/L at baseline to 1.07 g/L (reference range: 2–4 g/L) and remained low despite supplementation with cryoprecipitate and fibrinogen concentrate.

Right upper extremity deep vein thrombosis was diagnosed, and enoxaparin anticoagulation was initiated on day 15 at 4,000 IU every 12 h and later increased to 5,000 IU every 12 h. On the sixth day of anticoagulation (day 21 of admission), the patient developed hemodynamic instability, with hemoglobin decreasing from 110 to 68 g/L. Abdominal CT revealed bilateral rectus sheath hematomas with an estimated volume of approximately 1,100 mL (Fig. 2). Anticoagulation was immediately discontinued, and hemostatic therapy, red blood cell transfusions, fibrinogen supplementation, cryoprecipitate, and vasopressor support were administered. Her hemodynamic status subsequently stabilized.

The patient was successfully extubated on day 24. Although pulmonary lesions improved markedly (Fig. 1d), CK levels remained persistently elevated. Mycophenolate mofetil (MMF, 0.75 g twice daily) was added on day 29, and surgical evacuation of the hematoma was performed on day 33. Intraoperatively, local necrosis of the rectus sheath was observed. CK levels decreased from 945 U/L preoperatively to 510 U/L on postoperative day 36. At follow-up, the patient recovered uneventfully, with gradual

absorption of the hematoma, continued decline in CK levels, normalization of CRP, IL-6, and fibrinogen levels, and preserved respiratory function.

Discussion

ASS is a distinct subtype of idiopathic inflammatory myopathy, and anti-Jo-1 antibody is the most common associated autoantibody. When ASS is complicated by ILD, the disease may progress rapidly; some patients respond poorly to glucocorticoids alone and develop ARDS, with reported mortality rates of 40%–60% [1, 2]. The impact of chronic high-altitude hypoxia on autoimmune lung diseases has attracted increasing attention; however, systematic data regarding the clinical characteristics, immune-inflammatory changes, and optimal treatment strategies for high-altitude ASS-ILD remain limited.

Our patient, a long-term high-altitude resident with anti-Jo-1-positive ASS-ILD, initially responded to corticosteroids but rapidly deteriorated after steroid withdrawal, progressing to ARDS with markedly elevated IL-6 levels. This presentation was consistent with the high-inflammation phenotype of ASS-ILD, which has been associated with glucocorticoid resistance, rapid progression, and poor outcomes [8]. IL-6 promotes Th17 cell differentiation, suppresses regulatory T-cell (Treg) function, stimulates B-cell autoantibody production, and contributes to pulmonary fibroblast activation and collagen deposition [9]. Chronic hypoxia associated with residence at high altitude may activate inflammatory pathways through HIF-1 α , increasing the production of pro-inflammatory cytokines such as IL-6 and TNF- α , potentially aggravating autoimmune inflammation and lung injury [3, 4]. However, the specific role of high-altitude hypoxia in ASS-ILD progression requires further investigation.

TCZ, an IL-6 receptor antagonist, blocks both membrane-bound and soluble IL-6 receptors, reducing systemic and local IL-6 signaling [10]. Previous retrospective studies and case series have suggested that TCZ may improve lung function, high-resolution computed tomography findings, and oxygenation in patients with c potential steroid-sparing effects [2, 5, 6]. In our patient, who showed inadequate response to high-dose methylprednisolone, TCZ administration resulted in rapid improvement in inflammatory markers, oxygenation, and pulmonary lesions. This case suggests that IL-6 pathway inhibition may be a potential therapeutic option for severe ASS-ILD in patients living at high altitude. However, larger studies are needed to determine whether chronic hypoxia influences treatment response [9].

