

Clinical Image

TAFRO Syndrome

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05 March 2020

23 March 2020

DOI: 10.4274/balkanmedj.galenos.2020.2020.3.30

Cite this article as: Fujikawa H, Araki M. TAFRO Syndrome. *Balkan Med J*

A 54 year-old male patient presented with a 3-day history of fever. Physical examination revealed bilateral edema of lower extremities. Laboratory investigations showed hemoglobin level of 136 g/L (normal 135-176), platelet count of $62 \times 10^9/L$ (normal $131-362 \times 10^9$), lactate dehydrogenase level of 136 U/L (normal 130-240), alkaline phosphatase level of 428 U/L (normal 100-350), creatinine level of 0.67 mg/dL (normal 0.6-1.0) and C-reactive protein level of 22.23 mg/dL (normal 0-0.30). Serum immunoglobulins were within normal ranges, and monoclonal protein was not detected in serum and urine. Autoimmune workup was negative. Infectious workup was negative, including human herpesvirus-8 and human immunodeficiency virus. The level of vascular endothelial growth factor (VEGF) was elevated (175 pg/mL, normal <38.3). Computed tomography demonstrated mild splenomegaly (Figure 1A). 18F-fluorodeoxyglucose positron emission tomography-computed tomography revealed pleural effusion and systemic mild lymphadenopathy with increased 18F-fluorodeoxyglucose uptake (Figure 1B). Three weeks after

admission, fever lasted. Blood tests showed anemia (hemoglobin level of 97 g/L), deteriorated thrombocytopenia (platelet count of $28 \times 10^9/L$) and acute kidney injury (creatinine level of 1.57 mg/dL).

A biopsy of the right axillary lymph node revealed atrophic germinal centers with enlarged nuclei of endothelial cells, expanded interfollicular zone, proliferation of endothelial venules, and a relatively small number of mature plasma cells (Figure 1C). Bone marrow biopsy demonstrated hypercellular marrow, hyperplasia of megakaryocytes, and mild reticulin fibrosis (Figure 1D). We diagnosed TAFRO syndrome. The patient was treated with prednisolone (60 mg/d), which was gradually tapered and discontinued after approximately 3 years of treatment. The patient has no recurrence.

The TAFRO syndrome (thrombocytopenia, anasarca, fever, reticulin myelofibrosis and organomegaly) is a newly recognized disease concept (1). TAFRO syndrome is considered to be an uncommon subtype of idiopathic multicentric Castleman disease (iMCD), which is negative for both POEMS syndrome and HHV-8 (2). The pathogenesis of TAFRO syndrome has yet to be fully understood, but is assumed to be a cytokine storm including VEGF and interleukin-6 (3). TAFRO syndrome develops acutely or subacutely, and is frequently life-threatening, while non-TAFRO iMCD usually progresses chronically (2).

No optimal treatment has been established, but corticosteroids are the most commonly used first-line therapy. Other choices are immunosuppressants, immunomodulators and cytotoxic chemotherapy. Because late relapses are not long-term follow-up is warranted for patients with TAFRO syndrome.

The patient's consent was obtained.

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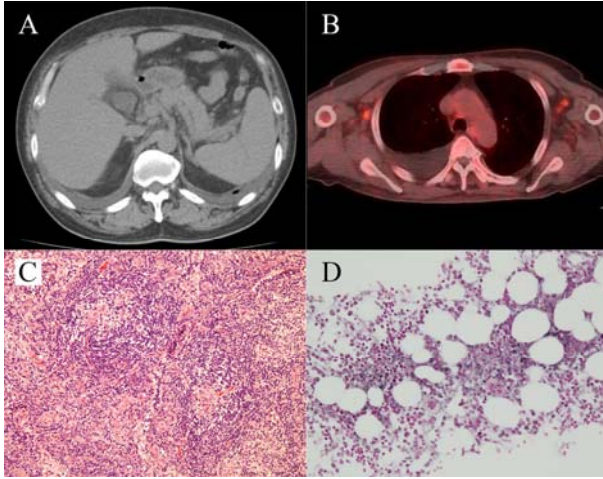


FIG. 1. (A) Computed tomography showing a slightly enlarged spleen. (B) 18F-fluorodeoxyglucose positron emission tomography-computed tomography showing pleural fluid and small lymphadenopathy with augmented 18F-fluorodeoxyglucose uptake. (C) Biopsy of the right axillary lymph node showing atrophic germinal centers with enlarged nuclei of endothelial cells, expanded interfollicular zone, proliferation in dense endothelial venules, and a few mature plasma cells (hematoxylin and eosin stain, original magnification x10). (D) Bone marrow biopsy showing hypercellular marrow and megakaryocytic hyperplasia along with the presence of reticulin fibrosis (silver stain, original magnification x20).

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