LETTER TO THE EDITOR
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Successful Tocilizumab Monotherapy for Steroid-Dependent TAFRO Syndrome with IgA Nephropathy

Steroide Bağımlı TAFRO Sendromunda IgA Nefropatisi Eşliğinde Başarılı Tosilizumab Tedavisi: Olgu Sunumu

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To the Editor,

TAFRO syndrome is a rare, potentially fatal systemic inflammatory disorder driven by excessive interleukin-6 (IL-6) signaling, and is now regarded as a clinical subtype of idiopathic multicentric Castleman disease (iMCD) (1-3). We report a patient with TAFRO syndrome, biopsy-confirmed IgA nephropathy, and increased bone marrow iron stores, who achieved sustained remission with tocilizumab.

A 70-year-old man presented with a 1-month history of malaise, fever, generalized edema, and ecchymosis. Laboratory tests showed hemoglobin 9.7 g/dL, platelets 29×10⁹/L, C-reactive protein 40 mg/L, ferritin 577.2 µg/L, and nephrotic-range proteinuria with renal dysfunction. Bone marrow aspirate/imprint showed no dysplastic changes; biopsy showed 70% cellularity, grade 2 reticulin fibrosis, and 3+ Perls-stained iron stores, with no prior red-cell transfusion. JAK2 V617F, CALR, and MPL were negative, and the rapid, complete reversal of cytopenias and marrow findings with immunosuppressive therapy argued against primary myelofibrosis or another myeloid neoplasm. Computed tomography showed hepatosplenomegaly, effusions, and small lymphadenopathies. Autoimmune serologies, ADAMTS13 activity, and blood/urine cultures were negative. Low-level CMV DNAemia (90 copies/mL) with high IgG avidity (92.7%) did not support acute infection; despite CMV-PCR clearance with valganciclovir, fever, anasarca, thrombocytopenia, and renal dysfunction persisted, excluding CMV as the driver of the clinical picture.

Methylprednisolone (1 mg/kg/day) produced rapid clinical improvement. Severe thrombocytopenia initially precluded any biopsy; once platelets recovered sufficiently for a safe, image-guided percutaneous renal biopsy, the lymphadenopathies had regressed markedly and no lymph node remained accessible for excision, so lymph node histopathology could not be obtained. This reflects the timing of platelet recovery relative to lymph node regression, not a lower inherent bleeding risk of renal biopsy, and remains an important limitation.

One week after steroid discontinuation, the disease relapsed (platelets 13×10⁹/L, recurrent anasarca, worsening renal function) with serum IL-6 76 pg/mL, over 10-fold the laboratory upper limit (<7 pg/mL), meeting the updated TAFRO diagnostic criteria (4). Renal biopsy showed mesangial hypercellularity with strong granular mesangial IgA (3+) and lower-intensity C3/lambda deposition, without thrombotic microangiopathy-like or membranoproliferative changes (Oxford MEST-C: M1E0S0T1C0); electron microscopy was unavailable, so subtle TAFRO-related endothelial injury cannot be fully excluded, and because biopsy followed corticosteroid therapy, the lesion's pre-treatment severity may have been underestimated.

Tocilizumab (8 mg/kg intravenously every 2 weeks) was started as monotherapy, without steroids. By month 3, platelets rose to 178×10⁹/L, creatinine normalized, and edema resolved, with sustained remission, supporting a treatment effect attributable to IL-6 blockade rather than residual steroid activity.

Renal involvement affects over half of TAFRO patients and typically shows thrombotic microangiopathy-like or membranoproliferative patterns (5,6); biopsy-confirmed IgA nephropathy is rarely reported (7). IL-6 dysregulation may promote aberrant IgA production and mesangial deposition, offering a plausible mechanistic link (7,8), though

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causality cannot be established from a single case. Increased marrow iron alongside reticulin fibrosis likely reflects IL-6-mediated hepcidin elevation and inflammatory iron sequestration rather than a defining TAFRO feature. This case highlights the rare TAFRO-IgA nephropathy association and supports IL-6 blockade as an effective steroid-sparing option in relapsing TAFRO syndrome (9,10).

