Coexistence of Ureteropelvic Junction Obstruction and Familial Mediterranean Fever in a Child with Recurrent Fever: A Case Report

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Abstract

Background: Familial Mediterranean fever (FMF) is an autoinflammatory condition characterized by recurrent fever and serositis, while ureteropelvic junction obstruction (UPJO) is a common cause of upper urinary tract obstruction in children. The coexistence of both conditions is rare. A 5-year-old girl presented with left flank pain and recurrent fever. Investigations revealed bilateral hydronephrosis, with more severe UPJO on the left side. She underwent left pyeloplasty with double-J stent placement. Despite this, the patient continued to experience recurrent fever and abdominal pain. Genetic testing confirmed FMF, with mutations in the MEFV gene. Colchicine treatment was initiated, which helped manage her fevers and abdominal pain more effectively. This case highlights the rare coexistence of UPJO and FMF in a pediatric patient. It emphasizes the importance of considering multiple diagnoses when symptoms persist and underscores the role of genetic testing in confirming FMF.

Keywords: Familial Mediterranean Fever; Hydronephrosis; Ureteropelvic Junction Obstruction; Recurrent Fevers; Pediatrics.

Introduction

Ureteropelvic junction obstruction (UPJO) is a common cause of hydronephrosis in the pediatric population. It impairs urine flow from the renal pelvis to the ureter due to partial or complete narrowing at the junction. If left untreated, UPJO can lead to complications such as chronic infections, urolithiasis, and progressive renal function decline. Although most cases are congenital, the condition may remain asymptomatic until adulthood.[1] Many UPJO cases are managed conservatively with regular monitoring and sequential imaging. However, surgical intervention is required for patients with declining renal function, recurrent infections, or persistent symptoms.[2,3]

Familial Mediterranean fever (FMF) is an autoinflammatory monogenic disease characterized by recurrent fever episodes accompanied by serositis, such as peritonitis, pleuritis and arthritis. Episodes usually last one to four days, with patients experiencing fever and serositis, but they remain asymptomatic between attacks. The frequency of episodes varies, occurring anywhere from once a week to once every three to four months. Symptoms of FMF manifest in the first decade of life in approximately 50% of patients. Typically, diagnosis is based on clinical presentation, ethnicity, family history, and response to colchicine therapy.[4] The disease is caused by mutations in the Mediterranean fever (MEFV) gene, located on the short arm of chromosome 16.[5,6] This gene encodes pyrin, a protein that plays a key role in regulating inflammation. Mutations in pyrin lead to an overproduction of interleukin-1β (IL-1β), which is a key mediator of inflammation.[7] FMF is known to coexist with a variety of other diseases, including inflammatory and disorders. According to Salehzadeh and Moghaddam (2020), FMF patients may present with a range of coexisting conditions, such as juvenile idiopathic arthritis, Behçet's disease, and Inflammatory bowel disease.[8] Diagnosing FMF remains challenging

due to its diverse clinical presentations and many variants of the MEFV gene are classified as variants of uncertain significance.[9,10]

We present the case of a 5-year-old girl diagnosed with UPJO who developed recurrent fevers and abdominal pain after undergoing pyeloplasty. Further investigations revealed the coexistence of FMF, a combination that, to our knowledge, has not been previously reported in the literature.

Case Report

A 5-year-old girl presented to the clinic with a history of fever and left flank pain lasting several days. The child had a two-year history of voiding dysfunction that was managed with Baclofen. She was initially treated with antibiotics for a suspected urinary tract infection (UTI), as the urine culture grew coagulase-negative Staphylococcus species; however, her symptoms persisted despite treatment. Renal ultrasound revealed bilateral hydronephrosis, with an anteroposterior diameter of 11 mm in the right kidney and 12.5 mm in the left kidney. A diuretic renal scan using 99mTc-DTPA revealed bilaterally enlarged kidneys with mildly decreased perfusion and parenchymal uptake. The excretory phase demonstrated significant delayed clearance in both kidneys, with a poor response to the diuretic challenge (furosemide) at the 10-minute mark. The time to half-maximum (T½) exceeded 15 minutes, more prominently on the left side, indicating severely impaired drainage. Both renal pelvises were dilated, suggesting pelvicalyceal dilatation. Calculated glomerular filtration rate (GFR) was 75 mL/min for the right kidney and 77 mL/min for the left kidney, with relative renal function of 49.3% for the right kidney and 50.7% for the left. These findings were consistent with bilateral impaired excretion, likely secondary to severe UPJO (Figures 1 and 2).

