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CASE REPORT

Spontaneous remission of iMCD-TAFRO: a case report

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Abstract
Idiopathic multicentric Castleman disease (iMCD)- TAFRO (thrombocytopenia, ascites, fever, reticulin fibrosis and organomegaly) is a clinically severe situation characterized by cytokine storms that are potentially fatal, necessitating prompt and decisive medical intervention. The International Castleman's Disease Collaborative Network (CDCN) prioritizes the combination of long-term siltuximab and high-dose steroids as the preferred therapeutic option for iMCD-TAFRO. Here, we report a rare case of spontaneous remission in iMCD-TAFRO. In this case, the patient diagnosed with iMCD-TAFRO experienced alleviation of clinical symptoms and normalization of laboratory test results without undergoing any etiological treatment. This case sheds new light on the therapeutic strategies for iMCD-TAFRO. Following the stabilization of the onset cytokine storm, a detailed evaluation of the patient's condition should be performed to determine the need for continuous medical treatment.

Keywords iMCD · TAFRO · CDCN · Spontaneous remission

Introduction

iMCD is a rare and severe lymphoproliferative disorder characterized by widespread lymphadenopathy, multi-organ dysfunction, and systemic inflammation [1]. One of its most aggressive clinical subtypes is iMCD-TAFRO, which, if left untreated, can often rapidly progress to multi-organ failure and even death [2].

Currently, the first-line regimen for iMCD-TAFRO consists of a combination of siltuximab and high-dose steroids [3]. While this treatment has shown efficacy in many cases, some patients may fail to respond or experience relapses [4]. Alternative therapies include immunosuppressive and cytotoxic regimen, as well as rituximab-based chemotherapy. However, the clinical course of iMCD-TAFRO can be variable.

Here, we present the first documented case of the spontaneous remission of iMCD-TAFRO. This patient achieved complete clinical and laboratory remission without receiving any disease-specific therapy. This case challenges the current understanding of iMCD-TAFRO as a condition that requires urgent and continuous medical intervention. It not only demonstrates the possibility of spontaneous remission of iMCD-TAFRO, but also underscores the importance of individualized patient assessment after the management of the initial cytokine storm.

Case presentation

A 29-year-old male with a 3-month history of fatigue and 1-month history of fever and oliguria was admitted to our hospital. When the fever started, he developed hepatosplenomegaly, gynecomastia, multiple lymphadenopathy and serous effusions. Laboratory results revealed thrombocytopenia, hypoalbuminemia, elevated alkaline phosphatase (ALP), normal transaminase levels, renal insufficiency, and

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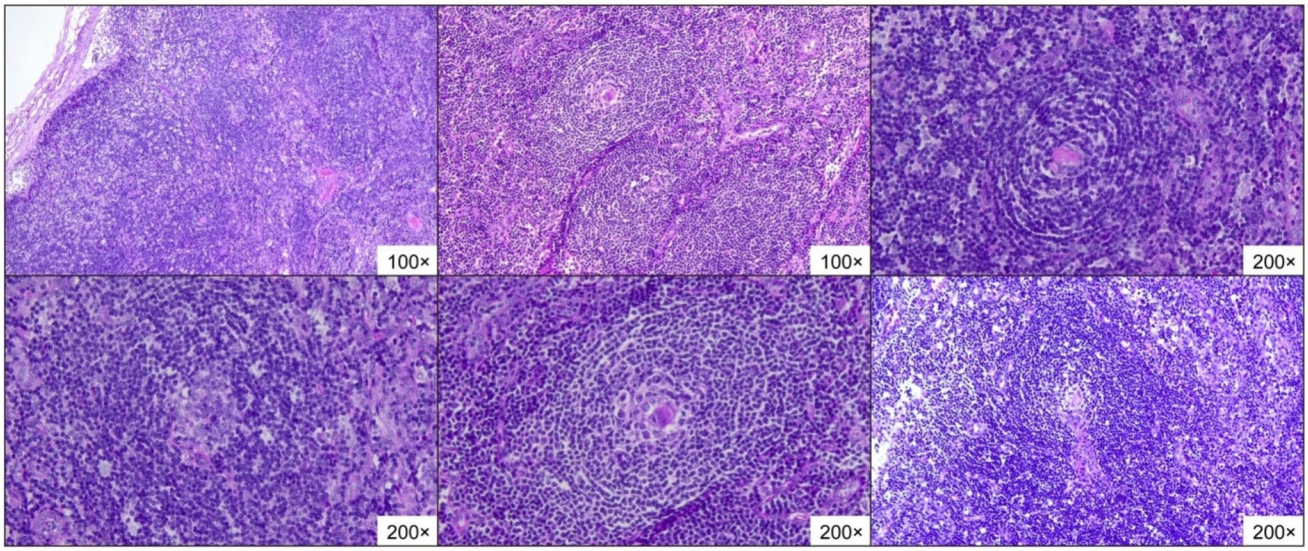

