Case Report

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Large Vessel Vasculitis as an Initial Manifestation of Acute Myeloid Leukemia: A Case Report

대혈관 혈관염이 첫 번째 징후로 나타난 급성 골수성 백혈병: 증례 보고

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Large vessel vasculitis is characterized by chronic inflammation within the aortic wall and its major branches. The inflammation is considered to occur as a result of immune dysregulation. Hematologic malignancy is one of the rare causes of secondary vasculitis. Herein, we report a rare case of large vessel vasculitis associated with acute myeloid leukemia mimicking primary vasculitis.

Index terms Acute Myeloid Leukemia; Autoimmune Diseases; Vasculitis

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INTRODUCTION

Large vessel vasculitis is inflammatory disorder characterized by chronic inflammation in vessel walls of aorta and it major branches. The inflammation is thought to be a result of immune dysregulation. It can typically occur as autoimmune disorders such as Takayasu's arteritis and giant cell arteritis. Large vessel vasculitis may also result from systemic rheumatologic disorders, infections, drugs and malignancies (1, 2). Vasculitis associated with malignancy is rare, and vasculitis with hematologic malignancy is more frequent than solid malignancy. It usually involves small and medium vessels (3). Here, we describe a rare case of large vessel vasculitis associated with acute myeloid leukemia (AML) confirmed by bone marrow biopsy and chromosomal study mimicking primary systemic vasculitis and present the imaging findings of CT and ultrasonography (US).

CASE REPORT

A 42-year-old female visited emergency department with a 8-day history of left-sided neck pain, headache and myalgia. Her body temperature was 36.8°C. On physical examination, there was tenderness in left neck. Laboratory test showed anemia with a hemoglobin level of 7.1 g/dL, thrombocytopenia with platelet count of 71 × 10^3/μL, elevation of both erythrocyte sedimentation rate (40 mm/hr) and C-reactive protein (8.09 mg/dL). Blood culture test was negative (Table 1).

Contrast-enhanced CT scan of neck revealed concentric wall thickening and diffuse enhancement along the left distal common carotid artery (CCA) and external carotid artery (ECA) (Fig. 1A). The Hounsfield units (HU) of the left distal CCA and ECA wall was measured about 30 HU on the pre-contrast image and 120 HU on the contrast-enhanced axial image. On US, there was increased echogenicity around left CCA and ECA. Right side was unremarkable (Fig. 1B). Additional CT scans of chest and abdomen showed no abnormal findings in aorta and major branches of vessels.