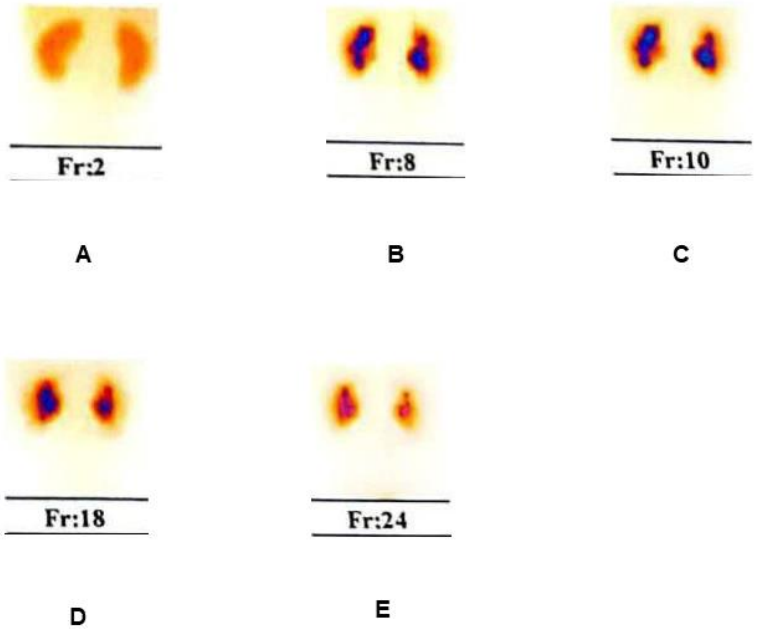

Figure 1: Preoperative sequential 99mTc-DTPA images of a 5-year-old girl with suspected ureteropelvic junction obstruction (UPJO). (A) Early perfusion image (Frame 2) shows symmetric bilateral renal perfusion with mildly reduced cortical uptake. (B, C) Cortical uptake images (Frames 8 and 10) demonstrate preserved but delayed parenchymal accumulation. (D) Post-furosemide image (Frame 18) shows persistent radiotracer retention in the pelvicalyceal systems of both kidneys, more prominent on the left. (E) Late excretory phase (Frame 24) confirms lack of drainage from the renal pelvises, especially on the left, despite diuretic stimulation.

