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Cascade of opportunistic infections in focal segmental glomerulosclerosis under dual immunosuppressive therapy: a case report

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Background: Focal segmental glomerulosclerosis (FSGS) is a heterogeneous glomerular disease frequently treated with high-dose glucocorticoids and calcineurin inhibitors, which can markedly increase susceptibility to opportunistic infections.

Case presentation: A 53-year-old previously healthy male presented with nephrotic syndrome and was diagnosed with FSGS on renal biopsy, for which he received high-dose prednisolone followed by cyclosporine. During dual immunosuppressive therapy, he developed sequential opportunistic infections, beginning with *Listeria monocytogenes* bacteremia and pneumonia, followed by probable Cytomegalovirus pneumonitis with high serum and bronchoalveolar viral loads, herpesvirus reactivation compatible with VZV, *Pneumocystis jirovecii* pneumonia, oral and intra-abdominal candidiasis, and onychomycosis. His course was further complicated by severe anemia and radiologic evidence of pneumoperitoneum; laparotomy revealed diverticulitis with microperforation but no overt bowel perforation. Management required intensive care unit admission, mechanical ventilation, broad-spectrum antibacterial and antifungal therapy, ganciclovir/valganciclovir, high-dose trimethoprim-sulfamethoxazole, and subsequent de-escalation of immunosuppression from prednisolone plus cyclosporine to lower-dose prednisolone plus mycophenolate mofetil. Targeted gene panel sequencing excluded common monogenic FSGS mutations, and anti-interferon- γ autoantibodies were absent. Absolute lymphocyte count, CD4 count, and immunoglobulin levels were not profoundly suppressed, supporting iatrogenic immunosuppression as the main driver of infection susceptibility. After optimization of immunosuppressive and anti-infective therapy, he stabilized without further opportunistic infections over nine months of follow-up, despite persistent nephrotic-range proteinuria and hypoalbuminemia.

Conclusions: This case illustrates how prolonged combined corticosteroid and calcineurin inhibitor therapy in FSGS can precipitate a cascade of severe

opportunistic infections, emphasizing the need for early pathogen-specific prophylaxis, vaccination, systematic infection surveillance, and dynamic reassessment of cumulative immunosuppression.

KEYWORDS

calcineurin inhibitors, case report, focal segmental glomerulosclerosis, immunosuppressive therapy, opportunistic infections, *Pneumocystis jirovecii* pneumonia

Introduction

Focal segmental glomerulosclerosis (FSGS) is a histopathologic pattern of glomerular injury characterized by segmental sclerosis involving portions of glomeruli and arising from diverse primary or secondary etiologies (1). This heterogeneity is reflected in variable pathogenesis, clinical course, and response to therapy, making timely diagnosis and tailored management crucial for renal outcome (2).

For primary FSGS, contemporary guidelines recommend high-dose oral glucocorticoids, typically prednisone at approximately 1 mg/kg/day, as first-line therapy for at least four weeks, and often up to 16 weeks, depending on the response (3, 4). In patients with steroid-resistant, steroid-dependent, or steroid-intolerant disease, calcineurin inhibitors (CNIs) such as cyclosporine or tacrolimus are widely used as alternative or adjunctive agents to achieve proteinuria reduction and preserve kidney function (3, 4). However, these regimens profoundly affect cell-mediated immunity, increasing susceptibility to a broad spectrum of opportunistic pathogens.

The risk of infection in glomerular disease is determined by the cumulative “net state of immunosuppression,” integrating drug exposure, underlying comorbidities, disruption of anatomic barriers, and prior colonization or latent infections. Glucocorticoids interfere with interleukin-2 signaling and T-cell activation (5). At the same time, cyclosporine further suppresses T-cell function and macrophage recruitment (6), creating a permissive environment for intracellular organisms such as *Listeria monocytogenes*, Cytomegalovirus (CMV), *Pneumocystis jirovecii*, and fungal pathogens. Recent work in nephrology and transplantation underscores the importance of baseline screening for latent viral infections, early *Pneumocystis* prophylaxis, and completion of recommended vaccinations in patients receiving prolonged corticosteroids and CNIs (7, 8).

