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CLINICAL REASONING: CASE REPORT

Granulomatous tubulointerstitial nephritis secondary to small lymphocytic lymphoma: a case report

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Summary

BACKGROUND: Granulomatous tubulointerstitial nephritis is an uncommon cause of acute kidney injury with a broad differential diagnosis that includes drug exposure, infections, autoimmune conditions, and sarcoidosis. Although renal infiltration by small lymphocytic lymphoma/chronic lymphocytic leukaemia (SLL/CLL) is frequently observed in autopsy series, it rarely results in clinically significant renal dysfunction. Granulomatous interstitial nephritis directly related to lymphomatous infiltration is particularly rare, with only a few cases described in the literature.

CASE PRESENTATION: A man in his seventh decade with indolent SLL developed rapidly progressive acute kidney injury. Extensive evaluation excluded obstructive, infectious (including tuberculosis), autoimmune, and drug-related causes, and sarcoidosis was considered unlikely in the absence of supportive clinical and laboratory findings. Immunohistochemistry and molecular techniques demonstrated a clonal B-cell population consistent with SLL, establishing the diagnosis of lymphoma-related granulomatous tubulointerstitial nephritis. Treatment with high-dose corticosteroids and acalabrutinib improved renal function, though targeted therapy was discontinued due to severe infectious complications.

CONCLUSION: Granulomatous tubulointerstitial nephritis secondary to lymphomatous infiltration should be considered in the differential diagnosis of unexplained acute kidney injury in patients with indolent CLL/SLL. Immunohistochemistry is crucial for confirming B-cell infiltration. Corticosteroids and targeted therapies may lead to renal improvement but require careful monitoring given the risk of infectious complications. This case adds a rare and well-documented presentation of SLL-associated granulomatous tubulointerstitial nephritis to the current medical literature.

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Introduction

Granulomatous tubulointerstitial nephritis is a rare renal condition, observed in approximately 0.3% to 0.9% of kidney biopsies. It is histologically defined by interstitial inflammation and the presence of granulomas. Renal involvement may be isolated or occur in the context of a systemic disease, which can help guide the diagnostic evaluation [1].

The aetiologies of granulomatous tubulointerstitial nephritis are diverse. Drug-induced forms are frequently reported among secondary causes and are primarily associated with non-steroidal anti-inflammatory drugs (NSAIDs), proton pump inhibitors (PPIs), diuretics, certain antibiotics, antiepileptic drugs, and some immune checkpoint inhibitors. Infectious causes, especially mycobacterial or fungal infections, should also be considered, particularly in endemic areas and in immunocompromised patients. Autoimmune and autoinflammatory diseases are other recognised aetiologies, including sarcoidosis, systemic lupus erythematosus, antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, tubulointerstitial nephritis with uveitis (TINU), and chronic inflammatory bowel diseases. Approximately 10% of granulomatous tubulointerstitial nephritis cases are idiopathic [1].

Chronic lymphocytic leukaemia (CLL) and small lymphocytic lymphoma (SLL) are mature B-cell malignancies characterised by the clonal proliferation of B lymphocytes and typically follow an indolent course. The term SLL is used when lymph node involvement is predominant without significant lymphocytosis in the peripheral blood, whereas CLL refers to cases with lymphocytosis, defined as a monoclonal B-cell count of at least 5 x 10^9/l in the peripheral blood. CLL and SLL are considered different clinical manifestations of the same disease entity. CLL/SLL is the most common leukaemia in adults in developed countries. It occurs more frequently in men (male-to-female ratio of 1.2:1) and typically presents at a median age of approximately 70 years. Most patients are asymptomatic at diagnosis, which is often made following the discovery of persistent lymphocytosis or, less commonly, cervical lymphadenopathy during routine evaluation [2].

Although renal involvement by CLL/SLL is common in autopsy series, reported in 60 to 90% of cases, it is typically subclinical and rarely leads to significant impairment of renal function [3, 4]. Consequently, CLL/SLL is rarely considered in the differential diagnosis of acute kidney injury. Within the spectrum of CLL-associated renal lesions, granulomatous tubulointerstitial nephritis is particularly rare. In a 25-year multicentre series, only a small fraction of patients with CLL/SLL-related kidney disease exhibited interstitial granulomas directly attributable to the malignancy [5]. In this context, the diagnosis of granulomatous tubulointerstitial nephritis as a direct manifestation of CLL/SLL represents an exceptional and diagnostically challenging clinical entity.

Here, we present a case of granulomatous tubulointerstitial nephritis secondary to renal infiltration by monoclonal B cells in a patient with SLL, along with a review of similar rare cases described in the literature.