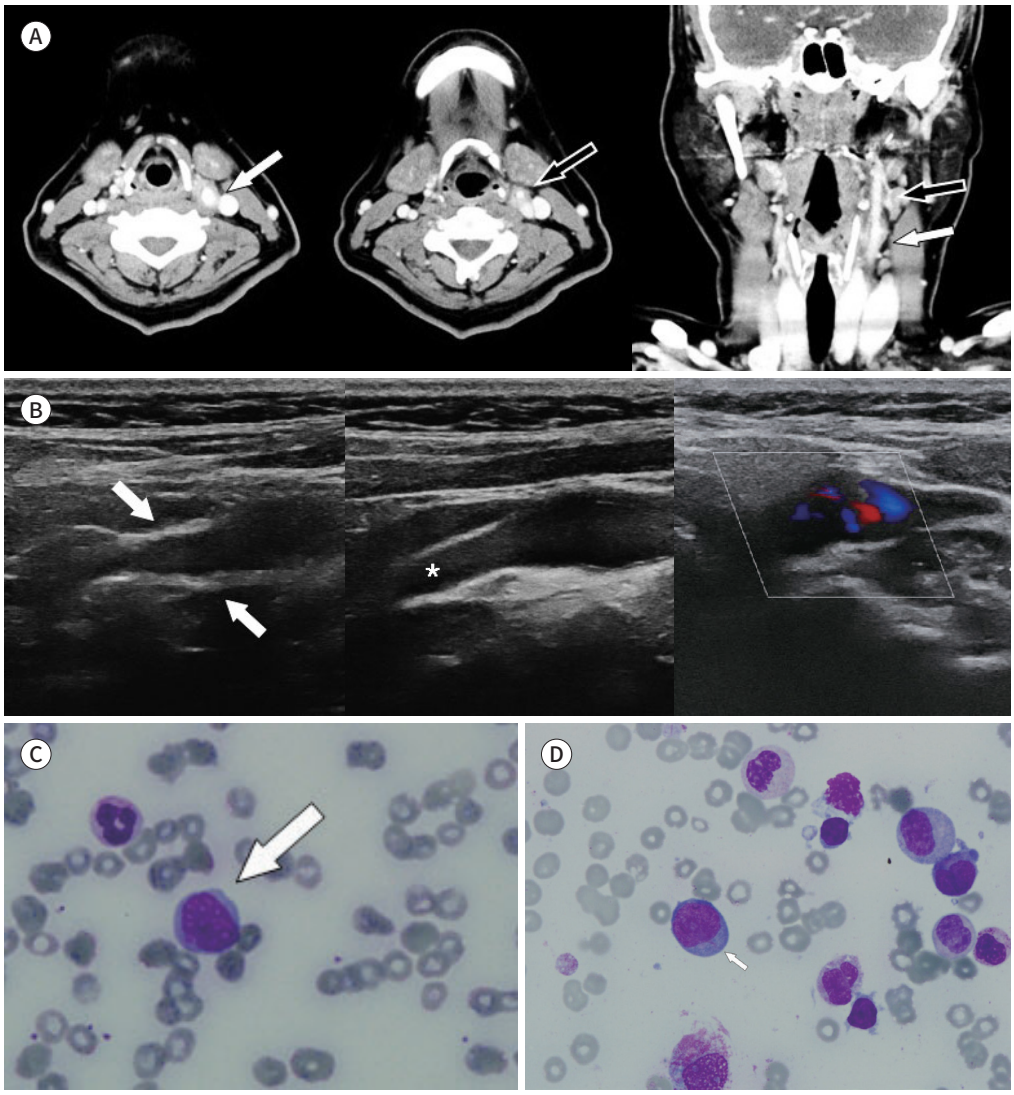
As she had no relevant medical history, we first suspected primary large vessel vasculitis such as giant cell arteritis. After high-dose steroid therapy (prednisolone 1 mg/kg/day), neck pain improved significantly. The extent of vessel involvement, prolonged anemia and thrombocytopenia, in spite of steroid treatment, however, had a distance from typical manifestations of these diseases. To reveal the cause of anemia and thrombocytopenia, she underwent additional studies. The laboratory tests for autoimmune serologies, including anti-nuclear antibodies, and anti-neutrophil cytoplasmic antibodies were negative (Table 1). Peripheral blood smear showed pleomorphic blasts (Fig. 1C). Bone marrow aspiration showed 12% blasts, and some of them had Auer body (Fig. 1D). Chromosomal study revealed t(8;21)(q22;q22.1), and finally she was diagnosed as AML. Therefore, we concluded that she had a

Table 1. Laboratory Studies on Admission

Laboratory Studies	Results	Reference Interval
CBC		
Hemoglobin, g/dL	7.1	12.3–15.3
Hematocrit, %	20.8	35.9–44.6
WBC, 10^3/μL	9.9	4.4–11.0
Platelets, 10^3/μL	61	150–450
ESR, mm/hr	40	0–20
CRP, mg/dL	8.1	0.0–0.5
ANA	Negative	Negative
Anti SS-A/Ro Ab, U/mL	Negative (0.5)	Negative (< 7.0)
ANCA, IU/mL		
Anti PR3 Ab (C-ANCA)	Negative (< 0.1)	Negative (< 2.0)
Anti MPO Ab (P-ANCA)	Negative (< 0.1)	Negative (< 3.5)

ANA = antinuclear antibody, ANCA = antineutrophil cytoplasmic antibody, Anti MPO Ab = anti-myeloperoxidase antibodies, Anti PR3 Ab = anti-proteinase 3 antibodies, Anti-SS-A Ab = anti–Sjögren's-syndrome-related antigen A autoantibodies, CBC = complete blood count, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, WBC = white blood cell

Fig. 1. A 42-year-old female with acute myeloid leukemia with t(8;21)(q22;q22.1) and large vessel vasculitis as the presenting manifestation.
A. Axial (left and middle) and coronal (right) contrast-enhanced CT images show diffuse enhancement and concentric wall thickening around the bifurcation of the left CCA (white arrows) and ECA (black arrows).
B. US shows concentric wall thickening of the left proximal ECA (arrows, left), whereas proximal internal carotid artery shows no abnormalities (star, middle). Increased echogenicity is observed around the bifurcation of the CCA on the color Doppler US (right).
C. Blood smear (× 1000) shows a blast (center) (arrow).
D. Bone marrow (× 1000) smear shows a blast with Auer rod (arrow).
CCA = common carotid artery, ECA = external carotid artery



secondary large vessel vasculitis associated with AML.

This report was conducted in compliance with the Helsinki declaration.

