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Case Report

Acutely deteriorated extravascular volume overload during peripheral blood stem cell mobilization in POEMS syndrome: A case series with cytokine analysis

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ABSTRACT

We describe two cases of polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes (POEMS) syndrome patients with deteriorated extravascular volume overload without increased levels of vascular endothelial growth factor after the administration of cyclophosphamide + granulocyte colony-stimulating factor for stem cell mobilization. We then measured the serum levels of 27 cytokines from these cases using a multiplex suspension array system. The analysis revealed the changes of cytokine profiles before cyclophosphamide + granulocyte colony-stimulating factor and after the development of capillary leak symptoms in both cases. This may improve our current level of understanding of the pathogenesis of POEMS syndrome not driven by vascular endothelial growth factor.

1. Introduction

Polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes (POEMS) syndrome is a rare plasma cell disorder characterized by the constituent ailments that comprise its name. Signs of extravascular volume overload, which are frequently observed in POEMS syndrome, are among the most common preterminal events in POEMS syndrome [1]. It has been speculated that elevated levels of vascular endothelial growth factor (VEGF) play a crucial role in inducing extravascular volume overload via angiogenesis and microvascular hyperpermeability [1,2]. However, discrepancies between disease activity and VEGF levels in POEMS syndrome patients have been reported [3]. Additionally, the efficacy of the anti-VEGF monoclonal antibody bevacizumab for POEMS syndrome patients has been a matter of controversy due to mixed study results [4–6]. Furthermore, several other cytokines, such as interleukin (IL)-6, IL-12, tumor necrosis factor-α, and hepatocyte growth factor, have been reported to be elevated in POEMS syndrome [7–9]. Therefore, VEGF may not be the driving force behind this disorder. Here we report two cases of patients with POEMS syndrome with acutely deteriorated extravascular volume overload without increased levels of VEGF after

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the administration of high dose cyclophosphamide (HD-CY) + granulocyte colony-stimulating factor (G-CSF) (CG) for peripheral blood stem cell (PBSC) mobilization. We then measured serum levels of 27 cytokines from these cases before and after CG using a multiplex suspension array system, and analyzed the changes in their cytokine profiles during their clinical courses.

2. Case 1

The first case (case 1) is a 61-year-old man who was diagnosed with POEMS syndrome and was referred to our institution in July 2008. His clinical course is shown in Fig. 1. The day of administration of G-CSF for PBSC collection is defined as day 0. The patient presented with monoclonal gammopathy (IgG-λ), a slight left pleural effusion, hepatosplenomegaly, and polyneuropathy with a performance status of 2. The level of serum VEGF was 8160 pg/mL on day minus 29. He was treated with high-dose dexamethasone (DEX: 40 mg/body; days minus 21 to minus 18), leading to an improvement in his systemic edema. He received HD-CY (2 g/m^2; days minus 13 to minus 12), followed by G-CSF (10 μg/kg; days 0–4) for PBSC collection. PBSC collection was performed on day 4. The required number of CD34$^+$ cells (5.12×10^6/kg) for autologous stem cell transplantation were harvested using the COBE Spectra cell separator (COBE Spectra, CaridianBCT, USA), although respiratory failure occurred 3 days after PBSC collection, and a computed

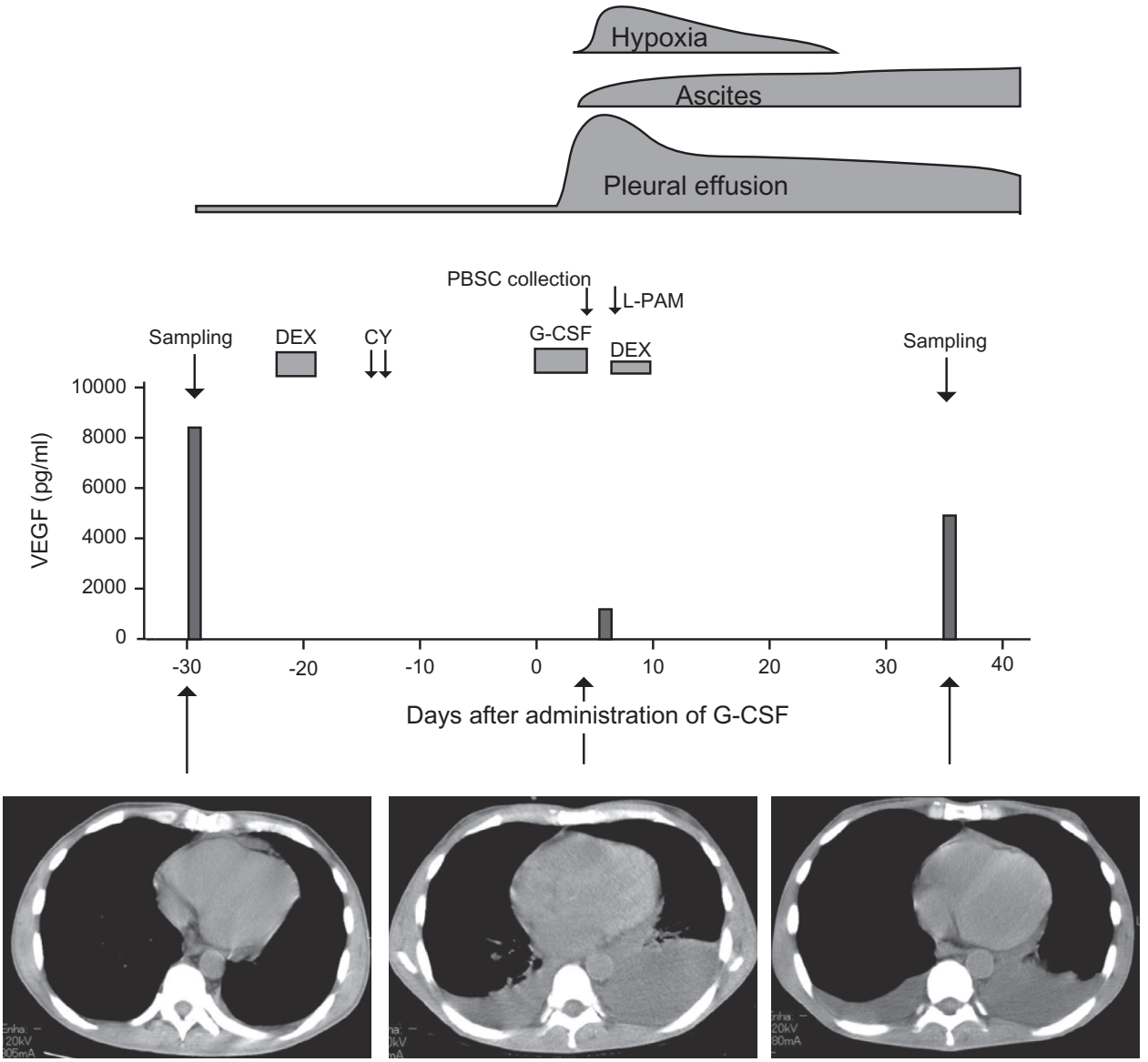

Fig. 1. Serial changes in computed tomography (CT) scan images and vascular endothelial growth factor (VEGF) level, and the therapeutic course of case 1. The sera sampling time points for the multiplex suspension array system are indicated by arrows. DEX, dexamethasone; CY, cyclosphosphamide; PBSC, peripheral blood stem cell; L-PAM, melphalan.