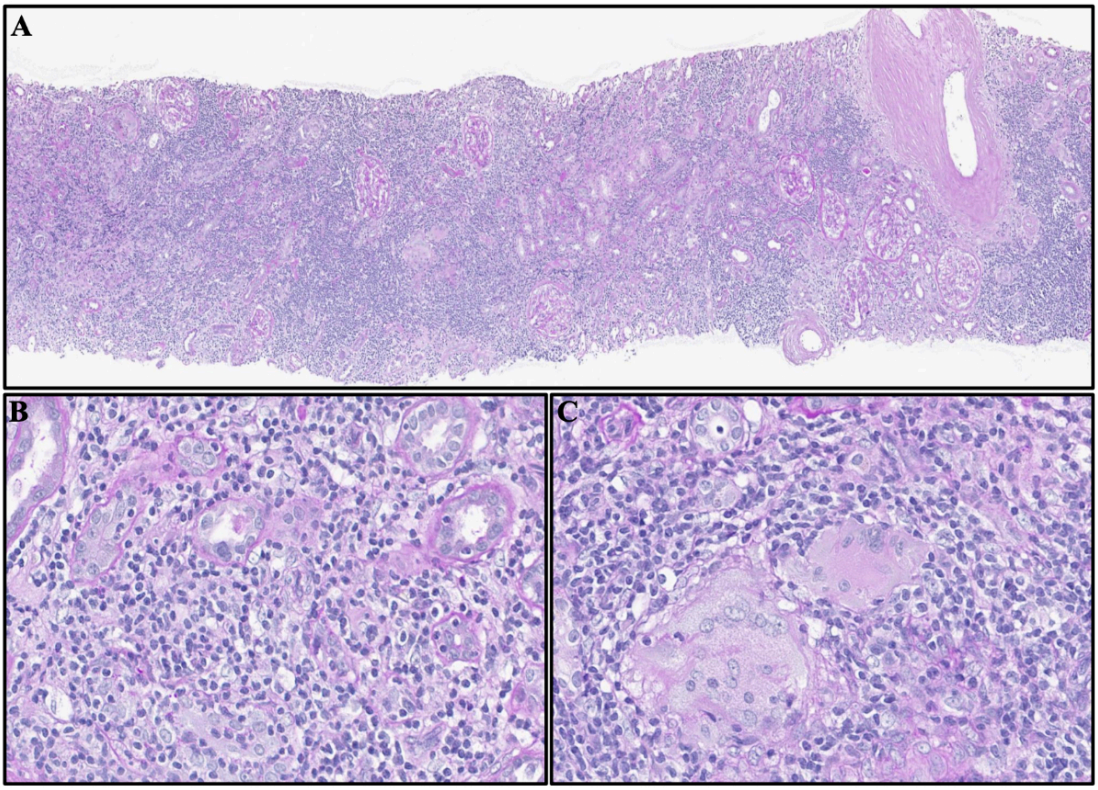
Case presentation

We report the case of a man in his seventh decade with a history of Parkinson's disease who was referred to a haematologist in 2023 following the incidental discovery of isolated cervical lymphadenopathy. At presentation, the patient reported weight loss without fever or night sweats and had no other symptoms. Physical examination revealed an extrapyramidal syndrome with bilateral cervical and axillary lymphadenopathy, with no evidence of inguinal lymphadenopathy or hepatosplenomegaly. The patient's general condition was preserved. A lymph node biopsy revealed clonal B-cell proliferation expressing CD5, CD19, CD22, CD23, CD43, CD52, CD79b, and surface IgM, with the absence of CD10, CD11c, CD25, CD38, CD103, or FMC7. Positron emission tomography-computed tomography (PET-CT) total body imaging showed additional lymphadenopathy in the cervical, mediastinal, and retroperitoneal regions, supporting the diagnosis of SLL. In the absence of lymphocytosis, clinical symptoms, or evidence of disease progression, close haematological surveillance was implemented without indication for specific therapy.

From early 2024, a gradual increase in serum creatinine was observed, rising from a baseline of 100 µmol/l to 196 µmol/l by October. The patient was referred to the nephrology outpatient clinic. To rule out ureteral obstruction secondary to retroperitoneal lymphadenopathy, MAG3 renal scintigraphy with a diuretic challenge was performed. The scan demonstrated bilateral impaired renal excretion, more pronounced on the right side.