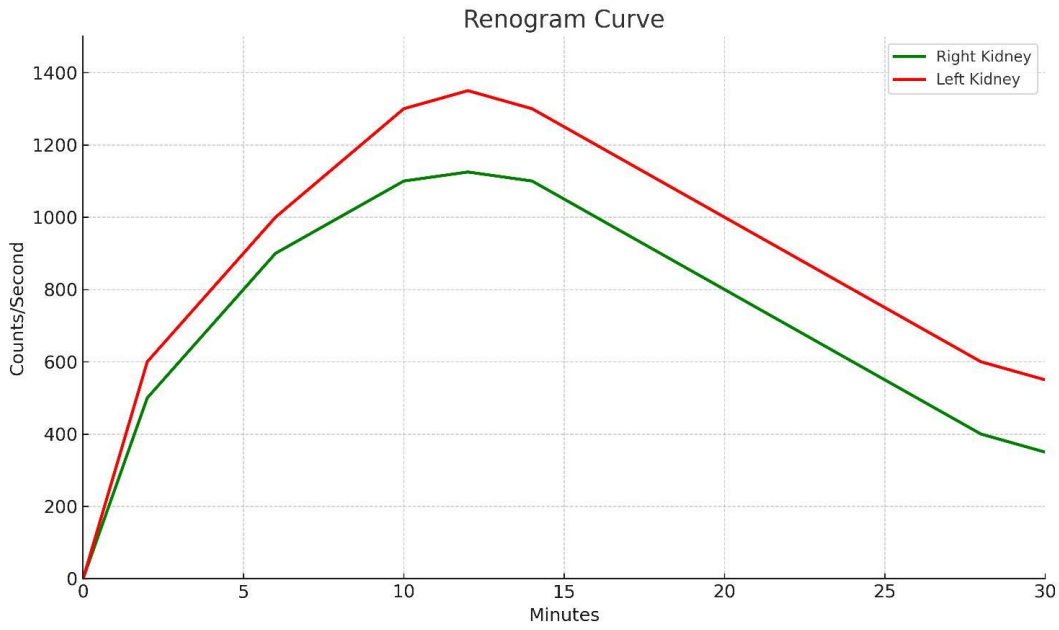

Figure 2: Preoperative time–activity curves from 99mTc-DTPA diuretic renography. Both kidneys demonstrate delayed excretion with a time to half-maximum (T½) exceeding 15 minutes, indicating impaired drainage. The left kidney (red curve) shows more pronounced retention and minimal response to furosemide administered at the 10-minute mark. The right kidney (green curve) also exhibits delayed clearance, but to a lesser extent. These findings support bilateral impaired excretory function, more severe on the left side, consistent with bilateral ureteropelvic junction obstruction (UPJO), predominantly affecting the left kidney.

A voiding cystourethrogram (VCUG) was performed, and it showed no evidence of vesicoureteral reflux (Figure 3). The patient was diagnosed with UPJO and, after completing a course of antibiotics, underwent open left pyeloplasty with the placement of a double J stent to correct the obstruction. However, one week postoperatively, she developed a recurrence of fever, which led to further imaging. Ultrasound revealed a 16.5 × 76 × 47 mm retroperitoneal collection adjacent to the left kidney. An abdominal CT scan confirmed the presence of an abscess measuring 47 × 52 × 21 mm, located anterior to the psoas muscle and adjacent to the left kidney. The abscess was drained, and appropriate antibiotic therapy was initiated. Despite these interventions, the fever and abdominal pain persisted, and a follow-up urine culture revealed Candida infection with a colony count of 100,000 CFU/mL. The patient was subsequently referred to a tertiary children's hospital for further evaluation and treatment.

Upon admission to a tertiary hospital, laboratory tests were as follows: BUN 13.3 mg/dL, creatinine 0.68 mg/dL, Sodium 138 mmol/L, potassium 4.2 mmol/L, calcium 10.6 mg/dL, phosphorus 4.6 mg/dL. Furthermore, ESR was 12 mm/h, CRP 1 mg/dL, Complete Blood Count (CBC): WBC 6.6 × 10^3/µL, hemoglobin 11.3 g/dL, platelets 384 × 10^3/µL, and liver enzymes AST 27 U/L and ALT 18 U/L.

