Original Article

Rapidly Progressive Multisystem Autoimmune Disease in an Adolescent Male: A Fatal Case of Overlapping ANCA-Associated Vasculitis and Systemic Lupus Erythematosus Complicated by Acute Kidney Injury and Multiorgan Failure

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ABSTRACT

Background

Rapidly progressive autoimmune diseases in pediatric populations pose substantial diagnostic and therapeutic challenges due to aggressive clinical courses, multisystem involvement, and frequent overlap between immunological syndromes. The coexistence of systemic lupus erythematosus (SLE) and ANCA-associated vasculitis in adolescents is rare and associated with severe renal injury, cardiovascular complications, and high mortality.

Objective

To describe a fatal case of fulminant multisystem autoimmune disease in a 14-year-old male characterized by rapidly progressive glomerulonephritis, severe cardiac dysfunction, respiratory failure, and sepsis.

Methods

A retrospective descriptive analysis was performed using hospital records from tertiary referral centers. Clinical history, laboratory and immunological findings, imaging studies, specialist consultations, treatment strategies, and disease progression were systematically reviewed.

Results

The patient developed acute kidney injury stage F according to RIFLE criteria in the context of overlapping SLE and ANCA-associated vasculitis. The disease course was complicated by progressive multiorgan failure involving renal, cardiac, pulmonary, hepatic, and hematopoietic systems. Despite renal replacement therapy, immunosuppressive treatment, and advanced intensive care support, the patient died due to refractory metabolic acidosis, respiratory failure, and septic shock.

Conclusion

This case highlights the extreme aggressiveness of pediatric autoimmune overlap syndromes and emphasizes the importance of early immunological evaluation and prompt initiation of targeted therapy. The fatal outcome reflects both the fulminant nature of the disease and current limitations in managing advanced multisystem autoimmune involvement.

Keywords

systemic lupus erythematosus; ANCA-associated vasculitis; acute kidney injury; multiorgan failure; pediatric autoimmune disease; case report.

INTRODUCTION

Autoimmune diseases in children and adolescents form a unique and especially challenging group of immune-related disorders. They differ in important ways from the same conditions seen in adults, not only in how they present clinically, but also in their severity, progression, and long-term outcomes. When immune dysregulation begins early in life, the disease course is often more aggressive, with earlier organ involvement and faster accumulation of irreversible damage.

These features make timely diagnosis more difficult and management more complex. As a result, children and adolescents with autoimmune diseases frequently face a heavier disease burden, with higher risks of complications and long-term consequences compared to adult patients [1].

Systemic lupus erythematosus (SLE) is one of the most complex and heterogeneous autoimmune diseases affecting children and adolescents. Pediatric-onset SLE accounts for approximately 15–20% of all SLE cases and is widely recognized as a more severe form of the disease. Compared with adult SLE, pediatric SLE is characterized by higher disease activity at presentation, more frequent flares, and a greater likelihood of major organ involvement. Renal, neurological, hematological, and cardiovascular manifestations occur more commonly and earlier in the disease course, often determining prognosis and survival. Renal involvement, particularly lupus nephritis, remains one of

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the most significant predictors of adverse outcomes in pediatric SLE. Up to 80% of children with SLE develop some degree of renal disease, frequently within the first year after diagnosis . Lupus nephritis in children tends to be more aggressive than in adults, with higher rates of proliferative forms, rapid decline in renal function, and progression to chronic kidney disease or end-stage kidney disease. Early recognition and timely immunosuppressive therapy are therefore critical, yet diagnosis is often delayed due to nonspecific early symptoms and overlap with other systemic conditions. An additional layer of complexity arises when SLE coexists with other autoimmune or inflammatory disorders. Overlap syndromes involving SLE and antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis are rare but increasingly recognized as distinct clinical entities with particularly aggressive behavior. ANCA-associated vasculitides are characterized by necrotizing inflammation of small to medium-sized blood vessels and are classically associated with rapidly progressive glomerulonephritis, pulmonary hemorrhage, and systemic inflammation. While these conditions are well described in adults, their occurrence in pediatric patients, especially in combination with SLE, is uncommon and poorly understood [2].