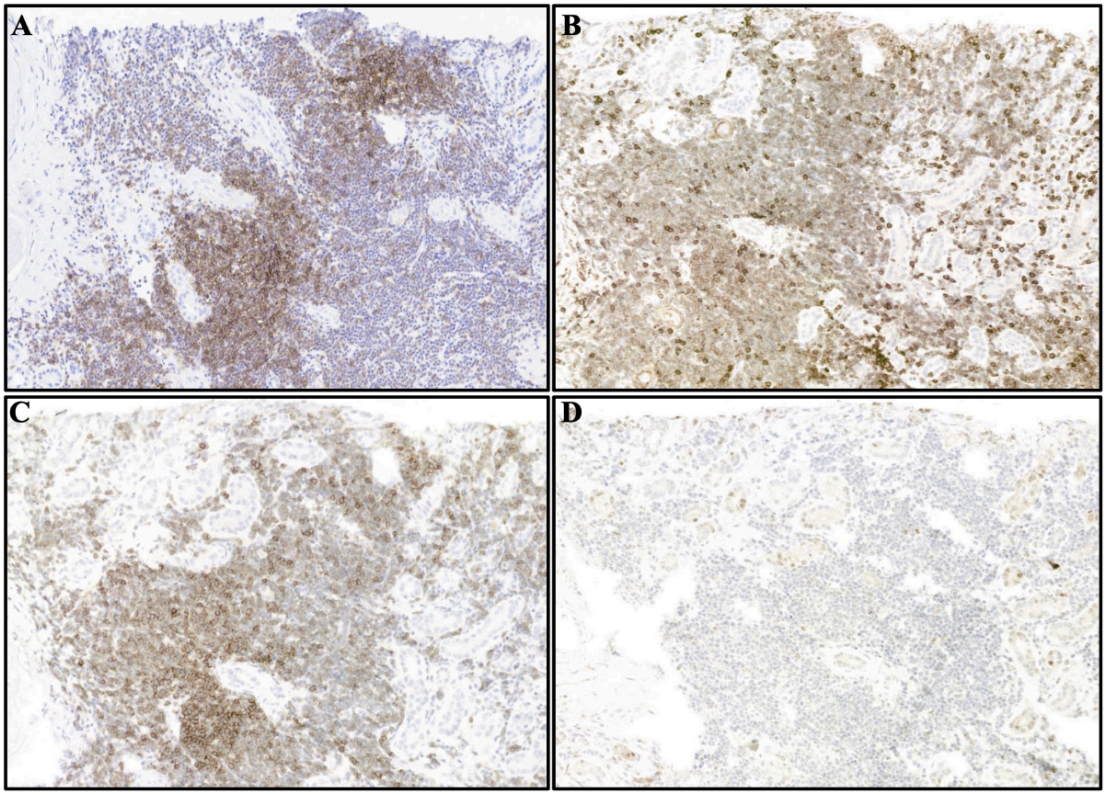
In January 2025, the patient was admitted for rapidly progressive acute kidney injury, with serum creatinine reaching 558 µmol/l. At admission, the patient reported only difficulty initiating voiding, which had been present for 2 months. He did not report oliguria, dysuria, or haematuria. He also denied asthenia, recent weight loss, or night sweats. Physical examination revealed supradiaphragmatic lymphadenopathy involving the cervical, supraclavicular, and axillary regions, without evidence of enlargement according to the haematologist following the patient in the outpatient setting. The remainder of the physical examination was unremarkable. Emergency placement of a right pigtail catheter did not improve renal function. A laboratory workup showed no systemic inflammation (CRP 4.45 mg/l) or electrolyte abnormalities. Urinalysis was unremarkable, without leukocyturia, and showed hyaline casts (++). Twenty-four-hour proteinuria was moderate (0.8 g/24 h), with a predominance of non-albumin proteins, suggesting a non-glomerular pattern of protein loss. Kidney biopsy revealed diffuse and severe tubulointerstitial nephritis with an abundant mononuclear cell-rich infiltrate and non-necrotising granulomas with multinucleated giant cells (figure 1).

Figure 1: A. Light microscopy revealed a severe and diffuse cellular interstitial infiltrate, with multiple non-necrotising granulomas. Haematoxylin-eosin/Jones stain. Formalin-fixed paraffin-embedded section; 10× magnification. B and C. The interstitial infiltrate consisted mainly of non-atypical mononuclear cells and a few poorly organised non-necrotising epithelioid granulomas with multinucleated giant cells (C). Haematoxylin-eosin stain. Formalin-fixed paraffin-embedded section; 40× magnification.