Keywords: Castleman Disease, tocilizumab, Glomerulonephritis, IGA, interleukin-6
Anahtar Kelimeler: Castleman Hastalığı, tosilizumab, Glomerülonefrit, IgA, interlökin-6

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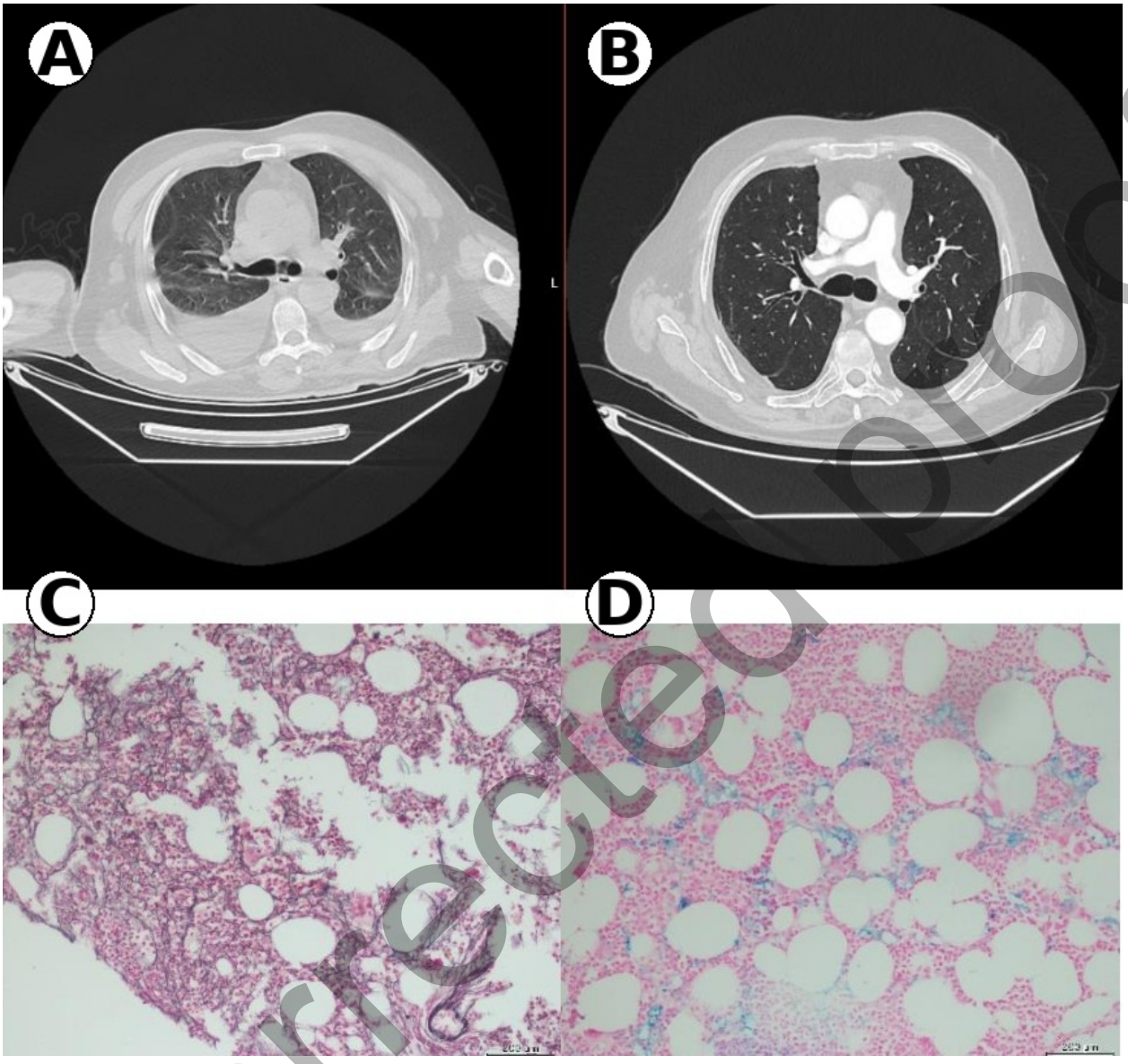


Figure 1. (A) Thoracic CT before and (B) after tocilizumab therapy, showing resolution of the pleural effusion. (C) Bone marrow biopsy showing reticulin fibrosis (reticulin stain) and (D) markedly increased iron stores on Perls' Prussian blue stain (light microscopy).

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