Despite these recommendations, reports detailing stepwise opportunistic infections in non-transplant FSGS patients on dual immunosuppression remain scarce. This case report describes a previously healthy adult with biopsy-proven FSGS who, under high-dose prednisolone and cyclosporine, developed a cascade of bacterial, viral, and fungal opportunistic infections, culminating in diverticulitis with microperforation. It discusses preventive strategies and therapeutic adjustments aiming at mitigating such complications.

Case description

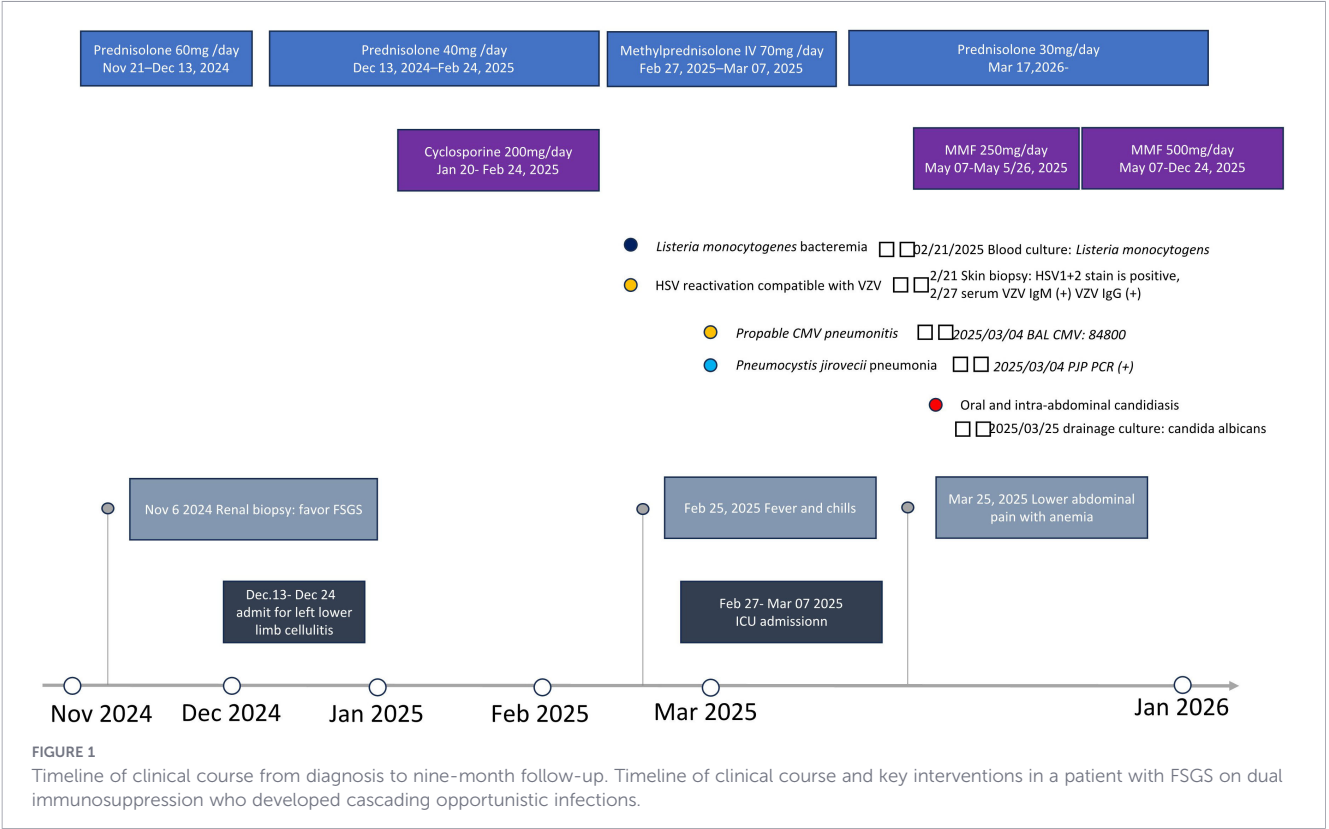
A 53-year-old male physical education teacher with a baseline body weight of approximately 82 kg and an ideal body weight (IBW) of

58.8 kg with no known past medical history, including chronic lung disease, prior TB exposure, or structural lung abnormalities, initially presented to a local hospital with progressive bilateral lower limb edema and was diagnosed with nephrotic syndrome. He was referred to the nephrology outpatient clinic of a tertiary center, where renal biopsy confirmed FSGS (Supplementary Figure 1), and he was admitted for further evaluation and initiation of therapy. The overall clinical course is summarized in Figure 1. Baseline laboratory investigations demonstrated nephrotic-range proteinuria, with a 24-hour urine protein of 11.1 g/day, serum creatinine of 1.48 mg/dL, serum albumin of 1.82 g/dL, urine protein-to-creatinine ratio of 11.6 g/g, and an estimated glomerular filtration rate (eGFR) of 55.8 mL/min/1.73 m².