Our patient developed deep vein thrombosis and received low-molecular-weight heparin anticoagulation; 6 days later, she developed RSH with hemorrhagic shock. Approximately 77% of RSH cases occur in patients receiving anticoagulation, and reported risk factors include female sex, immune abnormalities, and coughing [11]. Additionally, we observed a rapid decline in fibrinogen levels after TCZ administration. This may be related to inhibition of IL-6-mediated acute-phase responses, reduced hepatic fibrinogen synthesis, decreased coagulation factor XIII activity, and increased fibrinolytic activity [7, 12]. In this case, the development of life-threatening RSH was likely multifactorial, involving anticoagulation, persistent coughing, tissue vulnerability associated with severe illness, and TCZ-associated hypofibrinogenemia. Clinicians should closely monitor fibrinogen levels and coagulation parameters

during TCZ therapy, particularly when anticoagulation is required. Individualized anticoagulation strategies and timely fibrinogen supplementation may help reduce the risk of severe bleeding complications.

Another important finding in this case was the persistent elevation of CK despite normalization of inflammatory markers and improvement of pulmonary lesions. Active myositis was initially suspected; however, the patient had no myalgia or muscle weakness. Although MMF was initiated, the reduction in CK occurred only after surgical evacuation of the hematoma. Considering that the onset of action of MMF generally requires 4 to 8 weeks, the rapid postoperative decline in CK (from 945 to 510 U/L) suggested that CK elevation due to active myositis is usually accompanied by muscle symptoms, abnormal electromyography findings, and parallel changes in inflammatory markers and disease activity [13]. In contrast, CK elevation caused by local bleeding, tissue necrosis, rhabdomyolysis, drugs, toxins, or endocrine disorders may occur independently of pulmonary disease activity and requires evaluation using imaging or pathological findings [14]. This case highlights the importance of considering non-myositis causes of CK elevation in patients with ASS to avoid unnecessary escalation of immunosuppression and delays in treating potentially life-threatening complications.

Patient perspective

The patient expressed gratitude for the multidisciplinary care she received. She reported that her breathing difficulties improved significantly after tocilizumab treatment and that she was able to resume daily activities following recovery from surgery. She understood the risks associated with anticoagulation and agreed to the treatment decisions made by the medical team.

Conclusions

This case describes the successful management of severe ASS-ILD in a patient living at high altitude. It suggests that TCZ may be an effective treatment option for glucocorticoid-refractory ASS-ILD, even in a hypoxic high altitude environment. However, TCZ-associated hypofibrinogenemia, particularly when combined with anticoagulation, may increase the risk of life-threatening bleeding complications.

Close monitoring of fibrinogen levels and coagulation parameters is essential during TCZ therapy, especially in patients requiring anticoagulation. Individualized adjustment of anticoagulant therapy and timely correction of coagulopathy may have reduced bleeding risk. High-altitude hypoxia may contribute to an enhanced inflammatory response and potentially more aggressive disease progression in ASS-ILD, although further studies are needed to clarify this relationship. Early recognition and timely treatment remain critical in such settings. In addition, persistent elevation of CK during the course of ASS should prompt careful evaluation for non-myositis causes, including local tissue injury or bleeding, to avoid inappropriate escalation of immunosuppressive therapy. Overall, this case highlights the complexity of balancing immunosuppression, coagulation, and bleeding risk in the management of severe ASS-ILD, particularly in high-altitude environments.

Abbreviations

ARDS acute respiratory distress syndrome

ASS antisynthetase syndrome

CK creatine kinase

CRP C-reactive protein

CT computed tomography

ILD interstitial lung disease

PEEP positive end-expiratory pressure

RICU respiratory intensive care unit

RSH rectus sheath hematomas

Declarations

Ethics approval and consent to participate

This case report was approved by the Ethics Committee of Lhasa People's Hospital, Tibet (approval number: SYLL2226039). The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from the patient for participation in this study.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and materials

All clinical data supporting the findings of this case report are included within the manuscript. The datasets used and/or analyzed during the current study are available from the corresponding author, Dr. Yuntao Zhang (email: 412814726@qq.com), upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

LY : case management, data collection, and initial manuscript drafting; ZC: case management and data collection; DS: literature search and data organization; JYang: imaging data compilation and analysis; XS: clinical data acquisition and verification; YZ: study design, overall case management, manuscript review and revision, corresponding author. All authors read and approved the final manuscript.

