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**Systemic lupus erythematosus and antineutrophil cytoplasmic antibody-associated vasculitis overlap syndrome in a 77-year-old man: A case report**

Xu ZG *et al*. SLE and ANCA-AAV overlap syndrome

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**Abstract**

BACKGROUND

Systemic lupus erythematosus (SLE) and antineutrophil cytoplasmic antibody-associated vasculitis (AAV) are classically thought to cause renal impairment and small vessel vasculitis with different pathophysiologies. Their overlap constitutes a rare rheumatologic disease. To date, only dozens of such cases with biopsy-proven glomerulonephritis have been reported worldwide typically in women of childbearing age. Here, we present a unique clinical case due to its rarity and individualized treatment of a Chinese man in his eighth decade of life.

CASE SUMMARY

A 77-year-old man was admitted to several hospitals for shortness of breath and received nonspecific treatments over the past 3 years. As his symptoms were not completely relieved, he visited our hospital for further treatment. Laboratory examinations revealed kidney dysfunction, severe anaemia, hypocomplementemia, glomerular proteinuria, and microscopic haematuria. Antinuclear antibodies, as well as anti-dsDNA antibodies, were positive. Computed tomography of the chest showed right pleural effusion. Renal biopsy was performed, and histology suggested crescentic glomerulonephritis, pauci-immune type. After treatment with plasmapheresis, glucocorticoid, and cyclophosphamide, the disease was in remission, and the patient remained in a stable condition for over 3 years post-hospital discharge.

CONCLUSION

Due to its complexity and rarity, SLE and AAV overlap syndrome is easily misdiagnosed. An accurate diagnosis and treatment at the earliest stage may significantly improve the condition and reduce irreversible organ injury.

**Key Words:** Systemic lupus erythematosus; Antineutrophil cytoplasmic antibody-associated vasculitis; Overlap syndrome; Elderly male; Renal insufficiency; Case report

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**Core Tip:** Systemic lupus erythematosus and associated vasculitis overlap syndrome was first described in 1997, and only dozens of such cases have been reported to date worldwide. We report an elderly male patient who was not diagnosed with this disease in a timely manner due to hidden features. After treatment with plasmapheresis, glucocorticoid, and cyclophosphamide, the patient’s condition improved, even at his advanced age.

**INTRODUCTION**

Systemic lupus erythematosus (SLE) and associated vasculitis (AAV) overlap syndrome, first reported in 1997[1], is a rare disease characterized by simultaneous presentation of serological marker positivity, severe clinical manifestations (rapidly progressive glomerulonephritis and frequent pulmonary involvement)[2], or histopathology of SLE and AAV in the same patient, with the case fulfilling the classification criteria for both diseases. The disease is commonly seen in women of childbearing age. Those who have both overlapping syndromes commonly present with severe renal disease[3].

This case report describes the simultaneous manifestation of SLE and AAV. Based on our literature search, this overlap has rarely been reported in older men with biopsy-proven glomerulonephritis (GN).

**CASE PRESENTATION**

***Chief complaints***

This case report involves a 77-year-old Chinese man admitted to our hospital for recurrent shortness of breath for more than 9 mo.

***History of present illness***

The man was admitted to a local hospital for shortness of breath since February 2017. No clear diagnosis was made, and he was treated (the medication is unknown), but the symptom was recurrent. He felt worse and went to our hospital 2 mo later and was successively admitted to the Department of Cardiology and Respiratory. Laboratory examination showed mild renal insufficiency with serum creatinine (Scr) at 113 µmol/L. Anaemia with haemoglobin at 83 g/L, was present. Urinalysis revealed microscopic haematuria, but the urine protein was negative. Computed tomography (CT) of the chest showed right pleural effusion. For a correct diagnosis, the patient subsequently underwent thoracentesis and pleural biopsy. The hydrothorax was exudative, and the histological examination showed chronic inflammation. On the 14th day after admission, immunological tests revealed antinuclear antibodies (ANA) and anti-dsDNA antibody positivity, and myeloperoxidase (MPO)-antineutrophil cytoplasmic antibody (ANCA) was detected at 133 AU/mL using chemiluminescence. For further treatment, the patient went to a chest hospital and received nonspecific therapies. As his symptoms were not completely relieved in November 2017, he came to our hospital again.