High-dose oral prednisolone at approximately 1 mg/kg/day (30 mg twice daily) was started. Three weeks later, he required hospitalization for left lower limb cellulitis, leading to tapering of prednisolone to 40 mg/day. Over the subsequent two months, his clinical course was further complicated by steroid-related progressive weight gain, marked bilateral lower-extremity edema, prominent striae, and worsening finger numbness and stiffness. Due to his significant side effects from steroid use and persistent proteinuria (urine protein-to-creatinine ratio of 12.8 g/g), the nephrologist subsequently introduced cyclosporine 100 mg twice daily for FSGS control. At that time, the patient's body weight was approximately 80 kg, corresponding to a cyclosporine dosage of approximately 2.5 mg/kg/day. Therapeutic drug monitoring (TDM) was not performed during the initiation treatment period. Subsequent therapeutic drug monitoring performed during a later treatment episode with cyclosporine 50 mg twice daily in January 2026 demonstrated trough concentrations of approximately 35–50 ng/mL.

Approximately one month after starting dual immunosuppression, the patient presented to the emergency department with erythematous rashes and blisters on both lower limbs and was provisionally diagnosed with infectious folliculitis; blood cultures were obtained, and he was discharged for outpatient dermatologic evaluation and skin biopsy. He returned the next day with fever and chills, and chest radiography revealed bilateral lower-lobe infiltrates. Meanwhile, the previously drawn blood cultures had grown *Listeria monocytogenes*. Due to the unavailability of standalone ampicillin, he received intravenous ampicillin/sulbactam, with concomitant reduction of prednisolone and discontinuation of cyclosporine.

Despite early antimicrobial therapy, his respiratory status rapidly deteriorated, necessitating high-flow oxygen and subsequent transfer to the intensive care unit (ICU), where he was intubated for acute respiratory failure. Computed tomography (CT) angiography (Figure 2) excluded pulmonary embolism but showed bilateral infiltration. Given impaired renal function, meropenem was added to enhance *Listeria* coverage, while initial virologic and fungal testing