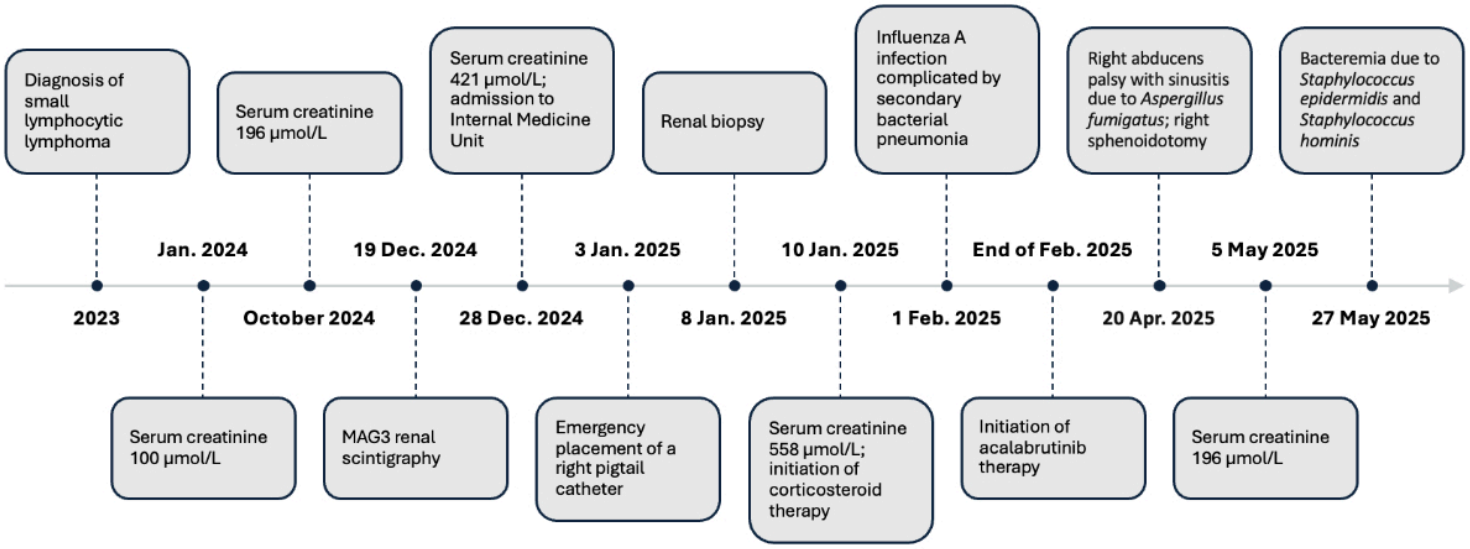
A thorough aetiological workup was undertaken. There was no recent change in the patient's usual medication and no exposure to medication known to induce interstitial nephritis. He was receiving calcium, vitamin D, vitamin B12, and folic acid supplementation, rosuvastatin, and, for Parkinson's disease, opicapone, pramipexole, and a combination of levodopa and benserazide. The patient had no risk factors for tuberculosis, no clinical or radiological signs of mycobacterial infection, and negative TB-Spot results. Polymerase chain reaction analysis performed on the kidney biopsy found no evidence of *Mycobacterium tuberculosis* complex DNA. Autoimmune evaluation was also non-contributory, with negative antinuclear antibodies and ANCA, as well as normal C3/C4 complement levels. Serum immunofixation revealed a small monoclonal IgG lambda peak, with a normal kappa/lambda free light chain ratio. Quantitative immunoglobulin testing revealed decreased levels of IgG at 3.98 g/l (reference range 7–16 g/l), IgA at 0.30 g/l (reference range 0.7–4 g/l), and IgM at <0.05 g/l (reference range 0.4–2.3 g/l). Sarcoidosis was deemed unlikely given the absence of hypercalcaemia, hypercalciuria, or elevated 25-(OH) vitamin D (87 nmol/l) and angiotensin-converting enzyme (46 U/l) levels. 1,25-$(OH)_2$ vitamin D and sIL2 were not measured. The ^{18}F-FDG PET-CT showed no signs of hypermetabolic lymphadenopathy, which is typically seen in sarcoidosis. PET-CT confirmed the presence of multiple non-hypermetabolic lymphadenopathies (cervical, axillary, and infra-diaphragmatic), consistent with SLL. Given the lack of alternative explanations, specific immunohistochemical staining was performed on the renal biopsy. This confirmed infiltration by CLL/SLL-type B-cell lymphoma with the following expression profile: CD20 low, CD5 positive, CD23 positive, and BCL1. The inflammatory infiltrate was heterogeneous, with a mixture of T cells (CD3-positive and CD5-positive) and, to a lesser extent, B cells (CD20-positive and CD79-positive). The spatial distribution appeared random rather than being localised to the periphery of granulomas (figure 2). Next-generation sequencing (NGS) identified a mutation in the SF3B1 gene, without a TP53 abnormality, strongly supporting the probability of an SLL B-cell clone [6].