DISCUSSION

Large vessel vasculitis refers to inflammatory disorder with chronic inflammation within

the aortic wall and its major branches. Immune dysregulation is thought to be a cause of vessel wall inflammation. Inflammatory large vessel vasculitis may result from systemic autoimmune disorders, such as giant cell arteritis, Takayasu arteritis, rheumatoid arthritis, Cogan disease, ankylosing spondylitis, and Behcet's disease (1). Malignancies can rarely be the cause of secondary large vessel vasculitis. Although the frequency of vasculitis secondary to malignancy is about 2.3%–8.0%, most manifestations of vasculitis are cutaneous involvements (2, 3).

Among secondary vasculitis occurring from malignancies, hematologic malignancies are more frequent than solid malignancies (2). Myelodysplastic syndrome (MDS), lymphoma and leukemia are common hematologic malignancies associated with secondary vasculitis (2). In MDS, existing along a continuous spectrum of AML, most associated secondary vasculitis was small vessel vasculitis (4, 5). Although several studies reported progression to AML in large vessel vasculitis with MDS patients, development of large vessel vasculitis in AML patients was very rare (4-6).

The pathogenesis of association between AML and vasculitis is unclear. In the setting of hematologic malignancy, abnormal expression of antigens can cause autoimmune dysregulations, which may result from abnormal functioning of B and T lymphocytes, gammopathies, reduced numbers and impaired natural killer cells and dendritic cells with abnormal antigen presentation (7, 8). Activation of T lymphocyte may result in the secretion of cytokines such as tumour necrosis factor-α and interferon-γ, which may result in the apoptosis of normal progenitor cells. Also, the patients with systemic vasculitis showed significantly more elevated serum tumour necrosis factor-α levels than healthy controls. Furthermore, abnormal activations of T cells by adventitial dendritic cells have a critical role in initiation of large vessel vasculitis, which can explain that autoimmune dysregulations may have a central role in development of associated large vessel arteritis (1, 8).

In previous reports of secondary large vessel vasculitis associated with hematologic malignancy, it presented similar imaging features of primary vasculitis, diffuse arterial wall thickening and contrast enhancement (6, 9, 10). Our case revealed diffuse enhancement and wall thickening of distal CCA and proximal ECA on contrast enhanced CT, which is indistinguishable from primary large vessel vasculitis such as Takayasu arteritis or giant cell arteritis. However, Takayasu arteritis usually affects the aorta and its major branches, and giant cell arteritis affects the small extra cranial branches of aorta such as temporal arteries. In our case, the affected lesions were distal CCA and proximal ECA, which had a distance from typical manifestations of Takayasu arteritis and giant cell arteritis (9).

Apart from anemia and thrombocytopenia, our patient did not show any other signs to suggest AML. Also she had no known relevant disease, which caused diagnostic confusion. In previous reports, the patients with large vessel vasculitis secondary to hematologic malignancies usually showed systemic symptoms such as high-grade fever, weight loss and arthralgia (5, 10). In our case, the chief complaint of patient was neck pain without fever or weight loss. Although our patient showed prompt improvement of neck pain with response of high dose steroid treatment, thrombocytopenia and anemia were persistent. Previous studies reported that, in the secondary vasculitis patients associated with hematologic malignancies, treatment of the vasculitis itself with steroid or immunosuppressant showed significant symptom improvements (6, 10). However, recurrence of vasculitis, renal involvement (microaneurysms or

glomerulonephritis), and steroid dependence were more common than vasculitis secondary to malignancy. Therefore, recognition and control of underlying hematologic malignancy is important for proper disease care (2).

In conclusion, we report a case of large vessel vasculitis combined with AML. It is challenging for radiologists to consider association between underlying hematologic malignancy and large vessel vasculitis without relevant medical history. However, if there exist unusual locations of vessel involvement and atypical clinical manifestations such as anemia and thrombocytopenia, the possibility of combined hematologic malignancy should not be overlooked.

Author Contributions

Conceptualization, Y.D.; investigation, J.G.; supervision, Y.D., J.J., K.J.; visualization, J.G.; writing—original draft, all authors; and writing—review & editing, all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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대혈관 혈관염이 첫 번째 징후로 나타난 급성 골수성 백혈병: 증례 보고

전가영[1] · 양동진[1*] · 장종창[1] · 강종완[2]

대혈관 혈관염은 대동맥과 이것의 주요 분지의 혈관벽에 만성 염증이 생기는 질환으로써 면역 이상반응에 의한 것이다. 혈액암은 이차적인 혈관염의 아주 드문 원인 중 한 가지다. 우리는 일차성 혈관염을 모방한 급성 골수성 백혈병과 연관된 드문 형태의 대혈관 혈관염에 대해서 보고하고자 한다.

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