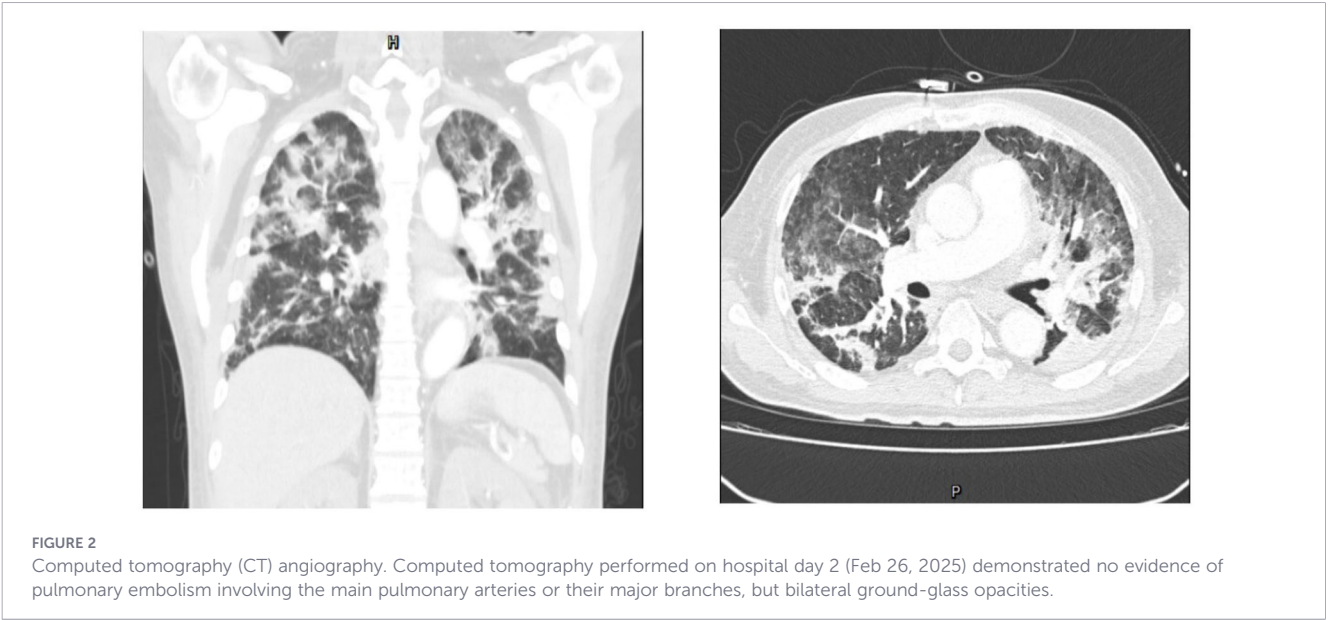


(including influenza, COVID-19, serum galactomannan, cryptococcal antigen, and HIV serology) was negative. Based on clinical suspicion of acute respiratory distress syndrome, intravenous methylprednisolone at 1 mg/kg/day was started.

On hospital day 4 in the ICU, serologic testing revealed markedly elevated CMV IgG and a serum CMV viral load of 27,500 copies/mL, leading to initiation of intravenous ganciclovir. Subsequent bronchoscopy with bronchoalveolar lavage (BAL) showed no bacterial or mycobacterial respiratory pathogens on multiplex polymerase chain reaction (PCR) testing, yet CMV viral

load in BAL was high (84,800 copies/mL), consistent with probable CMV pneumonitis. A previously obtained skin biopsy later demonstrated Herpes simplex virus (HSV)-1/2 positivity, while serology showed positive Varicella-zoster virus (VZV) IgG and IgM with negative HSV IgM. However, confirmatory testing, including PCR, immunohistochemistry, or direct fluorescent antibody (DFA) testing, was unavailable. Therefore, the episode was more conservatively interpreted as herpesvirus reactivation compatible with VZV.

The patient's pulmonary status gradually improved with ventilatory support and ganciclovir therapy, allowing extubation and



transfer to the general ward. However, attempts to taper corticosteroids and oxygen were limited by persistent infiltrates (Figure 3) and ongoing hypoxemia, prompting empiric initiation of high-dose intravenous trimethoprim-sulfamethoxazole (TMP-SMX) for suspected *Pneumocystis jirovecii* pneumonia (PJP). The results of PCR from BAL performed during stay at the ICU later confirmed PJP infection, and after continuation of therapy, his oxygen requirement decreased progressively, eventually reaching room air.

During the ward course, he developed oral candidiasis, which was treated with nystatin. Systemic antibacterial therapy was subsequently de-escalated once he completed a 14-day course targeting *Listeria*. After two weeks of Intravenous ganciclovir as the induction therapy, the patient transitioned to oral valganciclovir as the maintenance therapy with a response of declining CMV burden. Meanwhile, high-dose TMP-SMX was converted to oral therapy and subsequently to secondary prophylaxis.

Persistent anemia and a positive fecal occult blood test led to the performance of upper and lower gastrointestinal endoscopy, which revealed a tubular adenoma in the transverse colon and no evidence of CMV colitis. He was discharged clinically stable on valganciclovir, oral TMP-SMX for secondary PJP prophylaxis, and a tapering corticosteroid regimen.

At early post-discharge follow-up, he re-presented with severe anemia (hemoglobin 5.9 g/dL) and new lower abdominal pain. The patient also reported persistent bloody stool. Stool occult blood test was strongly positive for 4 +. Abdominal CT demonstrated mild pneumoperitoneum and ascites suggestive of hollow viscus perforation. Emergency laparoscopy converted to open laparotomy did not reveal an obvious perforation, but intra-abdominal drains were placed, and he was started on meropenem, continued high-dose TMP-SMX, and fluconazole for presumed complicated intra-abdominal infection and candidiasis. Valganciclovir for CMV pneumonitis was discontinued after 24 days, and corticosteroids were maintained at a lower dose of intravenous methylprednisolone to control FSGS.