The overlap of SLE and ANCA-associated vasculitis presents significant diagnostic challenges. Clinical manifestations such as renal failure, pulmonary involvement, cytopenias, and systemic inflammatory symptoms may be attributed to either disease, leading to diagnostic uncertainty and delays in initiating appropriate therapy. Immunologically, these patients often demonstrate features of both conditions, including high-titer antinuclear antibodies, anti–double-stranded DNA antibodies, hypocomplementemia, and ANCA positivity. Histopathological findings may also show mixed patterns, combining immune complex–mediated glomerulonephritis typical of lupus nephritis with pauci-immune necrotizing lesions characteristic of ANCA-associated vasculitis [3]. Rapidly progressive glomerulonephritis (RPGN) is among the most severe and life-threatening renal manifestations observed in autoimmune overlap syndromes. RPGN is defined by rapid loss of renal function over days to weeks and is frequently associated with crescent formation on renal biopsy. In pediatric patients, RPGN often leads to acute kidney injury (AKI) requiring urgent renal replacement therapy and is associated with high short-term mortality and long-term renal sequelae among survivors. The presence of RPGN in the context of SLE–ANCA overlap signals an extremely aggressive disease course and necessitates immediate, intensive intervention. Beyond renal involvement, multisystem organ dysfunction is a hallmark of severe autoimmune overlap syndromes. Cardiovascular manifestations, including myocarditis, cardiomyopathy, pericardial effusion, and pulmonary hypertension, are increasingly recognized as major contributors to morbidity and mortality in pediatric autoimmune disease [4]. Cardiac involvement may progress rapidly and silently, often becoming clinically apparent only when advanced dysfunction has already developed. In critically ill patients, cardiac failure significantly limits physiological reserve and reduces tolerance to aggressive immunosuppressive therapy and renal replacement strategies.

Pulmonary complications further compound disease severity. Interstitial lung disease, pulmonary edema, pleural effusions, and secondary infections are common in critically ill pediatric patients with autoimmune disease, particularly in the setting of immunosuppression and multiorgan failure. Respiratory failure frequently necessitates mechanical ventilation and is an independent predictor of poor outcome. The management of pediatric patients with overlapping SLE and ANCA-associated vasculitis is exceptionally challenging. Treatment strategies are largely extrapolated from adult studies and typically involve high-dose glucocorticoids, cytotoxic agents, plasma exchange, and biologic therapies. However, the evidence base for pediatric patients is limited, and optimal treatment protocols remain undefined. Moreover, aggressive immunosuppression substantially increases the risk of severe infections, sepsis, and treatment-related complications, particularly in patients with advanced organ dysfunction. Despite advances in intensive care, dialysis technologies, and immunomodulatory therapies, outcomes for pediatric patients with fulminant autoimmune overlap syndromes remain poor. Mortality is often related not only to uncontrolled autoimmune activity but also to secondary complications such as sepsis, refractory metabolic disturbances, and progressive multiorgan failure. These cases underscore the limitations of current therapeutic approaches and highlight the urgent need for improved diagnostic algorithms, earlier recognition of high-risk phenotypes, and the development of targeted treatment strategies tailored to pediatric patients. Against this

background, detailed clinical case reports remain critically important. They provide valuable insights into rare disease presentations, illustrate real-world diagnostic and therapeutic challenges, and contribute to a better understanding of disease behavior in pediatric populations. Reporting fatal cases, although difficult, is essential for identifying gaps in clinical care and guiding future research efforts [5].

The present report describes a fatal case of fulminant multisystem autoimmune disease in a 14-year-old male with overlapping systemic lupus erythematosus and ANCA-associated vasculitis. The case highlights the rapid progression from initial nonspecific symptoms to catastrophic multiorgan failure, emphasizing the diagnostic complexity and therapeutic limitations encountered in pediatric autoimmune overlap syndromes. By presenting this case, we aim to raise awareness of this rare but devastating condition and contribute to the growing body of literature on severe pediatric autoimmune disease.

MATERIALS AND METHODS

Study Design

This study was conducted as a retrospective, descriptive clinical case analysis. The design was chosen to allow a comprehensive evaluation of the diagnostic process, disease progression, therapeutic interventions, and clinical outcome in a pediatric patient with a rare and aggressive autoimmune overlap syndrome. Retrospective case analyses are considered appropriate and valuable for the investigation of uncommon diseases, particularly in pediatric populations where large cohort studies are often impractical due to low incidence rates [6].