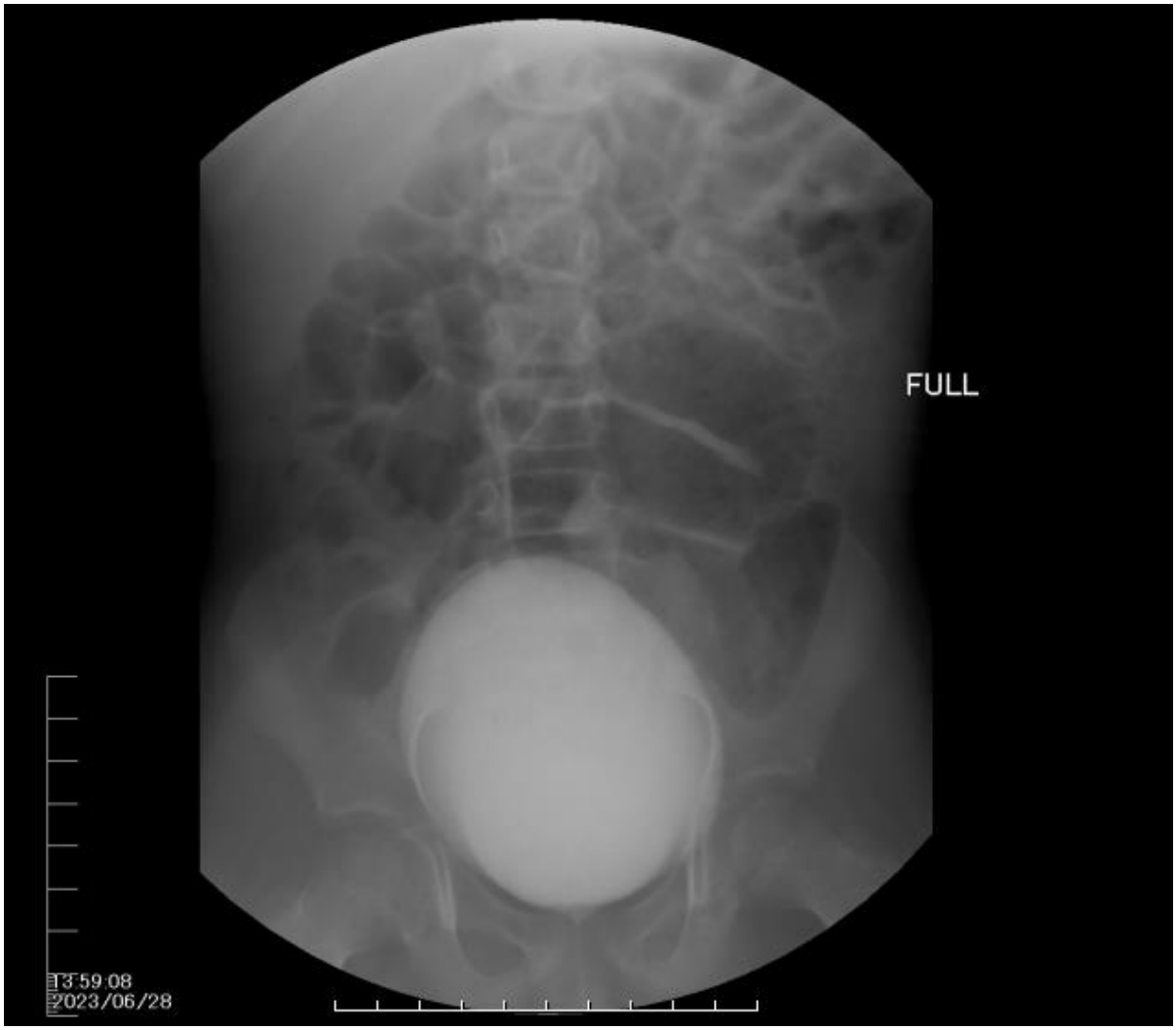

Figure 3: Postoperative VCUG with normal appearance of the bladder without evidence of vesicoureteral reflux.

Due to antibiotic resistant UTI, the double J stent was removed. Despite treatment, the patient continued to have persistent fever and ongoing flank and abdominal pain. A magnetic resonance urography (MRU) revealed mild hydronephrosis in the left kidney, accompanied by an extrarenal pelvis and inflammatory changes in the perirenal space, likely secondary to recent surgical intervention. MRU showed no evidence of obstruction post stent removal. The bladder appeared normal, with no filling defects or diverticula (Figure 4). A DMSA scan demonstrated normal cortical parenchyma in the right kidney, while the left kidney exhibited a dilated collecting system with cortical impairment localized to its lower one-third region.