Subsequently, *Candida albicans* grew from the drain fluid, leading to escalation of fluconazole dosing, while corticosteroids were further tapered to oral prednisolone 20 mg/day. The patient remained asymptomatic, tolerated oral intake, and was discharged on oral fluconazole and TMP-SMX prophylaxis. Over the following weeks, PJP prophylaxis was completed after one month, and

fluconazole was continued for a total of six weeks, constituting the antifungal course.

Because of ongoing nephrotic-range proteinuria, hypoalbuminemia, and edema, but in view of his history of multiple severe infections on previous dual high-dose prednisolone and cyclosporine, the treating team opted to maintain prednisolone at 15 mg/day and introduce mycophenolate mofetil as second-line therapy, with cautious dose escalation. During a nine-month follow-up on prednisolone (15 mg/day) and mycophenolate mofetil (500 mg/day), his edema gradually improved, and renal function remained stable, with persistent but non-progressive proteinuria and hypoalbuminemia and no further opportunistic infections. At that time, laboratory investigations showed a serum creatinine level of 2.13 mg/dL, serum albumin of 2.22 g/dL, urine protein-to-creatinine ratio of 9.7 g/g, and an estimated glomerular filtration rate (eGFR) of 35.9 mL/min/1.73 m².

To explore predisposing factors, we performed targeted gene panel sequencing, which screened 134 targeted genes associated with monogenic FSGS, nephrotic syndrome, Alport syndrome, and related podocytopathies (see [Supplementary Table 1](#) for representative genes included in the targeted gene panel). No pathogenic variants were identified in key genes including NPHS1, NPHS2, WT1, LAMB2, TRPC6, ACTN4, INF2, or APOL1, supporting a diagnosis of primary (non-genetic) FSGS (9–11). Immunologic evaluation demonstrated IgG, IgA, and IgM levels of 578, 109, and 169 mg/dL, respectively, with Absolute lymphocyte counts of 1678 cells/ μ L, and CD4+ T-cell counts of 403 cells/ μ L. In addition, a focused workup for autoantibodies, and anti-interferon- γ autoantibodies was negative. Collectively, these findings supported intensive iatrogenic immunosuppression with high-dose prednisolone and cyclosporine as the principal explanation for the infectious sequence.

Discussion

Infection cascade and immunopathogenesis

This case illustrates how aggressive immunosuppressive therapy for primary FSGS in an otherwise healthy adult can trigger a complex multi-pathogen infection course involving bacterial,



FIGURE 3
Serial chest radiograph changes during hospitalization. (A) Chest radiograph on admission showing minimal infiltrates. (B) Bilateral patchy infiltrates on hospital day 28 before TMP-SMX treatment for PJP. (C) Marked improvement after 2 weeks of PJP treatment on hospital day 42.

viral, and fungal pathogens. The temporal sequence—*Listeria monocytogenes* bacteremia and pneumonia followed by probable CMV pneumonitis, herpesvirus reactivation compatible with VZV, PJP pneumonia, and candidal infections—reflects progressive erosion of cell-mediated immunity under prolonged exposure to high-dose corticosteroids and a calcineurin inhibitor.

Glucocorticoids impair T-cell proliferation and cytokine signaling (5), while cyclosporine further inhibits T-cell activation and macrophage function (6), creating a permissive environment for intracellular organisms, such as *Listeria monocytogenes*. In this patient, *Listeria monocytogenes* infection was the first major opportunistic event, presenting as bacteremia and bilateral pulmonary infiltrates shortly after the onset of dual immunosuppression, consistent with impaired cell-mediated defenses. The subsequent development of probable CMV pneumonitis with high serum and BAL viral loads likely further amplified immunosuppression, given the known immunomodulatory effects of CMV, which can predispose to secondary infections, including PJP.

Diagnostic challenges in immunocompromised hosts

The diagnosis of opportunistic infections in this patient was complicated by attenuated inflammatory responses due to ongoing corticosteroid therapy. In particular, *Pneumocystis jirovecii* pneumonia presented with progressive hypoxemia and radiographic deterioration, which was initially difficult to distinguish from other infectious or inflammatory pulmonary processes in the setting of profound immunosuppression. Chest CT demonstrated diffuse bilateral ground-glass opacities, and the patient developed worsening oxygenation. Although serum β -D-glucan was not available in this case, which is a limitation, the overall clinical and radiologic findings supported the diagnosis of PJP. Empiric initiation of high-dose trimethoprim-sulfamethoxazole followed by confirmation via bronchoalveolar lavage PCR highlights the importance of maintaining a low threshold for initiating PJP-directed therapy in high-risk patients, especially those receiving combined corticosteroid and calcineurin inhibitor treatment without prophylaxis. BAL PCR positivity may also reflect colonization; however, in this case, the concordant clinical deterioration, imaging findings, and therapeutic response supported active infection rather than incidental colonization.