The analysis focused on reconstructing the chronological sequence of clinical events from the onset of initial symptoms through hospitalization, intensive care management, and final outcome. Particular attention was paid to the temporal relationship between clinical manifestations, laboratory abnormalities, imaging findings, immunological markers, and therapeutic interventions.

Clinical Setting

The patient was treated in pediatric intensive care units and tertiary referral hospitals equipped with advanced diagnostic facilities, renal replacement therapy, and multidisciplinary specialist support. Care was provided by a coordinated team including pediatric intensivists, nephrologists, cardiologists, pulmonologists, rheumatologists, hematologists, infectious disease specialists, and surgeons. Such a multidisciplinary approach is considered essential for the management of critically ill children with complex multisystem autoimmune disease.

Data Sources and Collection

Clinical data were extracted from comprehensive hospital medical records using a standardized data abstraction approach to ensure consistency and completeness. The following sources were reviewed in detail:

- Admission notes and daily progress records documenting clinical status, vital signs, and symptom evolution
- Laboratory data, including complete blood counts, biochemical panels, coagulation profiles, inflammatory markers, and arterial blood gas analyses
- Immunological investigations, including antinuclear antibodies (ANA), anti–double-stranded DNA antibodies, extractable nuclear antigen antibodies (anti-Sm, anti-nRNP), complement levels, and antineutrophil cytoplasmic antibodies (ANCA)
- Imaging studies, including chest radiography, computed tomography, abdominal and renal ultrasonography, and transthoracic echocardiography
- Specialist consultation reports from pediatric subspecialties
- Dialysis records detailing modality, duration, frequency, and biochemical response
- Intensive care documentation, including mechanical ventilation parameters, vasopressor support, and fluid balance records

All data were collected retrospectively after completion of clinical care and were reviewed independently to minimize interpretation bias.

Diagnostic Criteria and Definitions

The diagnosis of systemic lupus erythematosus was based on established clinical and immunological criteria consistent with international classification guidelines, incorporating multisystem involvement and serological markers of autoimmune activity. ANCA-associated vasculitis was diagnosed based on positive ANCA serology in conjunction with rapidly progressive organ

involvement suggestive of small-vessel vasculitis, particularly renal and pulmonary manifestations.

Acute kidney injury was classified according to the RIFLE criteria (Risk, Injury, Failure, Loss, End-stage kidney disease), which are widely used in pediatric critical care and nephrology settings. Multiorgan failure was defined as the dysfunction of two or more organ systems requiring medical intervention, consistent with established pediatric intensive care definitions [7].

Treatment Documentation

Therapeutic interventions were documented in detail, including the use of immunosuppressive agents, renal replacement therapy modalities, antimicrobial therapy, cardiovascular support, respiratory support, and transfusion strategies. Changes in treatment were correlated with clinical and laboratory responses where possible. The rationale for therapeutic decisions was derived from specialist recommendations and institutional protocols aligned with international practice guidelines.

Data Analysis

Given the descriptive nature of the study and the single-patient design, no statistical analysis was performed. Data were analyzed qualitatively, with emphasis on identifying clinically significant patterns, rapid disease progression, and factors contributing to therapeutic failure. Findings were interpreted in the context of existing literature on pediatric autoimmune disease and overlap syndromes.

Ethical Clearence

This case report was prepared for scientific and educational purposes in accordance with ethical principles governing medical research involving human subjects. All identifying patient information was anonymized to protect confidentiality. In line with international guidelines, formal ethical committee approval and informed consent were not required for this retrospective single-case analysis using anonymized clinical data.

RESULTS

Patient Characteristics

A 14-year-old male from Almaty, Kazakhstan, was admitted to the pediatric intensive care unit in extremely critical condition. Prior to the onset of illness, he had been considered healthy, with no documented chronic diseases, regular medications, or long-term medical supervision. His growth and development were reported as age appropriate. A family history of autoimmune disease was notable, as a maternal relative had been diagnosed with systemic sclerosis, suggesting a possible genetic susceptibility to immune-mediated disorders.