***History of past illness***

He had no history of coronary heart disease, metabolic disease, rheumatic disease, or liver disease, but had over 50 years of water pipes smoking history.

***Personal and family history***

He has no special personal and family history.

***Physical examination***

His blood pressure, heart rate, and temperature were normal. A moderate anaemic appearance and decreased breathing sounds in the right lower lung were noted. Heart auscultation and abdominal examination were normal. No pitting oedema in the extremities was detected. He had no skin involvement, lymphadenopathy, or synovitis.

***Laboratory examinations***

On admission, serum laboratory results revealed the following values: Haemoglobin (Hb), 57 g/L; white blood cells, 5.9 × 109/L, platelets, 156 × 109/L; Scr, 310 µmol/L; serum albumin, 39 g/L; complement C3, 0.72 g/L; C4, 0.17 g/L; C-reactive protein, 32.1 mg/L. Liver function was normal. The patient was positive for ANA and anti-dsDNA antibodies. MPO-ANCA was detected at 180.62 AU/mL using chemiluminescence, and cANCA was positive by indirect immunofluorescence. Proteinase (PR3)-ANCA and pANCA were normal. We detected no anti-glomerular basement membrane or anti-phospholipase A2 receptor antibodies. Urinalysis revealed glomerular proteinuria (24-h urine protein, 0.887 g/d) and microscopic haematuria.

***Imaging examinations***

CT of the chest showed right pleural effusion, and Doppler echocardiography indicated decreased left ventricular diastolic dysfunction and moderate pulmonary hypertension. Kidney ultrasound examination revealed normal-sized kidneys, renal cysts, and right kidney stones, with obstruction excluded.

***Renal biopsy***

Lymph nodes or AVV was considered, leading us to perform a renal biopsy. Histological examination of the renal biopsy demonstrated 36 glomeruli, of which 13 were globally sclerotic and 14 were crescent, including 3 cellular, 1 fibro-cellular, 8 fibrous, 1 small cellular, and 1 small fibro-cellular, with some lesions of capillary fibrinoid necrosis (Figure 1). No marked mesangial cell proliferation, matrix proliferation, or fuchsinophilic protein deposits were found in the remaining glomeruli. Part of the interstitial region was infiltrated with inflammatory cells. Immunohistology showed negativity for immunoglobulin (Ig) M (+), IgA, IgG, C3, and C1q. Vacuolar degeneration in endothelial cells was observed by electron microscopy, and part of the glomerular capillary loops were compressed.

**FINAL DIAGNOSIS**

We corrected the previous diagnosis result to SLE and AAV overlap syndrome.

**TREATMENT**

As the diagnosis was clear, we started injections of methylprednisolone (500 mg/d, 3 d in total), cyclophosphamide (CTX) (0.4 g/d, 2 d in total), and γ-globin (15 g/d, 5 d in total). Plasmapheresis (double plasmapheresis, exchange dosage: 800 mL fresh frozen plasma) and continuous renal replacement therapy were immediately initiated. Although MPO-ANCA did not decrease apparently after five plasmapheresis sessions, the patient’s condition improved, the reexamination image was also evidently promoted, and the value of Scr was stable at approximately 270 µmol/L.

**OUTCOME AND FOLLOW-UP**

After being discharged, the patient was maintained on tapering PO doses of prednisone that was eventually suspended one year later. He was administered nine courses of 800 mg intravenous CTX (7.2 g in total) and was transitioned to oral daily azathioprine (100 mg), which continues to date. Further results, including urine protein-to-creatinine ratio, urinary erythrocyte, Scr, Hb, and images, revealed effective relief (Figures 2 and 3).