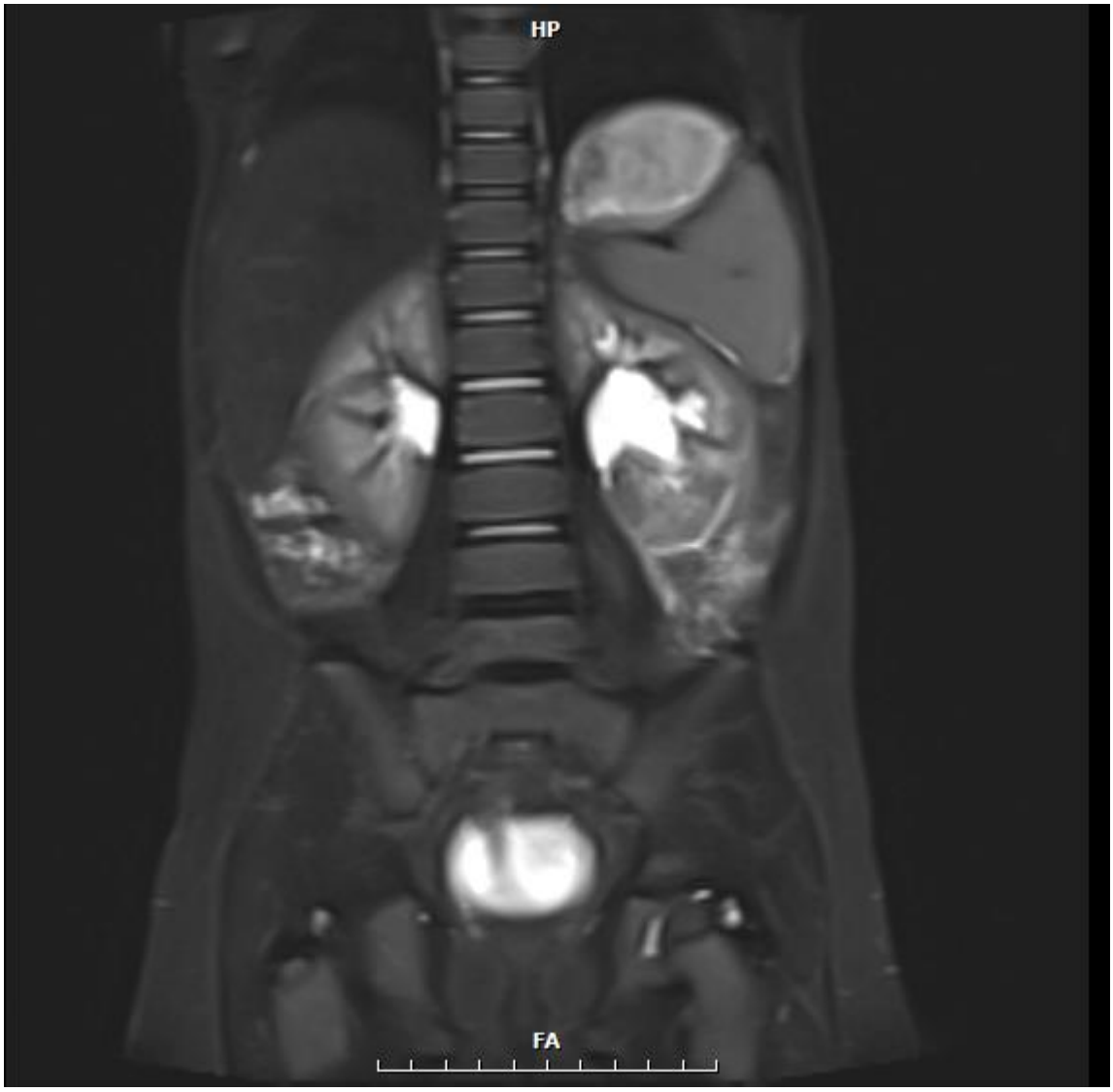

Figure 4: Postoperative MRU show mild left hydronephrosis with an extrarenal pelvis and inflammatory changes in the left perirenal space.

In spite of completing extended courses of antibiotic and antifungal treatments that effectively resolved the urinary infection, the patient's fever persisted. Her voiding dysfunction worsened, presenting with urinary retention. Clean intermittent catheterization (CIC) was initiated. Urodynamic studies revealed high-pressure voiding (Pvesical: 90 cm H_2O), a dysfunctional voiding pattern. Consequently, a rheumatology consultation was requested to investigate possible underlying causes.

Rheumatologic laboratory tests revealed the following results: antinuclear antibody (ANA) titer was <1:40, within the normal range (<1:80), and anti-dsDNA levels were 55 IU/mL, also within normal limits (<100 IU/mL). Complement levels were normal, with C3 at 140 mg/dL (reference: 90–180 mg/dL) and C4 at 27 mg/dL (reference: 10–40 mg/dL). Wright and 2-ME tests were negative. Neutrophil oxidative burst testing (NBT) was 100. In addition, coagulation studies showed a mildly elevated D-dimer level of 400 ng/mL (normal: <200 ng/mL), while fibrinogen was within the normal range at 303 mg/dL (reference: 200–400 mg/dL). Ferritin level was 103 ng/mL, within the normal range (8.5–148.9 ng/mL). Immunoglobulin levels were as follows: IgG 869 mg/dL (reference: 700–1600 mg/dL), IgM 135 mg/dL (reference: 10–300 mg/dL), IgA 119 mg/dL (reference: 4–806 mg/dL), and IgE 10 mg/dL (reference: <10 mg/dL).

