CASE REPORT

Acute Myeloid Leukemia Complicated by Giant Cell Arteritis

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Abstract

Giant cell arteritis (GCA), a type of systemic arteritis, is rare in Japan. We herein report a case of acute myeloid leukemia (AML) complicated by GCA that manifested during chemotherapy for AML. A 77-year-old woman with severe back pain was diagnosed with AML. She achieved complete remission with the resolution of her back pain following induction chemotherapy. However, she developed a headache and fever after consolidation chemotherapy. A diagnosis of GCA was made based on a biopsy of the temporal artery and arterial imaging. GCA should therefore be included in the differential diagnosis in AML patients complicated with a headache and fever of unknown origin.

Key words: giant cell arteritis, acute myeloid leukemia, fever of unknown origin, headache, jaw claudication

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Introduction

Giant cell arteritis (GCA) is a common type of systemic vasculitis in adults over 50 years of age in Western countries. However, the incidence of this vasculitis is low among Asian populations, especially in Japan (1). The association between GCA and malignancy is well-known; however, only four well-documented cases of concomitant acute myeloid leukemia (AML) and GCA have been reported to date (2-5). We herein describe the case of an AML patient who developed GCA during chemotherapy treatment.

Case Report

A 77-year-old woman was referred to our hospital due to severe back pain that had begun one week earlier, with general malaise and appetite loss. The results of a physical examination were unremarkable; the back pain was spontaneous, but no pain on motion. The patient also reported neither knocking pain nor tenderness in the back, and both skin lesions and arthrocele were absent. A hematological examination revealed a white blood cell (WBC) count of 9.1×10⁹/L, with 11.3% blast-like cells, 4.3% promyelocytes, 5.3% myelocytes, 33.7% neutrophils, 6.3% monocytes and 35.1% lymphocytes, a hemoglobin concentration of 13.4 g/dL and a platelet count of 124×10⁹/L. The serum concentrations of lactate dehydrogenase (LDH) and C-reactive protein (CRP) were elevated at 381 IU/L (normal: 120 to 230 IU/L) and 3.59 mg/dL (normal: below 0.3 mg/dL), respectively. A hematologic examination showed a serum concentration of fibrinogen of 270 mg/dL (normal: 160 to 350 mg/dL), while the level of D-dimer was elevated at 31.9 μg/mL (normal: below 1.0 μg/mL). A bone marrow aspirate showed hypercellularity, with blasts or promyelocytes, without Auer rods, comprising 60% of marrow nucleated cells (Fig. 1). An immunophenotypic analysis revealed that these immature cells expressed CD34, CD13 and CD33 antigens and cytoplasmic myeloperoxidase (MPO), but not HLA-DR. A chromosomal examination showed a normal karyotype of 46, XX, and the PML-RARA fusion gene was not detected on a fluorescence in situ hybridization (FISH) analysis. A diagno-

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Figure 1. Leukemic cells in the bone marrow. Morphologically, the majority of cells are promyelocytes, some of which contain coarse azurophilic granules.

sis of AML-M2 was therefore made according to the French-American-British (FAB) classification. Computed tomography (CT) of the chest and abdomen demonstrated no abnormal findings regarding the cause of the back pain. We thus chose to administer low-dose chemotherapy consisting of cytarabine (30 mg/day, continuous intravenous infusion, days 1-14) and aclacinobine (20 mg/day, days 1-5) as induction chemotherapy. During this treatment, the absolute neutrophil count reached 10.2×10^9/L, which led to the prompt resolution of the patient's back pain (Fig. 2). However, she subsequently developed a headache, jaw claudication and a low-grade fever during the recovery period of myelosuppression after the second consolidation chemotherapy. The laboratory findings revealed normochromic and normocytic anemia (Hb: 8.5 g/dL), a platelet count of 134×10^9/L, and a WBC count of 9.4×10^9/L, with a normal differential count. The CRP level was elevated at 6.44 mg/dL, and the erythrocyte sedimentation rate (ESR) was 129 mm/h. A blood and spinal fluid culture yielded negative results, and Herpes simplex virus (HSV)-1, HSV-2 and varicella zoster virus (VZV) were not detected in the spinal fluid on a multiplex virus polymerase chain reaction (PCR) analysis, which was performed at our institution (6).