**DISCUSSION**

SLE and AAV are classically thought to cause renal impairment and small vessel vasculitis with different pathophysiologies. Both affect the kidneys, but the mechanism of SLE involves massive deposition of immune complexes under the endothelium of glomerular capillaries. It is a classical immune complex-mediated kidney injury[4]. In contrast, AAV leads to necrotizing and crescentic glomerulonephritis without immune complex deposition[5].

SLE and AAV overlap syndrome was first described in 1997. It is typically seen in women of childbearing age. Our case is unique because to our knowledge, this overlap is rarely observed in older men with biopsy-proven GN worldwide. The clinical manifestations of this patient were multisystem involvement, the associated autoantibodies were positive, and the histological examination of the renal biopsy revealed AAV-renal impairment. After assessment, the case fulfilled both SLE and AAV classification criteria.

Many factors have been known to cause SLE, including smoking, alcohol[6], ultraviolet light[7], virus infection[8], certain drugs[9], silica[10], *etc.* In this case, the patient was not exposed to intense ultraviolet light. There was no evidence to suggest that he was infected with viruses before the onset of this overlap syndrome. Procainamide, hydralazine, phenytoin sodium, isoniazid, propylthiouracil, penicillamine, and other special drugs have not been taken recently. However, given his water pipes smoking history, we suspect that it might be a potential trigger for SLE. Like SLE, there are a number of factors that contribute to serum ANCA positivity. *Staphylococcus aureus* is a common bacterium that has been implicated in the genesis of ANCAs[11]. Cigarette smoking and drugs that we mentioned above are also involved in inducing ANCA production[12,13]. There was no evidence that this patient had been infected with bacteria according to the physical examination upon admission. Therefore, in this case, water pipes smoking seems to be the common cause of SLE and ANCAs.

Corticosteroids, immunosuppressive agents, and plasmapheresis are recommended as regular therapies for this overlap. In this case, a high dose of glucocorticoid (GC) and CTX were given to diminish inflammation and prevent permanent organ damage. After we detected ANCA in the patient’s circulation, plasma exchange was used to rapidly remove the pathogenic autoantibodies and prevent the deterioration of renal function. When he was in complete remission, azathioprine was used after CTX withdrawal due to its lower toxicity. Further results, including urine protein, Scr, Hb, and images, showed effective relief in 3 years.

This case reveals that early diagnosis and timely treatment for this overlap syndrome are critical. The patient had been misdiagnosed and received nonspecific treatments for 6 mo before visiting our department. Thus, early diagnosis and proper treatments are crucial for renal function preservation. In addition, it is generally believed that elderly patients are vulnerable to the adverse effects of the GC to treat autoimmunological diseases. In a recent study, Sada *et al*[14] divided the elderly AAV patients into three groups according to initial GC dose. They found that there were no statistically significant intergroup differences in remission or relapse, but serious infection developed more frequently in the high-dose group (prednisolone ≥ 0.8 mg/kg per day). Considering that the patient was elderly and prone to GC-related side effects such as serious infection and gastrointestinal bleeding, we treated him with only 0.5 g methylprednisolone QD for 3 d and achieved satisfactory results. Thus, a conservative dose for GC therapy may be an appropriate option for the elderly.

**CONCLUSION**

In conclusion, SLE and AAV overlap syndrome is a rare autoimmune disease involving multiple systems. It usually damages small vessels and causes renal impairment. Due to the complexity of this disease, it is easily misdiagnosed. An accurate diagnosis and treatment at the earliest stage may significantly improve the patient’s condition and reduce irreversible organ injury.

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**Footnotes**

**Informed consent statement:** Written informed consent was obtained from the patient for publication of this report and any accompanying images.