Figure 2: Immunochemistry study revealed kidney infiltration by small lymphocytes with a characteristic immunophenotype showing diminished CD20 expression (A), aberrant CD5 expression (B), along with CD23 expression (C), and the absence of significant BCL1 staining (D), consistent with small lymphocytic lymphoma. Formalin-fixed paraffin-embedded section with DAB as chromogen; 20× magnification.



The diagnosis of granulomatous tubulointerstitial nephritis secondary to renal infiltration by SLL was established. Treatment was initiated with intravenous methylprednisolone (500 mg/day for three days), followed by oral prednisone at 1 mg/kg/day. In parallel, and after multidisciplinary discussion with the haematology team, acalabrutinib, an oral Bruton tyrosine kinase inhibitor, was started due to the lymphomatous renal infiltration. The initial evolution was favourable, with progressive improvement in renal function and stabilisation of serum creatinine at 190 µmol/l four months after treatment initiation and at the time of corticosteroid tapering. However, acalabrutinib had to be discontinued early because of major infectious complications that occurred in the weeks following its initiation. The patient first developed influenza A pneumonia, which was rapidly complicated by bacterial superinfection with an unidentified pathogen. A few weeks later, he developed invasive fungal sinusitis due to *Aspergillus fumigatus*, with secondary bony erosion resulting from the *Aspergillus* infection, complicated by a right abducens nerve palsy in April 2025. The patient underwent urgent sphenoidotomy due to cranial nerve involvement. Due to osseous involvement, treatment with posaconazole and anidulafungin was initiated and continued for two weeks, followed by therapy with inhaled amphotericin B and oral posaconazole. One month later, the patient presented with bacteraemia due to *Staphylococcus epidermidis* (3 out of 4 blood culture sets) and *Staphylococcus hominis* (3 out of 4 blood culture sets), secondary to bacterial sphenoidal sinusitis and a persistent bony defect following invasive aspergillosis. Management required prolonged hospitalisation and a one-week course of cefazolin, with a favourable clinical outcome. The patient underwent serial sinus imaging follow-up after hospital discharge. Given the favourable clinical and radiological evolution, inhaled amphotericin B was continued for a total of three months, and posaconazole for ten months. Due to the severity of the infectious complications, after further discussion with the haematologists, acalabrutinib was suspended, and therapy with obinutuzumab, a humanised type II anti-CD20 monoclonal antibody, and venetoclax, a selective BCL-2 inhibitor, was planned. This therapy has not yet been started because of the recent infections (timeline shown in figure 3).

Figure 3: Timeline from the diagnosis of small lymphocytic lymphoma to the acute care episode.



Discussion

This study reports a new case of granulomatous tubulointerstitial nephritis in a patient with renal infiltration by SLL. In patients with CLL/SLL, the most commonly reported causes of acute kidney injury include acute tubular necrosis, uric acid crystal nephropathy, light chain nephropathy, obstructive nephropathy, amyloidosis, hypercalcaemia, certain forms of glomerulonephritis, and cryoglobulinaemia [7]. By contrast, granulomatous interstitial nephritis related to lymphomatous renal infiltration has only been described in isolated case reports and small series, with ten cases reported to date [8–14].

The diagnosis of granulomatous tubulointerstitial nephritis remains particularly challenging. Aleckovic-Halilovic et al. proposed a diagnostic framework for biopsy-proven cases, emphasising that although renal biopsy is essential for the aetiological evaluation, it lacks specificity [15]. Histopathological patterns may provide guidance: non-necrotising granulomas suggest sarcoidosis or drug-induced nephritis, whereas necrotising granulomas are more commonly associated with ANCA-associated vasculitis or infections such as tuberculosis.

In the context of lymphoproliferative disorders, additional diagnostic complexity arises. Sarcoidosis–lymphoma syndrome, including paraneoplastic sarcoidosis, has been described [16]. Although sarcoidosis cannot be formally excluded, the absence of systemic, radiological, and biological features makes this diagnosis unlikely, with findings more consistent with renal involvement secondary to SLL infiltration. Patients with lymphoproliferative disorders are also at increased risk of opportunistic infections (e.g. tuberculosis, histoplasmosis, and parasitic infections) related to both disease-induced and treatment-induced immunosuppression. Furthermore, drug-induced granulomatous tubulointerstitial nephritis must be considered, as polypharmacy and prolonged antimicrobial therapy are frequent in haematological malignancies [17].