Fig. 1 Histopathological findings of the patient which is consistent with Castleman disease (hyaline-vascular subtype) (hematoxylin-eosin (HE) staining). Follicles with expanded mantle zones containing atrophic germinal centers. Residual germinal center penetrated by hyalinized vessel rendering a " lollipop " appearance to the follicle. Small lymphocytes palisade around the germinal centers (onion-skin like appearance)

a high inflammatory state, with no evidence of infection and autoimmune diseases (Supplementary Table 1). Biopsy of a left cervical lymph node suggested Castleman's disease (CD) of hyaline-vascular subtype (Fig. 1), and serum human herpes virus-8 (HHV-8) DNA was negative. Meanwhile, his platelet count (PLT) continued to decline to a minimum of $43 \times 10^{\wedge}9$/L. Except for the absence of bone marrow fibrosis in the patient's bone marrow biopsy, the patient met all the major and minor diagnostic criteria for iMCD-TAFRO [5]. Therefore, a diagnosis of iMCD-TAFRO was made. However, the patient refused treatment targeting iMCD-TAFRO and would like to go to another hospital due to personal concerns. Following treatment with diuretics and platelet transfusion, his symptoms gradually improved, and was then referred to our hospital. On examination, his body temperature, PLT, albumin, serum creatinine, and interleukin (IL)-6 all returned to normal (Supplementary Table 1). Further evaluation including bone marrow biopsy, electromyogram, serum protein electrophoresis and endocrinology assessment ruled out POEMS syndrome. According to the International Castleman's Disease Collaborative Network (CDCN) diagnostic criteria [6], he was diagnosed with iMCD-TAFRO. Yet, his symptoms relieved and laboratory results returned to normal without receiving any treatment for the primary disease, and the patient's condition has remained stable since (Supplementary Table 1).

Discussion and conclusion

First described by Kazue Takai in 2010 [7], TAFRO syndrome is a systematic inflammatory status characterized by thrombocytopenia, anasarca, fever, reticulin fibrosis and organomegaly. It is generally believed that iMCD-TAFRO arises from dysregulation of cytokine secretion and autoimmune processes, primarily associated with serum IL-6 and vascular endothelial growth factor (VEGF) level [8]. Other driving factors of the disease include chemokine ligand 13 (CXCL13), IL-1, IL-2, IL-10, tumor necrosis factor (TNF)-α, and type 1 interferon (IFN-1) [9]. Patients with iMCD-TAFRO often undergo a rapid clinical course, with a poor prognosis and a high mortality rate. To our limited knowledge, this is the first reported case of spontaneous remission in iMCD-TAFRO, which is typically regarded as a severe subtype in need of immediate therapy initiation. CDCN recommends siltuximab, an anti-IL-6 monoclonal antibody, with or without corticosteroids as the first-line therapy for iMCD-TAFRO. In addition, the BCD regimen (subcutaneous bortezomib, oral cyclophosphamide and dexamethasone) has a high response rate in iMCD-TAFRO [10]. For relapsed cases of iMCD-TAFRO, sirolimus, which targets the mTOR pathway, may be considered [11]. However, in this case, the patient achieved complete remission without any etiological treatment. Still, it should be noted that patients with iMCD-TAFRO require immediate medical intervention due to the potential lethality of the onset cytokine storm. Once the cytokine storm is controlled, these patients may not need lifelong siltuximab treatment as

CDCN recommends, suggesting that a novel pathogenesis of iMCD-TAFRO may remain to be discovered and further research is needed to differentiate these patients from those requiring long-term medical intervention.

In conclusion, this case demonstrates the potential for spontaneous remission in iMCD-TAFRO. Despite the timely medical intervention needed for the initial cytokine storm, it's feasible to monitor and determine the need for lifelong treatment once the initial cytokine storm is under control in iMCD-TAFRO patients.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00277-025-06324-y.

Author contributions Y.Q., M.Z. and L.Z. took care of the patient. C.J. performed the pathological analysis. Y.Q. wrote the manuscript. L.Z. and J.L. reviewed and edited the manuscript. J.L. supervised the project.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.