**Conflict-of-interest statement:** The authors declare that they have no conflict of interest to disclose.

**CARE Checklist (2016) statement:** The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

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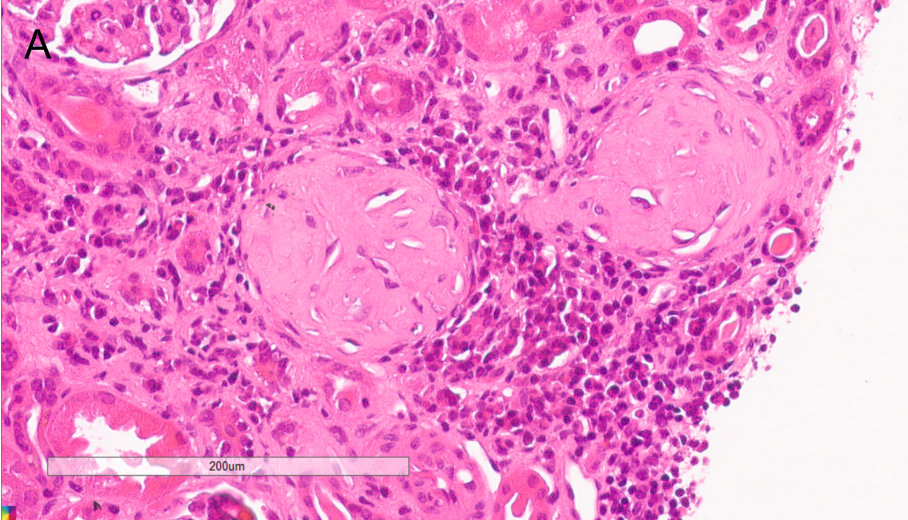
Grade C (Good): C, C