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Figures

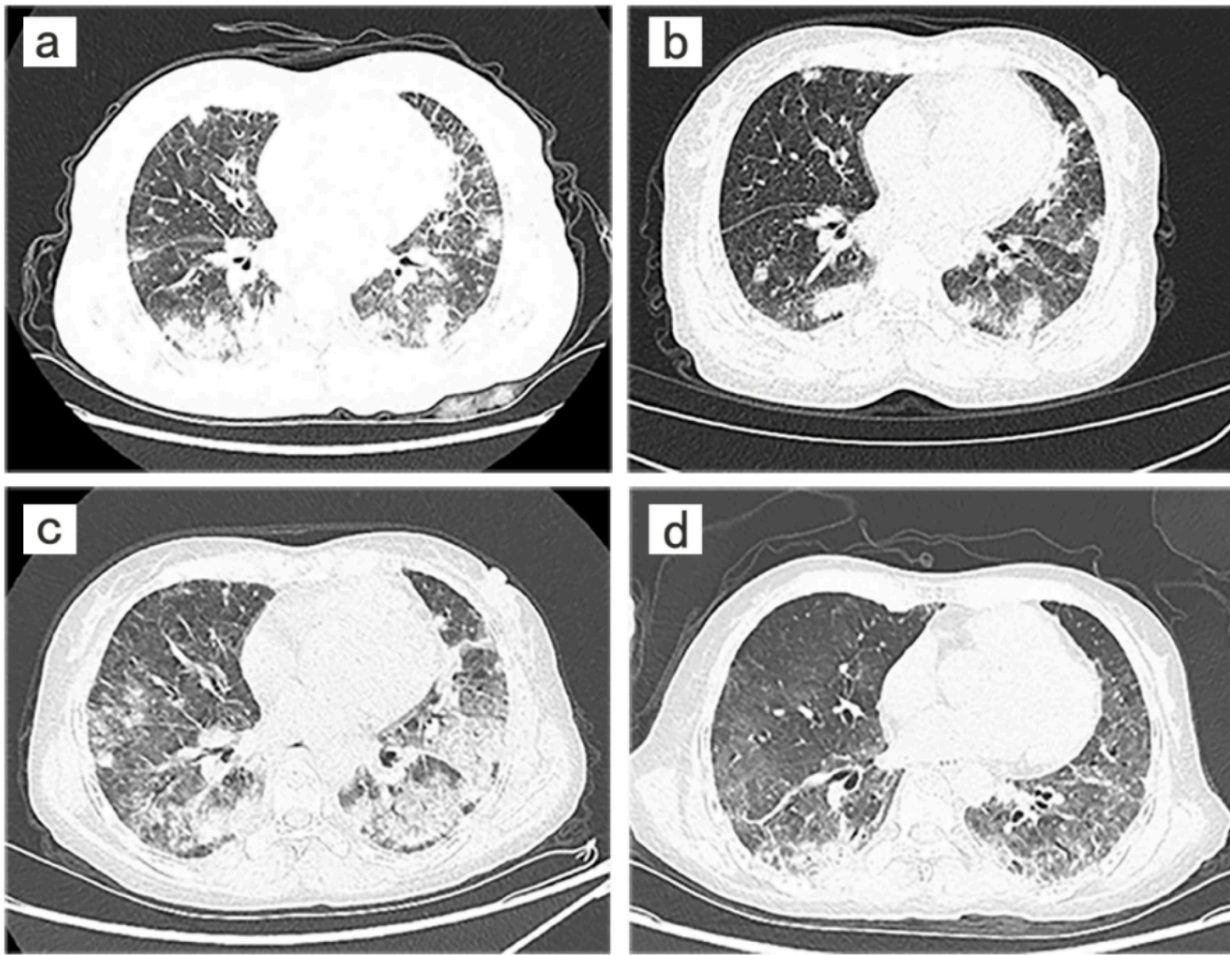


Figure 1

(a) At initial presentation, showing bilateral patchy nodular opacities. (b) After initial methylprednisolone therapy (day 7), demonstrating partial absorption of the lesions. (c) After glucocorticoid withdrawal (day 13), revealing marked exacerbation with diffuse ground-glass opacities. (d) Following a single dose of tocilizumab (day 24), showing significant radiological improvement.