Serological tests, including those for antinuclear antibodies (ANA), rheumatoid factor, cytoplasmic and myeloperoxidase anti-neutrophil cytoplasmic antibodies (ANCA), and tests of the thyroid function were all unremarkable, and a bone marrow examination showed no evidence of AML recurrence. The patient was treated with broad-spectrum antibiotics, without any improvements in the symptoms or laboratory findings. When making a differential diagnosis, she complained of pain in the left temporal region, and an ultrasound examination showed wall thickening and segmental stenosis of the left temporal artery. Giant cell arteritis was therefore suspected. Contrast CT of the chest and abdomen also demonstrated a thickening of the arterial walls from the aortic arch to the abdominal aorta and the bilateral subclavian and right iliac arteries (Fig. 3A, B). Magnetic resonance angiography (MRA) revealed a stenosis of the right temporal artery, and fat-suppressed T2-weighted magnetic resonance imaging (MRI) of the head showed regions of hyperintensity, indicating the inflammation of the fat surrounding the bilateral temporal arteries (Fig. 3C). A biopsy of the superficial temporal artery was performed, and the histological findings of the artery showed marked hyper trophy of the vascular endothelium, stenosis of the arterial lumen (Fig. 4A, B) and granulomatous inflammation with giant cells in the tunica media and tunica externa of the artery (Fig. 4C, D). These findings were consistent with the diagnostic criteria of GCA. The patient was treated with oral prednisolone (20 mg), which led to the prompt resolution of her symptoms and the normalization of her CRP value. We completed the consolidation chemotherapies, and the patient’s AML remains in a state of sustained CR. The GCA showed a complete response to treatment with prednisolone (15 mg) as of December 2014.

Discussion

GCA is a type of systemic arteritis that mostly affects elderly people. The incidence of GCA in Japan is significantly different from that observed in Europe and North America. The prevalence of GCA in Japan among people older than 50 years of age is 1.47 per 10 million (7). In contrast, the prevalence in the United States and Spain is 200 and 60 per 10 million people, respectively (8, 9). Hence, GCA is a rare form of vasculitis in Japan. Although the association between GCA and malignant disease is well-known, the incidence of malignancy during follow-up in patients with GCA varies from 0-15%, depending on the cohort investigated (10-15). An association between GCA and AML has been described in four patients as a case report. Interestingly, three of whom were from Japan (2-4), presumably reflecting the low incidence of GCA in Japan. On the other hand, a large Swedish cohort study reported that patients with GCA were at significant risk of AML development (16), this risk is also indicated by the US Surveillance Epidemiology and End Results (SEER)-Medicare database (17). Thus, the association between GCA and AML does not appear to be rare in Western countries, presumably due to differences in the genetic background or lifestyle factors of Western and Japanese individuals.

The criteria for a diagnosis of GCA proposed by the American College of Rheumatology are as follows: an age over 50 years, new onset of localized headaches, abnormalities of the temporal artery (temporal artery tenderness, reduced pulsation), an increased ESR (≥50 mm/1st hour) and abnormal findings on an arterial biopsy (vasculitis with predominantly mononuclear cell infiltration, granulomatous inflammation or evidence of giant cells) (18). The present case
was accompanied by typical symptoms and sufficiently fulfilled the GCA diagnostic criteria.

Although the etiology of GCA is unknown, its development shows seasonal fluctuations and/or a cyclic pattern, suggesting environmental effects, such as infection, on its development (19). Genetic factors, such as HLA-DRB1*04 alleles (20) and tumor necrosis factor microsatellite polymorphisms (21), have also been reported. Histologically, GCA is characterized by granulomatous inflammation with lymphocytes, macrophages and giant cells in the vessel wall; it has therefore been suggested that proinflammatory cytokines, such as interferon-γ, interleukin-1 (IL-1) and IL-6, play a pivotal role in the pathogenesis of GCA (22). In the present patient, it is possible that the systemic inflammatory response at the onset of AML and during the period of febrile neutropenia due to consolidation chemotherapy in the CR state brought about the inflammatory changes in the vessel wall and thus contributed to the development of GCA. Methylprednisolone, which was administered to relieve the inflammatory response of unknown cause during the induction chemotherapy may have masked the manifestations of GCA.

The causes of GCA-related symptoms can be divided into three categories: cranial vascular involvement, arteritis of large vessels, and systemic inflammation. Cranial vasculitis typically causes headaches, jaw claudication and scalp tenderness, whereas large vessel arteritis and systemic inflammation induce chest or back pain and the onset of fever or general fatigue, respectively. The severe back pain demonstrated by the present case suggests the co-existence of polymyalgia rheumatica (PMR); however, her clinical findings did not fulfill the 2012 PMR classification criteria of the European [European League Against Rheumatism (EULAR)] and American [American College of Rheumatology (ACR)] rheumatology societies (23). Clinically, 40-60% of patients with GCA exhibit PMR-related symptoms at di-
The authors state that they have no Conflict of Interest (COI).

References


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