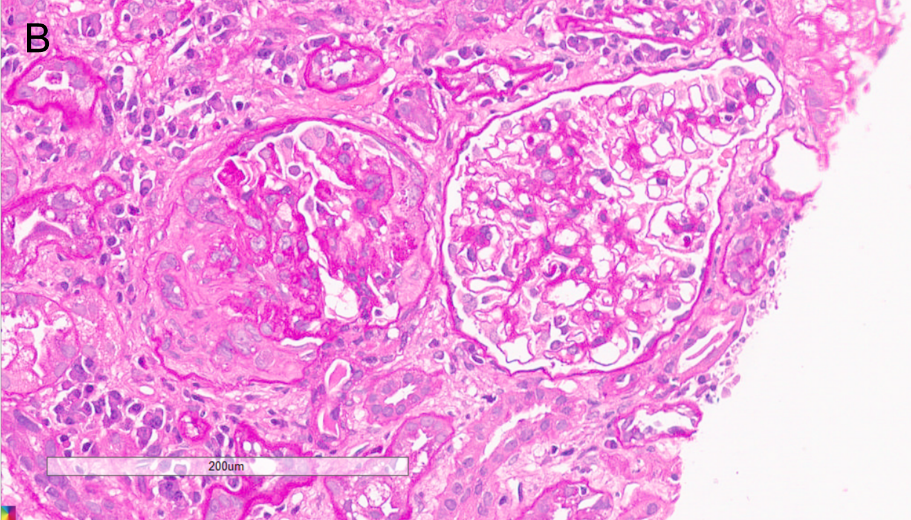
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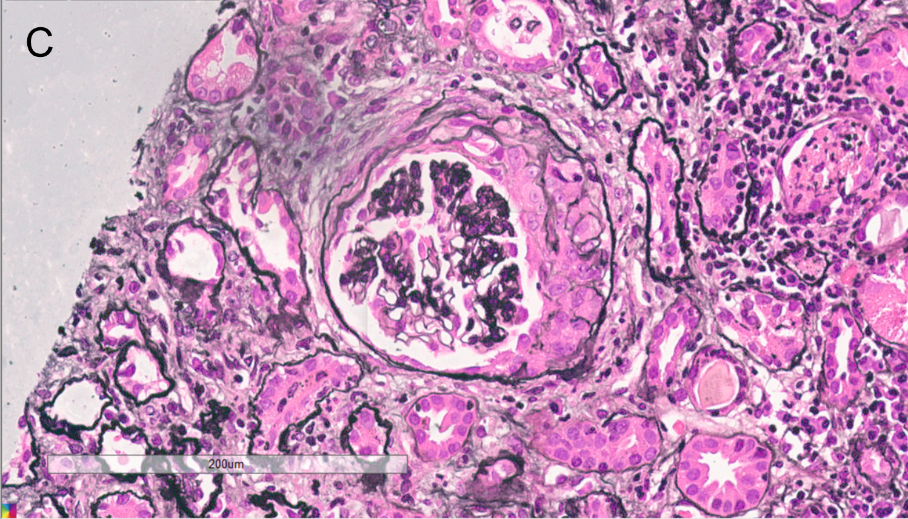
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