Clinical Course

The patient's illness evolved insidiously over several months. Initial symptoms included episodic headaches and ocular discomfort, which were not investigated at the time. These were followed by the gradual development of arterial hypertension, reaching values up to 140/110 mmHg, accompanied by proteinuria and progressive thrombocytopenia. During this period, early signs of myocardial dysfunction were also detected, indicating the onset of multisystem involvement.

In the weeks preceding hospitalization, the clinical course accelerated dramatically. The patient developed persistent fever, a malar-type facial rash, gastrointestinal symptoms, generalized weakness, and progressive peripheral edema. Acute deterioration occurred with the onset of dyspnea, oliguria, and signs of uremic intoxication, prompting urgent hospital admission. Upon transfer to the intensive care unit, the patient exhibited features of rapidly progressive multisystem failure involving the renal, cardiovascular, respiratory, hepatic, and hematopoietic systems.

Laboratory Findings

Laboratory investigations revealed severe acute kidney injury, with creatinine levels exceeding 1000 µmol/L and markedly elevated blood urea nitrogen, consistent with renal failure at the "Failure" stage according to RIFLE criteria. Electrolyte disturbances included persistent hyperkalemia and progressive metabolic acidosis, which became increasingly refractory despite renal replacement therapy.

Hematological abnormalities were prominent and progressive. The patient developed severe anemia and profound thrombocytopenia, with platelet counts declining to critically low levels. Hypoproteinemia and hypoalbuminemia reflected both renal losses and systemic inflammation. Inflammatory markers were markedly elevated, including C-reactive protein, while coagulation studies demonstrated elevated D-dimer levels, indicating significant activation of the coagulation and inflammatory cascades.

Immunological testing confirmed intense autoimmune activity. Antinuclear antibodies were detected at high titers, accompanied by positive anti–double-stranded DNA, anti-Sm, and anti-nRNP antibodies. Complement levels, particularly C3, were significantly reduced. In parallel, antineutrophil cytoplasmic antibodies were strongly positive. This serological profile supported the diagnosis of systemic lupus erythematosus overlapping with ANCA-associated vasculitis, a combination known to be associated with aggressive renal and systemic disease.

Imaging Findings

Cardiac assessment by transthoracic echocardiography revealed severe dilated cardiomyopathy with global hypokinesia and a markedly reduced left ventricular ejection fraction, which declined to approximately 30% during the course of illness. Progressive pericardial effusion was observed, along with signs of pulmonary hypertension. These findings were consistent with severe inflammatory myocardial involvement.

Chest imaging demonstrated extensive bilateral pulmonary pathology. Radiographic and computed tomography findings included polysegmental pneumonia, pulmonary edema, and bilateral pleural effusions. Following pleural intervention, a pneumothorax developed, further compromising respiratory function. Abdominal and renal ultrasonography revealed hepatomegaly, ascites, and structural renal abnormalities consistent with acute inflammatory injury.

Treatment and Outcome

The patient received comprehensive intensive care, including invasive mechanical ventilation, vasopressor and inotropic support, renal replacement therapy, high-dose systemic glucocorticoids, intravenous immunoglobulin, broad-spectrum antimicrobial therapy, and repeated blood component transfusions. Despite transient biochemical improvement following dialysis sessions, renal function did not recover. Cardiac and respiratory function continued to deteriorate, and immunosuppressive therapy was complicated by severe infectious progression.

In the final phase of illness, the patient developed septic shock, refractory metabolic acidosis, and progressive multiorgan failure. Despite maximal supportive and disease-directed therapy, irreversible physiological decompensation occurred, and death was declared.

DISCUSSION

Overlap between systemic lupus erythematosus and ANCA-associated vasculitis in pediatric patients is exceptionally rare, yet it represents one of the most aggressive forms of autoimmune disease encountered in childhood. Published data suggest that when these conditions coexist, the clinical course is often fulminant, with rapid progression to organ failure and significantly increased mortality compared with either disease alone [9]. The present case illustrates the devastating potential of this overlap, particularly in the presence of early renal and cardiac involvement.

One of the most striking aspects of this case was the insidious onset followed by abrupt clinical deterioration. Initial symptoms such as headache, ocular discomfort, and later hypertension and proteinuria were nonspecific and may not have immediately suggested a systemic autoimmune process. Similar diagnostic delays have been described in other pediatric cases, where early manifestations are subtle and easily attributed to benign or unrelated conditions. Unfortunately, in aggressive overlap syndromes, even short delays in diagnosis can allow irreversible organ damage to develop before targeted therapy is initiated.