In addition, the coexistence of oral, cutaneous, and intra-abdominal candidiasis, as well as onychomycosis, and isolation of *Candida* species from surgical drain cultures, underscore the breadth of fungal risk in the setting of broad-spectrum antibiotics, mucosal disruption, and sustained immunosuppression.

The diagnosis of CMV pneumonitis in this case should also be interpreted cautiously. Although elevated serum CMV viral load and detection of CMV in BAL fluid raised strong clinical suspicion for pulmonary CMV involvement, definitive evidence of invasive CMV lung disease, including histopathology, cytopathic changes, immunohistochemistry, or highly specific radiographic features, was unavailable. Therefore, the pulmonary manifestations were considered a mixed pulmonary infectious process involving bacterial pneumonia, PJP, and possible CMV involvement.

Last but not least, the clinicopathologic correlation of the vesiculobullous skin lesions was limited. Skin biopsy demonstrated HSV-1/2 positivity; however, confirmatory PCR testing or viral subtyping was unavailable, precluding definitive differentiation between HSV and VZV. Considering the clinical presentation and subsequent serologic findings, the episode was more conservatively classified as probable herpesvirus reactivation compatible with VZV.

Gastrointestinal complications and corticosteroid-associated fragility

The episode of diverticulitis with microperforation and radiologic pneumoperitoneum following extended steroid exposure likely reflects cumulative gastrointestinal toxicity and impaired healing capacity associated with corticosteroids (12). Similar associations between long-term glucocorticoid therapy and diverticular perforation have been reported (13), supporting the concept that steroid-related fragility can exacerbate otherwise limited diverticular disease into complicated intra-abdominal pathology.

Treatment strategy reconsideration

From a preventive and retrospective perspective, this case highlights several important considerations regarding immunosuppressive strategy and infection risk management. The absence of *Pneumocystis jirovecii* pneumonia prophylaxis during the period of combined high-dose prednisolone and cyclosporine therapy represents a potential gap in infection prevention, as the overall immunosuppressive burden would typically meet criteria for prophylaxis in non-HIV immunocompromised patients.

In addition, baseline evaluation, including vaccination history and latent infection screening (e.g., Varicella-zoster virus, Cytomegalovirus, and tuberculosis), was not systematically performed before escalation of immunosuppressive therapy. This limitation was, in part, related to the absence of a standardized institutional protocol for infectious risk stratification in this clinical setting.

Finally, the subsequent development of infectious complications underscores the importance of continuous reassessment of both the necessity and intensity of dual immunosuppression. Earlier implementation of cyclosporine therapeutic drug monitoring (TDM), together with more timely adjustment of immunosuppressive therapy, might have allowed better balancing between disease control and infection risk.

Systemic and host susceptibility factors

Extensive evaluation excluded intrinsic immunodeficiency conditions, including common monogenic forms of Focal Segmental Glomerulosclerosis and anti-interferon- γ autoimmunity. While iatrogenic immunosuppression likely played a major contributory role, we acknowledge that additional baseline factors may have further contributed to impaired host immunity, including severe nephrotic syndrome with hypoalbuminemia, probable urinary immunoglobulin loss, prolonged hospitalization, and broad-spectrum antibiotic exposure.

Subsequent therapeutic drug monitoring performed during a later lower-dose treatment episode demonstrated trough levels below the target range. However, these measurements may not accurately reflect cyclosporine exposure during the initial treatment period, when therapeutic drug monitoring was not performed. Therefore, supratherapeutic exposure cannot be ruled out as a contributing factor to the patient's susceptibility to infection. Accordingly, these later trough concentrations should not be interpreted as representative of drug exposure during the initial treatment period.

This observation is consistent with the concept of the “net state of immunosuppression,” in which the cumulative effect of multiple immunosuppressive agents, rather than any single drug exposure, drives the risk of opportunistic infections in patients with glomerular disease and other immunosuppressed populations.