In our patient, alternative causes such as renal sarcoidosis, drug-induced nephritis, infectious causes (particularly tuberculosis), and autoimmune disease were reasonably excluded. Subsequent specific immunohistochemical staining confirmed renal infiltration by lymphoma, supporting the suspected diagnosis [15]. Granulomatous involvement can therefore be considered a direct manifestation of CLL/SLL.

Granulomatous reactions are common in Hodgkin lymphoma, reported in 9–29% of cases, but are much rarer in non-Hodgkin lymphomas, including CLL/SLL, where the reported prevalence does not exceed 7.3% [18]. The most frequent sites are the lymph nodes, spleen, liver, and skin [19].

Importantly, granulomatous lesions may precede, coincide with, or follow the diagnosis of lymphoma. In a series by De Charry et al., some patients initially received a misdiagnosis of sarcoidosis when granulomatous lesions were, in fact, the first clinical manifestation of lymphoma. Given the non-specific nature of the histological findings, granulomatous inflammation alone cannot reliably distinguish between aetiologies. Therefore, features atypical of sarcoidosis (e.g. older age, the absence of thoracic involvement, or histological atypia) should prompt reconsideration of the diagnosis. Histological features atypical of sarcoidosis include few, poorly formed epithelioid granulomas, the lack of a predominantly perivascular distribution, a more random spatial distribution pattern rather than distribution at the periphery of granulomas, and a non-T-cell predominance of the surrounding inflammatory infiltrate [20]. In suspected lymphoma cases, immunohistochemistry to demonstrate B-cell infiltration should always be performed [17].

The pathophysiological mechanism underlying granulomatous reactions in lymphomatous infiltration remains poorly understood. One hypothesis involves a T-cell–mediated hypersensitivity response to tumour antigens, leading to monocyte activation, a cytokine cascade, and the differentiation of monocytes into epithelioid histiocytes, resulting in granuloma formation. Another hypothesis suggests direct cytokine secretion, particularly interferon-gamma, by neoplastic B cells, driving macrophage differentiation into epithelioid histiocytes and granuloma development [16].

In the literature, we identified seven publications describing ten patients with granulomatous tubulointerstitial nephritis secondary to CLL/SLL infiltration, with or without a suspected drug-related trigger (table S1 in the appendix) [8–14]. The earliest reports, published in 1994 and 1995, described patients with CLL/SLL who had granulomatous lesions initially attributed to nitrofurantoin and allopurinol exposure [8, 9]. In one case, no immunostaining or assessment of lymphomatous infiltration was performed, whereas the other described renal lymphoma involvement. A subsequent report in 2009 described granulomatous nephritis following alendronate therapy in a patient with biopsy-proven lymphomatous renal involvement [11]. Overall, most cases, including ours, have not shown a direct link to drug exposure, although treatment may have acted as a potential trigger for granulomatous inflammation.

CLL/SLL is typically indolent at the time of acute kidney injury onset. In 7 of the 10 reported cases, patients were under active surveillance without specific haematological treatment. However, some cases showed renal function deterioration in parallel with haematological progression. For example, Nasr et al. described acute kidney injury episodes coinciding with marked leukocytosis, reflecting active CLL/SLL [13]. This was not observed in our patient, who showed stable lymphadenopathy and no leukocytosis.

At diagnosis, renal involvement is typically severe, with a mean serum creatinine level of 609 μmol/l and dialysis required in 70% of cases (7/10). Histological analysis frequently reveals non-necrotising granulomas with a predominantly perivascular distribution, moderate to diffuse interstitial infiltration, tubulitis, and tubular atrophy; some biopsies have also shown advanced interstitial fibrosis.

Because of its rarity and heterogeneous causes, no randomised trials have established an optimal treatment strategy for granulomatous tubulointerstitial nephritis. In clinical practice, management typically includes the discontinuation of suspected offending agents, treatment of the underlying disease, and the initiation of corticosteroid therapy in the absence of infectious contraindications. In a retrospective study, Joss et al. analysed 18 granulomatous tubulointerstitial nephritis cases of various aetiologies; 16 patients were treated with corticosteroids, with renal function improving or stabilising in 15, suggesting a potential therapeutic benefit, although prospective validation is lacking [21].