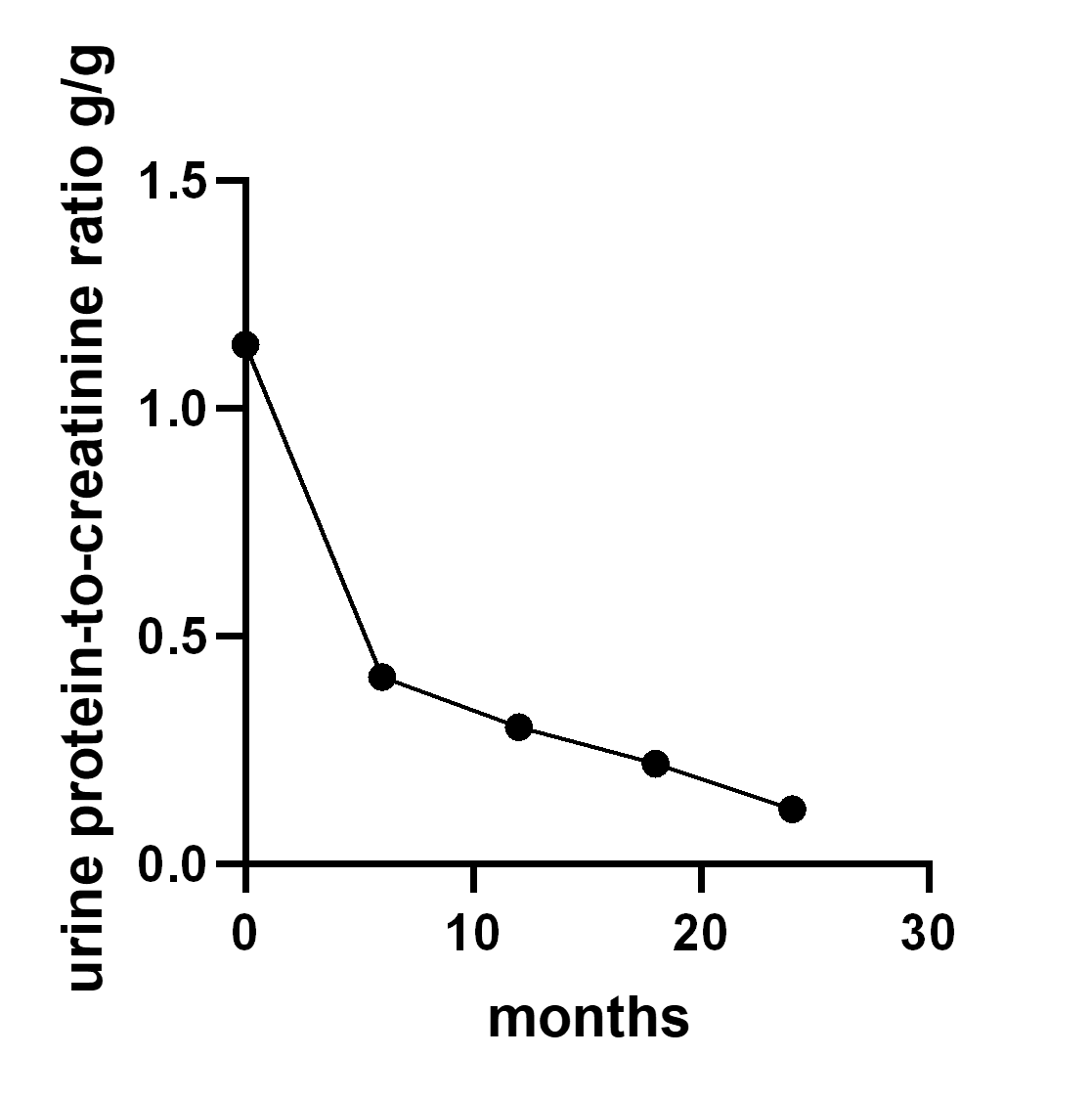
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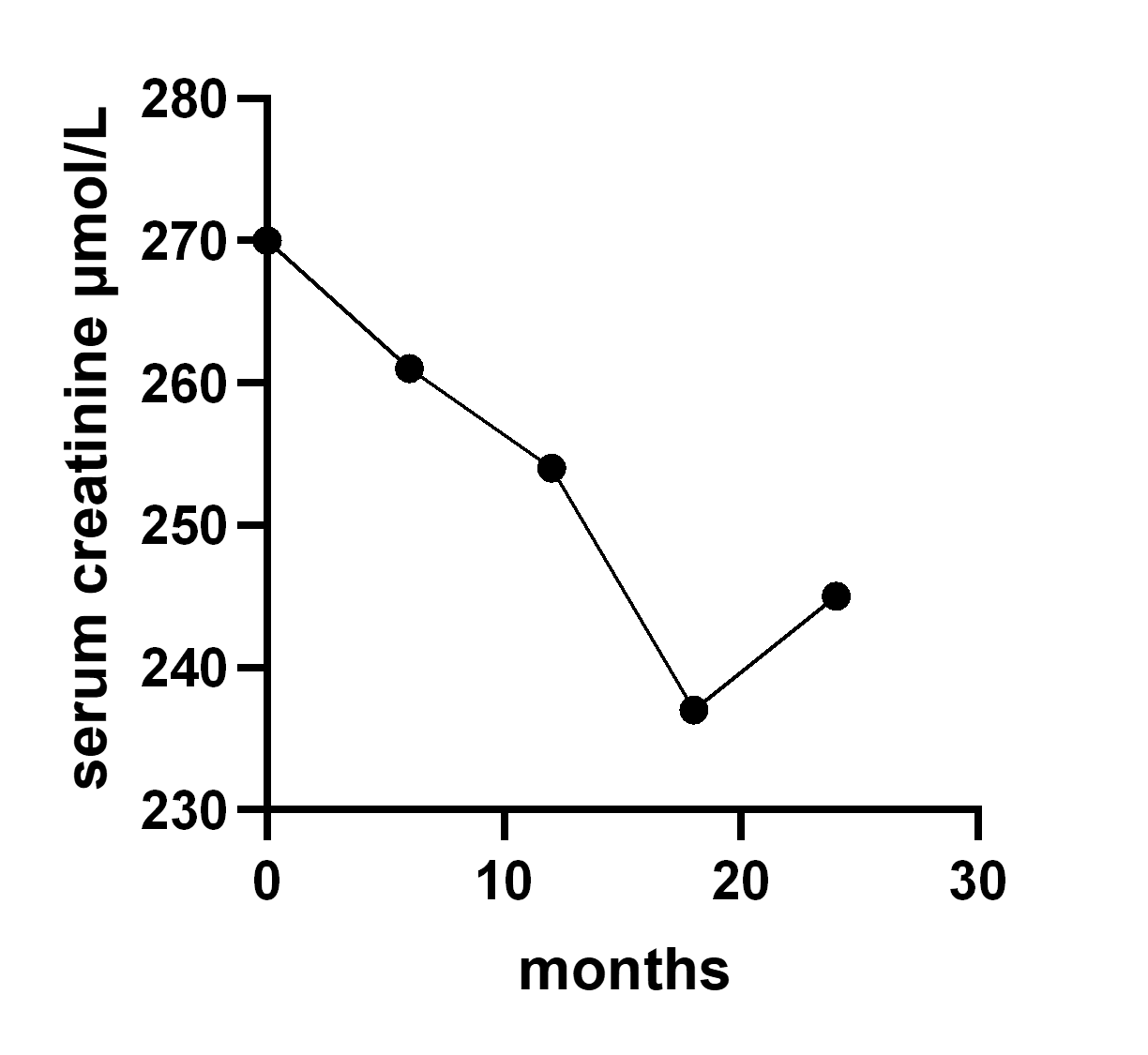