Clinical outcome and literature context

Following modification of immunosuppressive therapy, including reduction of corticosteroid dosage and transition from cyclosporine to mycophenolate mofetil, combined with targeted antimicrobial therapy and short-term prophylaxis (4), was associated with clinical stabilization and the absence of further opportunistic infections over nine months. This suggests that tailoring immunosuppression to the lowest effective intensity and periodically re-evaluating the risk–benefit balance are critical for minimizing infectious complications (14), particularly in patients with persistent nephrotic syndrome who may require long-term therapy.

To our knowledge, this represented a rare and extensive cascade of opportunistic infections in a non-transplant FSGS patient. Previous case reports have described individual infections such as PJP or CMV in nephrotic syndrome (15, 16), but simultaneously bacterial, viral, and fungal pathogens with surgical complications have rarely been reported in this population.

Conclusion

This case highlights how prolonged combined high-dose corticosteroid and calcineurin inhibitor therapy for FSGS in a previously healthy adult can lead to a cascade of severe opportunistic infections, including *Listeria monocytogenes* bacteremia, probable CMV pneumonia, herpesvirus reactivation compatible with VZV, PJP, and invasive candidiasis, as well as diverticulitis with microperforation. The clinical course emphasizes that infection risk is driven by the cumulative immunosuppressive effect and can be amplified by diagnostic delays and the absence of pathogen-specific prophylaxis.

Early identification of high-risk patients, systematic screening for latent infections, implementation of PJP prophylaxis, optimization of vaccinations, and vigilant surveillance for early signs of infection should be integral components of care for individuals receiving prolonged corticosteroids and CNIs. Regular reassessment of immunosuppressive intensity and timely modification of regimens, as illustrated by the eventual shift to lower-dose prednisolone plus mycophenolate mofetil in this patient, are essential to prevent similar cascades and improve outcomes in patients with glomerular disease requiring long-term immunosuppressive therapy.

Take-away lessons

In patients with FSGS requiring high-dose corticosteroids (≥ 20 mg/day for >1 month) plus calcineurin inhibitors, clinicians should (1): initiate PJP prophylaxis with TMP-SMX before dual therapy; (2) screen for latent CMV, VZV, and tuberculosis at baseline; (3) ensure vaccination completion before immunosuppression; (4) maintain high clinical suspicion for opportunistic infections during therapy; and (5) consider early transition to lower-intensity regimens (e.g., mycophenolate mofetil) in patients developing infectious complications.

Patient perspective

When the kidney disease was first diagnosed, and medications were started, I just worried about leg swelling and fatigue, and did not realize how seriously my immune system could be weakened. The sudden onset of fever, breathing difficulty, and painful skin blisters, followed by admission to the intensive care unit and mechanical ventilation, was terrifying and left me feeling that my body was under attack from multiple infections simultaneously.

After prolonged and multiple hospitalizations, mechanical ventilation, surgeries, and numerous antimicrobial treatments, I felt fortunate to have survived and to be back at home, but I still worried about both the relapse of the kidney disease and the possibility of serious re-infections. I appreciate that my current treatment regimen maintained a better balance between controlling kidney disease and preserving immune function, and I valued the detailed examinations and thorough explanations from the medical team, which gave me confidence facing the future.

Data availability statement

The original contributions presented in the study are included in the article and its [Supplementary Material](#). Further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by Institutional Review Board, Kaohsiung Medical University Hospital (KMUH IRB). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

C-HW: Writing – original draft, Writing – review & editing. J-JL: Writing – original draft, Writing – review & editing, Formal analysis. D-YH: Formal analysis, Writing – original draft, Writing – review & editing, Data curation. C-YW: Writing – original draft, Writing – review & editing, Methodology. S-YL: Writing – original draft, Writing –

review & editing. J-JT: Writing – original draft, Writing – review & editing, Conceptualization, Data curation, Formal analysis, Supervision.

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Generative AI statement

The author(s) declared that generative AI was not used in the creation of this manuscript.