Genetic testing for FMF was advised and revealed heterozygous mutations in the MEFV gene: a missense variant (ACG > ATG, Thr309Met) and a synonymous variant (GAG > CAG, Glu148Glu). Whole exome

sequencing confirmed the heterozygosity of both variants. The Thr309Met variant is a rare missense change of uncertain clinical significance, while the Glu148Glu variant is a synonymous substitution generally considered benign, although its clinical relevance remains uncertain. Therefore, the diagnosis of FMF was primarily established based on clinical presentation and supported by genetic testing identifying heterozygous MEFV variants of uncertain significance.[11,12]

Colchicine treatment was initiated, which helped manage the patient's fevers and abdominal pain more effectively. She continued to receive multidisciplinary care, addressing both her renal and rheumatologic needs.

In summary, persistent fever following treatment of the initial UPJO and UTI, along with unremarkable rheumatologic laboratory results, prompted genetic testing. Identification of heterozygous MEFV variants, together with clinical features, led to a diagnosis of FMF. Colchicine treatment resulted in marked symptom improvement.

Discussion

UPJO is a common cause of hydronephrosis in children and may present with flank pain, UTI, or incidental findings on prenatal or postnatal imaging.[1-3] If untreated, UPJO may result in progressive renal deterioration, necessitating prompt diagnosis and intervention. Indications for pyeloplasty in UPJO include symptomatic obstruction (e.g., pain, recurrent UTIs), decreased differential renal function (DRF) <40%, progressive increase in anteroposterior diameter (APD) of the renal pelvis on imaging, renal cortical atrophy, or a deterioration of >10 percentage points in DRF on serial radionuclide scans.[2,13] In infants, progressive hydronephrosis is a critical determinant for surgical decision-making, even in asymptomatic cases. Notably, even severely impaired kidneys with DRF <20% may show functional improvement after surgical correction.[14,15] In our patient, the decision to proceed with pyeloplasty was based on symptomatic presentation and imaging findings consistent with significant left-sided UPJO. Postoperative complications included the formation of a retroperitoneal abscess and persistent flank pain, which are recognized but uncommon outcomes of pyeloplasty. Complications of this procedure may include urinary leakage, infection, stent-related discomfort, and, rarely, deterioration in renal function despite surgical repair.[2,3]

FMF is the most common monogenic autoinflammatory disorder, caused by mutations in the MEFV gene.[4,7] The hallmark features include recurrent fevers and serositis, with most cases presenting in early childhood. Importantly, patients are asymptomatic between attacks, which can further complicate diagnosis when symptoms overlap with structural conditions like UPJO.

Bladder involvement in FMF may manifest as urinary tract infections, irritative symptoms, or voiding dysfunction, with findings such as pyuria and hematuria commonly observed during attacks (Yener, 2025). In a recent study by Yener et al., hydronephrosis was observed in 5.9% of FMF patients, and over 80% exhibited impaired voiding based on urodynamic studies.[16] In a study by Salehzadeh et al., only one out of 400 FMF patients -a 5-year-old male- had vesicoureteral reflux (VUR), highlighting the rarity of true structural abnormalities of the urinary tract in patients with FMF.[8] In our patient, the bladder dysfunction may be attributable to both her underlying urological condition and FMF. Although FMF is classically inherited in an autosomal recessive pattern, heterozygous individuals may still exhibit significant symptoms, particularly in high-prevalence populations.[9,10] While common pathogenic MEFV mutations such as M694V or M680I were not identified in our patient, atypical or rare variants—such as Thr309Met—have occasionally been reported in symptomatic individuals; however, their pathogenicity remains uncertain. This case highlights the importance of clinical judgment when genetic findings are inconclusive or of uncertain significance.[12]

To our knowledge, this is the first pediatric case describing the coexistence of UPJO and FMF. Recognizing such overlap is crucial to avoid unnecessary interventions, reduce morbidity, and initiate appropriate treatment, such as colchicine, which can prevent complications in FMF.

Conclusion

This case underscores the diagnostic complexity when structural abnormalities such as UPJO coexist with systemic autoinflammatory diseases like FMF. Persistent or recurrent symptoms following surgical correction should prompt clinicians to re-evaluate the differential diagnosis beyond anatomical causes, especially when

symptoms such as fever and abdominal pain remain unexplained. Early integration of rheumatologic evaluation may accelerate diagnosis in such complex presentations.

Disclosure

Informed consent was obtained from the patient's legal guardian for participation and publication of this case report.

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