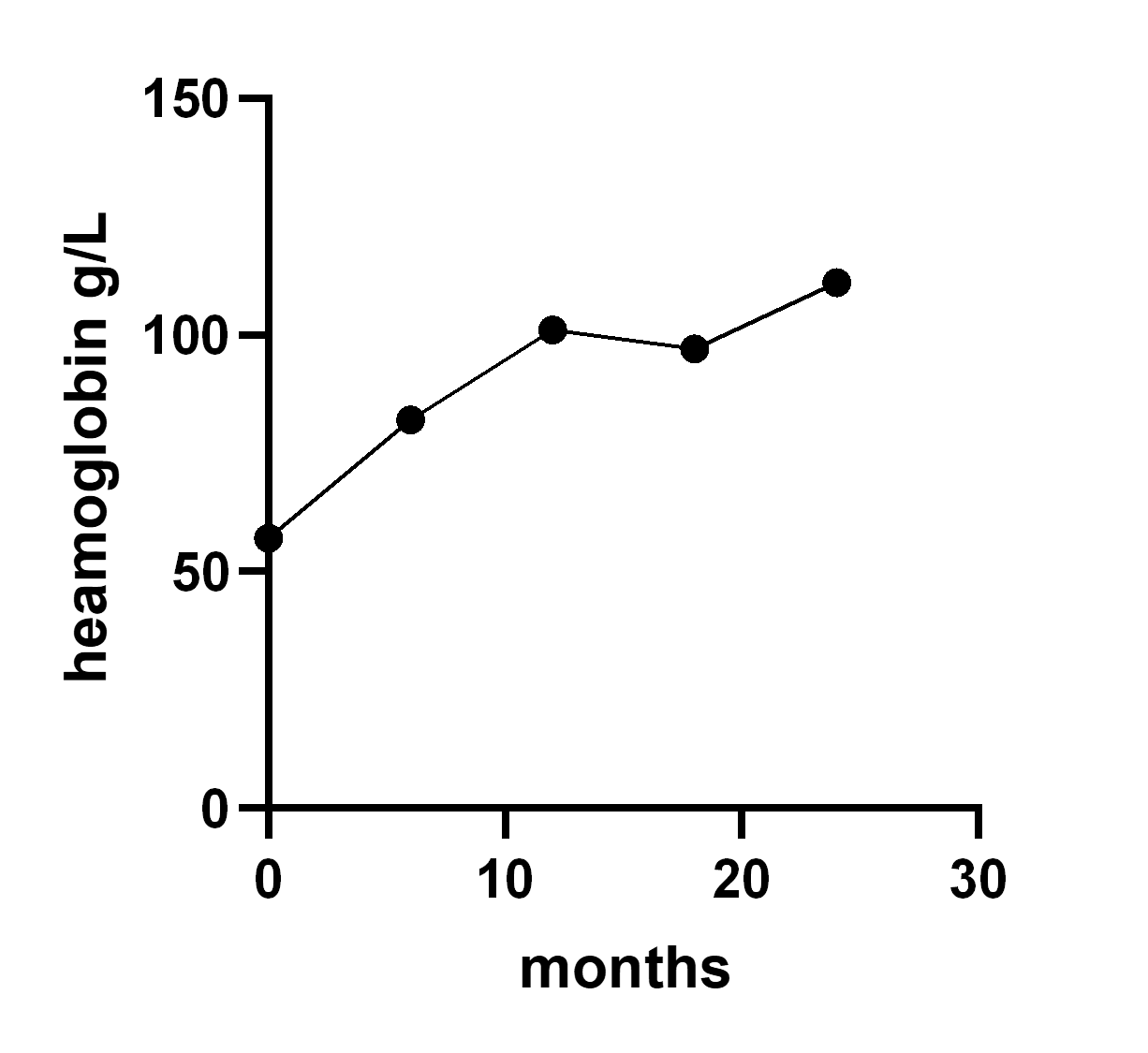




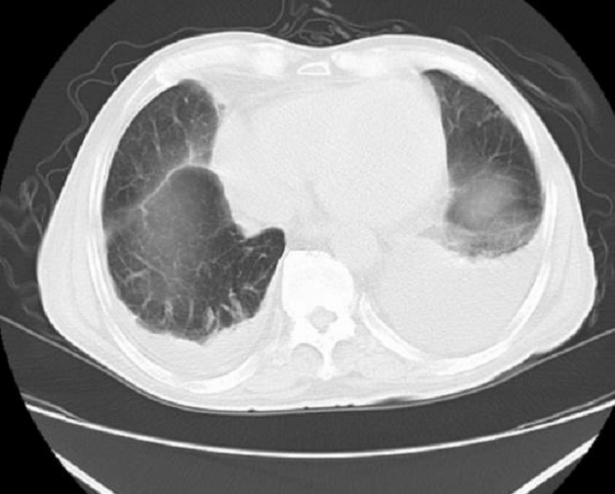
**Figure 1 Sections of kidney samples taken at autopsy showing sclerotic glomerulus, fibro-cellular crescent, and cellular crescent.** A: Haematoxylin and eosin stained image; B: Periodic acid-Schiff reaction; C: Periodic acid-Schiff-methenamine