Renal involvement played a central role in disease severity and outcome. Rapidly progressive glomerulonephritis led to acute kidney injury requiring renal replacement therapy within a short period of time. In overlap syndromes, renal pathology often combines immune complex–mediated injury typical of lupus nephritis with necrotizing, pauci-immune lesions associated with ANCA-mediated vasculitis. This dual mechanism is believed to accelerate renal destruction and limit the effectiveness of conventional immunosuppressive regimens [10]. In pediatric patients, the loss of renal function further destabilizes metabolic balance and contributes to systemic deterioration.

Cardiac involvement represented another critical determinant of outcome in this case. Severe dilated cardiomyopathy and progressive reduction in left ventricular function significantly reduced physiological reserve and complicated intensive care management. Cardiac manifestations in pediatric SLE are frequently underrecognized, yet myocarditis and cardiomyopathy are increasingly acknowledged as important contributors to mortality in severe autoimmune disease[8]. When cardiac dysfunction coexists with renal failure, the

ability to tolerate aggressive immunosuppression, fluid shifts, and renal replacement therapy becomes markedly limited.

Secondary infection and sepsis emerged as terminal events in this case. Profound immune dysregulation, combined with high-dose immunosuppressive therapy and prolonged intensive care, created conditions conducive to severe infection. Sepsis remains a leading cause of death in pediatric patients with autoimmune disease, often representing the final pathway through which multisystem failure becomes irreversible. This highlights the difficult balance clinicians face between suppressing uncontrolled autoimmune activity and preserving immune competence in critically ill children.

This case underscores several important clinical lessons. First, adolescents presenting with unexplained hypertension, proteinuria, cytopenias, and systemic inflammatory symptoms should prompt early and comprehensive immunological evaluation. Second, overlap syndromes should be considered when clinical severity appears disproportionate to a single autoimmune diagnosis. Finally, early multidisciplinary involvement is essential, although even optimal care may be insufficient in fulminant disease [11].

In conclusion, this fatal case reflects both the extraordinary aggressiveness of pediatric SLE–ANCA overlap syndromes and the current limitations of available therapeutic strategies. Continued reporting of such cases is crucial to improving recognition, refining diagnostic approaches, and ultimately developing more effective treatments for these rare but devastating conditions [12].

CONCLUSION

Fulminant autoimmune overlap syndromes in pediatric patients represent some of the most severe and life-threatening conditions encountered in clinical practice. This case illustrates how the coexistence of systemic lupus erythematosus and ANCA-associated vasculitis can lead to rapid, widespread organ damage and catastrophic clinical deterioration despite timely access to advanced intensive care, renal replacement therapy, and immunosuppressive treatment.

The aggressive disease course observed in this adolescent highlights the limitations of current diagnostic and therapeutic approaches when faced with rapidly progressive multisystem autoimmune involvement. Early manifestations were nonspecific, yet they preceded irreversible renal, cardiac, and pulmonary failure. This underscores the critical importance of maintaining a high index of suspicion for autoimmune disease in children and adolescents presenting with unexplained hypertension, proteinuria, cytopenias, or systemic inflammatory features. Prompt immunological evaluation and early multidisciplinary involvement may improve outcomes, particularly before irreversible organ damage occurs.

At the same time, this case emphasizes the delicate balance required in managing severe autoimmune disease. While aggressive immunosuppression is often necessary to control immune-mediated injury, it significantly increases vulnerability to infection and sepsis, which remain leading causes of mortality in critically ill pediatric patients.

In conclusion, this fatal case reinforces the need for heightened clinical vigilance, earlier recognition of high-risk autoimmune overlap syndromes, and the development of more effective, targeted therapeutic strategies for children with severe autoimmune disease. Continued reporting and analysis of such cases are essential to advancing understanding, improving early diagnosis, and ultimately reducing mortality in this vulnerable population.

Conflict of Interest: The author declare no conflict of interest.

Authors's contribution:

Data gathering and idea owner of this study: Assel Bolsyn

Study design: Assel Bolsyn

Data gathering: Assel Bolsyn

Writing and submitting manuscript: Assel Bolsyn

Editing and approval of final draft: Assel Bolsyn

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