References

- Gembillo G, Sessa C, Santoro D. Advances in the pathophysiology and treatment of focal segmental glomerulosclerosis: The importance of a timely and tailored approach. *World J Nephrol.* (2025) 14:103039. doi: 10.5527/wjn.v14.i2.103039
- Shabaka A, Tato Ribera A, Fernández-Juárez G. Focal segmental glomerulosclerosis: State-of-the-art and clinical perspective. *Nephron.* (2020) 144:413–27. doi: 10.1159/000508099
- Liew A, Gibson KL. How I treat focal segmental glomerulosclerosis. *Clin J Am Soc Nephrol CJASN.* (2022) 17:1814–6. doi: 10.2215/cjn.06850622
- Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group, Rovin BH, Adler SG, Barratt J, Bridoux F, Burdge KA, et al. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. *Kidney Int.* (2021) 100(Suppl 4):S1–S276. doi: 10.1016/j.kint.2021.05.021
- Albarracín Melo LT, Abdulkhakov N, Han I, El-Bizri A, Brunner-Weinzierl M, Schraven B, et al. The immunosuppressive effect of glucocorticoids in human primary T cells is mainly mediated via a rapid inhibition of the IL-2/IL-2R signaling axis. *Cell Comm Signaling CCS.* (2025) 23:268. doi: 10.1186/s12964-025-02266-0
- Matsubara Y, Kiwan G, Liu J, Gonzalez L, Langford J, Gao M, et al. Inhibition of T-cells by cyclosporine A reduces macrophage accumulation to regulate venous adaptive remodeling and increase arteriovenous fistula maturation. *Arteriosclerosis Thrombosis Vasc Biol.* (2021) 41:e160–74. doi: 10.1161/atvbaha.120.315875
- Schweitzer L, Miko BA, Pereira MR. Infectious disease prophylaxis during and after immunosuppressive therapy. *Kidney Int Rep.* (2024) 9:2337–52. doi: 10.1016/j.ekir.2024.04.043
- Windpessl M, Kostopoulou M, Conway R, Berke I, Bruchfeld A, Soler MJ, et al. Preventing infections in immunocompromised patients with kidney diseases: Vaccines and antimicrobial prophylaxis. *Nephrol Dialysis Transplant Off Publ Eur Dialysis Transplant Assoc - Eur Renal Assoc.* (2023) 38:ii40–9. doi: 10.1093/ndt/gfad080
- Bierzyńska A, McCarthy HJ, Soderquest K, Sen ES, Colby E, Ding WY, et al. Genomic and clinical profiling of a national nephrotic syndrome cohort advocates a precision medicine approach to disease management. *Kidney Int.* (2017) 91:937–47. doi: 10.1016/j.kint.2016.10.013
- Malone AF, Phelan PJ, Hall G, Cetincelik U, Homstad A, Alonso AS, et al. Rare hereditary COL4A3/COL4A4 variants may be mistaken for familial focal segmental glomerulosclerosis. *Kidney Int.* (2014) 86:1253–9. doi: 10.1038/ki.2014.305
- Sambharia M, Rastogi P, Thomas CP. Monogenic focal segmental glomerulosclerosis: A conceptual framework for identification and management of a heterogeneous disease. *Am J Med Genet Part C Semin Med Genet.* (2022) 190:377–98. doi: 10.1002/ajmg.c.31990
- Narum S, Westergren T, Klemp M. Corticosteroids and risk of gastrointestinal bleeding: A systematic review and meta-analysis. *BMJ Open.* (2014) 4:e004587. doi: 10.1136/bmjopen-2013-004587
- Broersen LHA, Horváth-Puhó E, Pereira AM, Erichsen R, Dekkers OM, Sørensen HT. Corticosteroid use and mortality risk in patients with perforated colonic diverticular disease: A population-based cohort study. *BMJ Open Gastroenterol.* (2017) 4:e000136. doi: 10.1136/bmjgast-2017-000136
- Glenn DA, Zee J, Mansfield S, O'Shaughnessy MM, Bomback AS, Gibson K, et al. Immunosuppression exposure and risk of infection-related acute care events in patients with glomerular disease: An observational cohort study. *Kidney Med.* (2022) 4:100553. doi: 10.1016/j.xkme.2022.100553
- Zhou L, You X, Zhang J, Zhang W. Pneumocystis pneumonia in patients with primary nephrotic syndrome. *Clin Nephrol.* (2022) 97:226–31. doi: 10.5414/cn110679
- Cao Y, Li L. Long-term prognosis following cytomegalovirus respiratory infection in immunocompromised and immunocompetent patients: A retrospective single-centre study. *BMC Infect Dis.* (2025) 25:756. doi: 10.1186/s12879-025-11162-4

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