silver staining. Original magnification × 400.

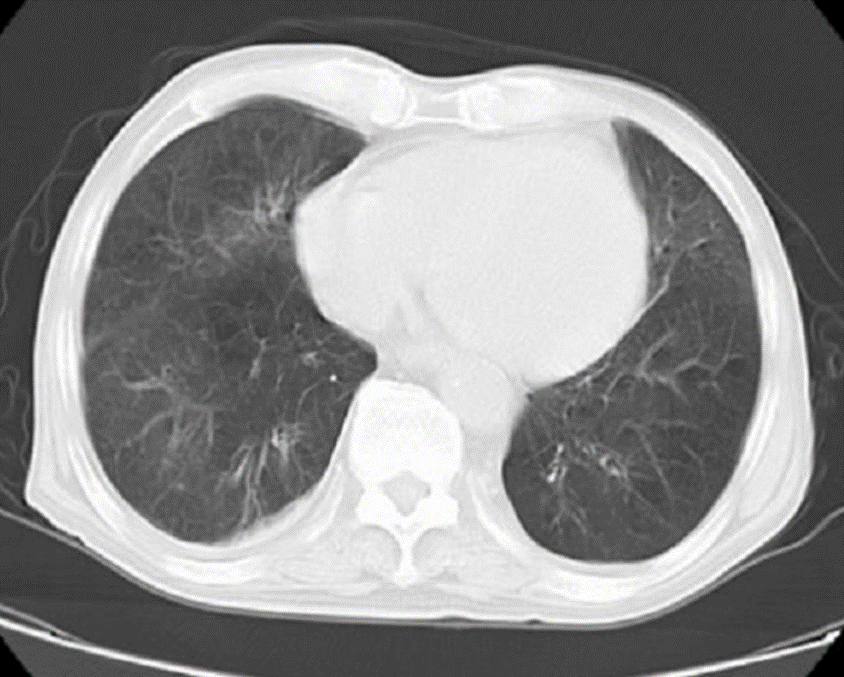






**Figure 2 Trends of urine protein-to-creatinine ratio, serum creatinine, and haemoglobin.**

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**Figure 3 Computed tomography of the chest showing pleural effusion.**