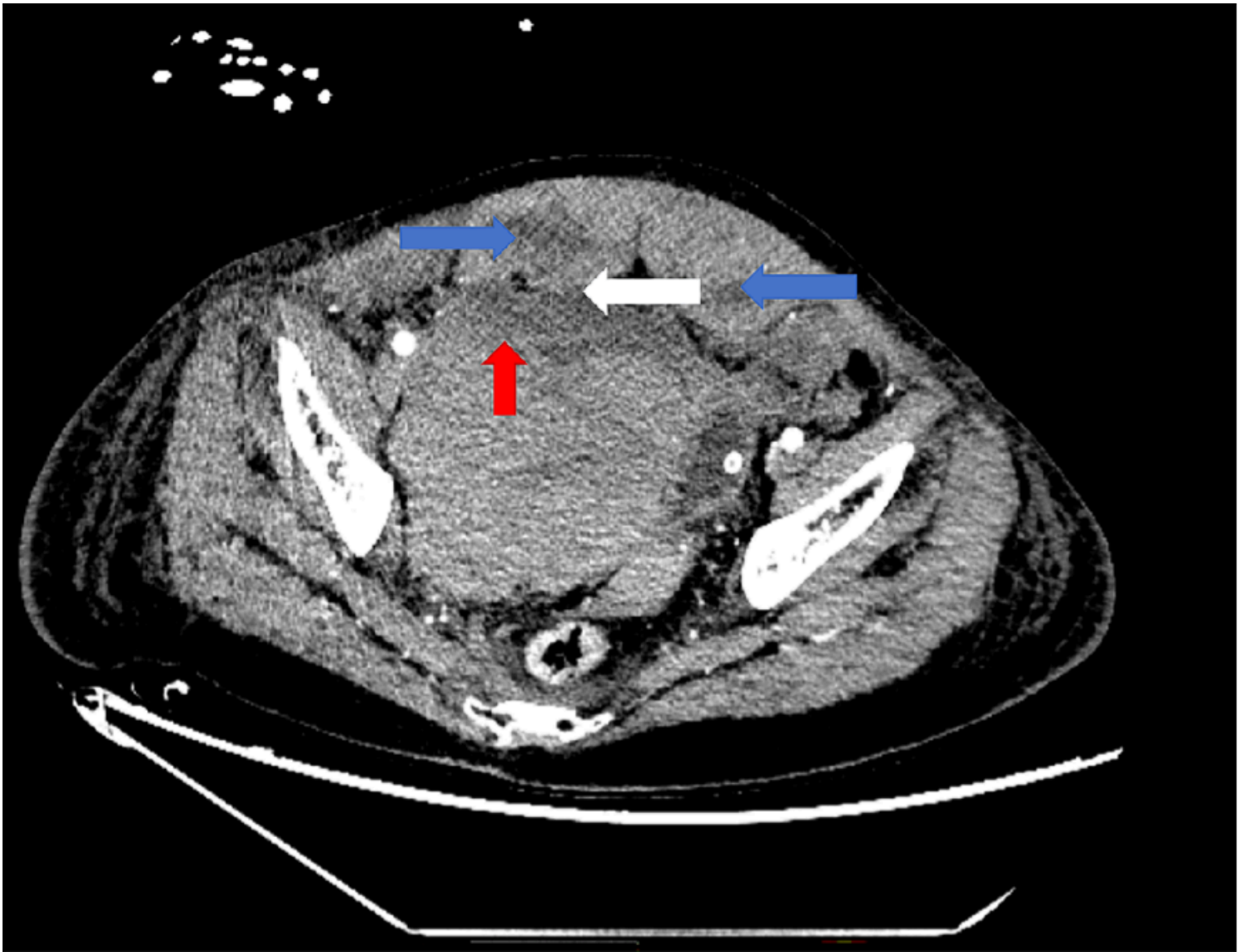


Figure 2

Abdominal contrast-enhanced CT of the same patient demonstrating bilateral rectus sheath hematomas (blue arrows) and encapsulated pelvic fluid/blood collection (red arrows), which is continuous with the right rectus sheath (white arrow).