In our case, a multidisciplinary approach between nephrology and haematology led to the initiation of combined corticosteroid and acalabrutinib therapy, resulting in rapid renal improvement. Among the six previously published cases of granulomatous tubulointerstitial nephritis secondary to CLL/SLL treated with corticosteroids, alone or in combination with lymphoma-directed therapy, five experienced improved renal function [9, 13]. The only non-responder had extensive lymphomatous infiltration on renal biopsy [10]. By contrast, in patients who did not receive corticosteroids, the renal outcome was poor: one patient improved after discontinuation of the suspected drug [8], whereas the remaining three patients treated only with targeted therapy progressed to end-stage renal disease requiring dialysis [12–14]. These observations suggest that corticosteroids may be beneficial in granulomatous tubulointerstitial nephritis, but their efficacy appears limited when extensive lymphomatous infiltration or advanced chronic renal damage is present [14].

Our patient developed multiple severe infections, including an episode of sepsis one month after the initiation of immunosuppressive therapy with corticosteroids, secondary to influenza A pneumonia complicated by bacterial superinfection. Four months after the diagnosis of granulomatous tubulointerstitial nephritis and seven weeks after the initiation of acalabrutinib, the patient developed invasive fungal sinusitis caused by *Aspergillus fumigatus*, complicated by a sixth cranial nerve palsy and *Staphylococcus hominis* and *Staphylococcus epidermidis* bacteraemia. Management required aggressive antifungal therapy and surgical sphenoidotomy, leading to the discontinuation of acalabrutinib. Invasive fungal infections, particularly those caused by *Aspergillus fumigatus*, have been reported in patients treated with acalabrutinib [22, 23]. Corticosteroid therapy is also a risk factor for the development of invasive aspergillosis [24]. In previously reported cases, several patients developed serious infections such as recurrent pulmonary infections or cellulitis-related sepsis. These patients had received corticosteroid therapy alone or corticosteroids in combination with rituximab or with chlorambucil, cyclophosphamide, and vincristine [10, 13].

These infectious complications likely result from multiple converging factors. Beyond the intrinsic immune dysfunction of CLL/SLL – characterised by hypogammaglobulinaemia, complement deficiencies, and impaired cellular immunity – immunosuppressive therapies further increase the risk of infection [25]. Advanced age and renal dysfunction, both common in this population, may represent additional vulnerabilities. Consequently, patients treated for granulomatous tubulointerstitial nephritis secondary to CLL/SLL require close monitoring, particularly after the initiation of immunosuppressive or targeted therapies.

Conclusions

In conclusion, unexplained acute kidney injury in a patient with CLL/SLL should raise clinical suspicion. Renal biopsy with immunohistochemistry is essential to assess for lymphomatous infiltration. In cases of granulomatous tubulointerstitial nephritis, a thorough diagnostic work-up must be conducted to rule out sarcoidosis and drug-related, infectious, or autoimmune causes. When lymphomatous infiltration is confirmed, treatment with corticosteroids and lymphoma-directed therapy may lead to renal improvement. The management of these patients should be multidisciplinary, and close follow-up is required due to the notable risk of infection, which appears to be related to the underlying haematological disease and to the immunosuppressive and lymphoma-directed treatments.

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Authors' contributions: IP, AH, DDS, SDS, and LB were involved in patient follow-up and contributed to the diagnosis. GA was responsible for the pathological examination of the kidney biopsies and contributed to writing the pathology section. IP drafted the manuscript. AH, DDS, CRO, SDS, and LB critically revised the manuscript. All authors read and approved the final manuscript.
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Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest related to the content of this manuscript was disclosed.

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Appendix

Table S1. Characteristics of patients with granulomatous tubulointerstitial nephritis secondary to infiltration by CLL/SLL.

First author, year of publication	Sex, age (years)	Haematologic diagnosis, year of diagnosis, treatment initiated	Time between CLL/SLL diagnosis and GIN diagnosis	Possible contributing factors	sCr at the time of biopsy (µmol/l)	Biopsy findings	Treatment initiated	Response to treatment	Need for dialysis	Complications, death
Korzet 1994	Male, 76	CLL 1985	5 years	Nitrofurantoin	827	Normal glomeruli, tubules, and interstitium. One non-caseating epithelioid granuloma. No lymphoma markers.	Nitrofurantoin discontinuation.	sCr 203 µmol/L within 6 weeks	No	No / not described
Martinez-Vea 1995	Male, 70	CLL Binet B, 1985, prednisone and allopurinol	Unknown	Allopurinol and progression of CLL	884	17% glomerulosclerosis. Interstitial inflammatory infiltrate (lymphocytes, monocytes, some eosinophils). Numerous non-caseating granulomas. Lymphocyte markers: T-cell-specific UCHL-1 Ab and B-cell-specific CD20 Ag.	Prednisone 70 mg/day and CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone).	sCr 212 µmol/L	Yes (temporary)	No / not described

