Pediatric Nephrology
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CLINICAL QUIZ

A patient presenting with fever after graft loss: Answers

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Answers

1. *What is your preliminary diagnosis for this patient?*

Initially, peritonitis should be suspected in a patient on peritoneal dialysis admitted with fever and abdominal pain; it was excluded in our patient. Also, urinary tract infection was excluded with normal urine microscopy and culture. She was evaluated for long COVID syndrome since she had a diagnosis of COVID-19 and MIS-C 4 months before her admission. Long COVID syndrome is the chronic persistence of symptoms associated with COVID-19, and studies have reported cases with symptoms lasting >12 weeks [1–3]. Long COVID syndrome in children also presents with persistent headache and fatigue, sleep disturbance, difficulty in concentrating, abdominal pain, myalgia, or arthralgia [4]. In the cluster analysis of clinical symptoms in long COVID syndrome, the prevalence of fever was 2.9–4.8, and the prevalence of abdominal pain was 3.7–6.0 [2]. Re-emergence of fever, increased acute phase reactants, and presence of erythropoietin-unresponsive anaemia were noteworthy, so we have updated our diagnosis list again. In addition to the above findings, the patient was diagnosed with graft intolerance syndrome due to the presence of tenderness on the graft.

2. *Which tests will support the diagnosis?*

Graft intolerance syndrome (GIS) is a clinical condition that occurs after the loss of graft function after kidney transplantation; the patients have a fever, flu-like symptoms, malaise, haematuria, localized pain, enlarged kidney size, elevated C-reactive protein, and resistant anaemia. Other possible aetiologies should be excluded before a diagnosis of GIS [5, 6]. In a series of 55 patients with GIS, approximately one-third of patients had an increase in graft size [6]. In our patient, there was no increase in graft size, but the parenchyma echo was increased by grade 1–2. Luna et al. confirmed a diagnosis of GIS with ^{18}F-FDG PET/CT in three patients with non-functional grafts who developed intolerance syndrome [7]. In the ^{18}F-FDG PET/CT imaging of our patient, a diffuse heterogeneous hypermetabolic activity of low level was observed in the subcapsular area of the transplanted kidney (Fig. 1), supporting the presence of inflammation on the graft.

3. *What are the treatment options?*

Treatment options for GIS include re-administration (if discontinued) or increasing the dose of immunosuppressants, graft embolization, or transplant nephrectomy [8]. In some cases, prednisolone and low-dose mycophenolate mofetil were administered to control inflammation; however, most of the patients required nephrectomy at follow-up [9]. Percutaneous renal artery embolization was performed successfully in 15 patients with symptomatic non-functioning kidney allograft, and only minor complications were reported in 4 patients [10]. In our patient, the dose of prednisolone was increased to 1 mg/kg/day and continued at the same dose for 1 month, gradually decreasing to 0.3 mg/kg/day. In the 5th month after the diagnosis of GIS, she had no fever and abdominal pain; haemoglobin was 11.1 g/dL and her C-reactive protein level was 3.48 mg/L.

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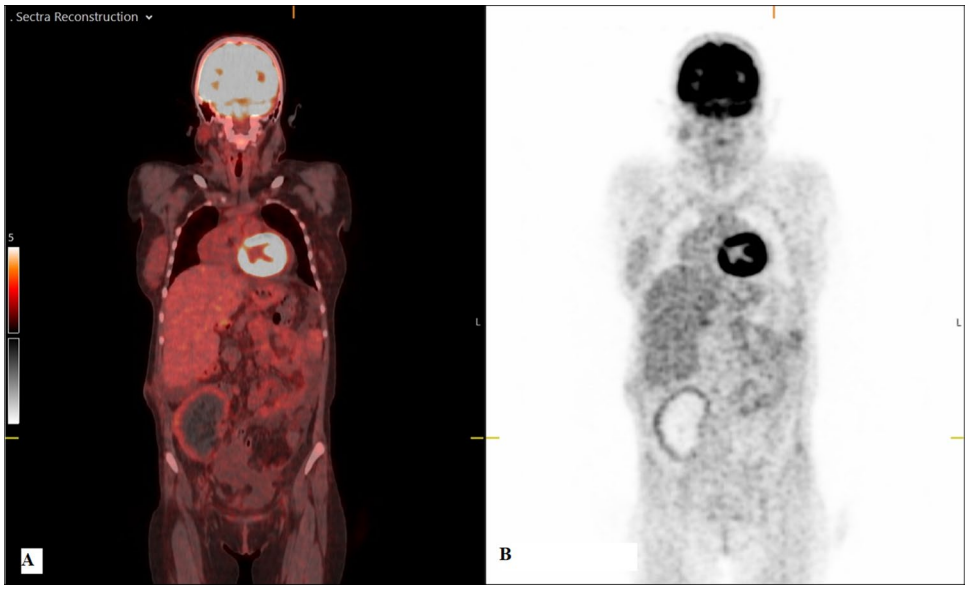

Fig. 1 Coronal image demonstrating diffuse low-level heterogeneous hypermetabolism in the transplanted kidney subcapsular area (SUVmax = 3.1). No activity was observed in the medial and medullary area of the transplanted kidney parenchyma. (**A**, fusion PET/CT; **B**, PET/CT)

Discussion

The incidence of GIS ranges from 12 to 37% in adults [6]. It mostly occurs within the first year after graft loss [11]. In a report with 74 patients who underwent graft nephrectomy, 48 of whom had GIS, the factors associated with GIS were age at graft failure, duration of dialysis, donor age, HLA mismatch, and several rejections [11]. Our patient was diagnosed with GIS 16 months after graft loss, and she had a history of acute rejection. We speculate that MIS-C, which occurred at follow-up after graft loss, may have stimulated the immune response, leading to reactivation of the inflammatory pathways in the graft, which had a silent course after the discontinuation of immunosuppressive treatments. It has been shown that inflammatory pathways are stimulated following COVID-19 infection [12, 13].

Conclusion

For a kidney transplant patient who has lost his/her graft; presents with fever, constitutional symptoms, and graft tenderness; and has increased inflammatory markers, resistant anaemia, and enlarged graft size, graft intolerance syndrome should be suggested. Although clinical findings may guide the diagnosis, ^{18}F-FDG PET/CT can also be used for the diagnosis.

Declarations

Conflict of interest The authors declare no competing interests.

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