Kamat 2007	Male, 72	CLL Binet A	Unknown	Initial suspicion of sarcoidosis	860	Hyaline casts with lymphocytic tubulitis. Interstitial inflammatory infiltrate (lymphocytes, plasma cells, eosinophils). Numerous non-necrotising epithelioid granulomas. One biopsy showed diffuse leukemic infiltration on a background of chronic tubule-interstitial disease. Lymphocyte markers: CD5, CD20, CD23, CD79a, BCL-2. Mononuclear cell markers: CD3, CD68 (PGM1).	Initial suspicion of sarcoidosis. Prednisolone, then chlorambucil, cyclophosphamide, vincristine, and prednisolone.	No improvement	Yes	Recurrent chest infections. Died of cellulitis-acquired sepsis
Inoue 2010	Male, 50	CLL	18 months	None	445	Interstitial inflammatory infiltrate (lymphocytes) with several nodular granulomas. Normal glomeruli. Lymphocyte markers: CD20, CD23, BCL-2. CLL infiltration accompanied by infiltration of reactive CD3+/CD5+ T cells forming nodular granulomas	Fludarabine phosphate for 3 days.	Progression of renal involvement	Yes	No / not described
Nasr 2015, 1st case	Male, 57	CLL Rai I	2 years	None	519	Diffuse interstitial inflammatory infiltrate, tubulitis, mild tubular atrophy, and interstitial fibrosis. Small, ill-defined non-necrotising granulomas with giant cells. Focal (20%) interstitial CLL involvement.	Corticosteroids, rituximab, and cyclophosphamide.	sCr 203 µmol/L, followed by worsening of renal function closely linked to lymphocytosis	No	Alive (81 months post-biopsy)
Nasr 2015, 2nd case	Female, 74	CLL Rai 0	4 years	Alendronate sodium	1311	Diffuse interstitial inflammatory infiltrate, mild tubular atrophy, interstitial fibrosis. Large, well-defined non-necrotising granulomas with giant cells. Focal (30%) interstitial CLL involvement.	Pulsed IV methylprednisolone, followed by prednisone 60 mg/day tapered over 6 weeks, plus cyclophosphamide.	sCr 186 µmol/L	Yes (for 2 months)	Died of breast cancer (31 months post-biopsy)

Nasr 2015, 3rd case	Male, 78	CLL Rai 3, IVIG	8 months	None	607	Patchy reactive interstitial inflammation, tubulitis, moderate tubular atrophy, and interstitial fibrosis. Large, well-defined non-necrotising granulomas, also involving interlobular arteries, with giant cells. Focal (10%) interstitial CLL/SLL involvement. Focal segmental glomerulosclerosis.	Corticosteroids (1 mg/kg/day).	sCr 283 µmol/L	No	Died of cellulitis (2 months post-biopsy)
Nasr 2015, 4th case	Male, 79	CLL Rai 1	18 months	None	506	Diffuse reactive interstitial inflammation, tubulitis, moderate tubular atrophy, and interstitial fibrosis. Small to large, ill-defined non-necrotising granulomas with giant cells. Focal (20%) interstitial CLL involvement.	Corticosteroids and rituximab.	sCr 186 µmol/L	Yes (for 4 months)	Died of pneumonia and acute renal injury (49 months post-biopsy)
Nasr 2015, 5th case	Male, 63	CLL Rai 4, chemotherapy (data not available) at diagnosis and rituximab 2 years later for recurrence	4 years	Lisinopril	889	Diffuse reactive interstitial inflammation, tubulitis, severe tubular atrophy, and interstitial fibrosis. Large, well-defined non-necrotising granulomas with giant cells. Diffuse (80%) interstitial CLL involvement.	Rituximab.	No improvement	Yes	Alive (43 months post-biopsy)
Suzuki 2017	Male, 55	CLL Rai 2	3.5 years	None	234	56% glomerulosclerosis. Diffuse (90%) tubulointerstitial inflammatory infiltrate (lymphocytes). Some non-caseating epithelioid granulomas. Lymphocyte markers: CD5, CD20, CD3.	Cyclophosphamide.	No improvement	Yes	No / not described

Abbreviations: sCr, serum creatinine; GIN, granulomatous interstitial nephritis; CLL, chronic lymphocytic leukaemia; IVIG, intravenous immunoglobulins.