Autoimmune Vasculitis Causing Acute Bilateral Lower Limb Paralysis

Ayuko Tokonami 1, Ryuichi Ohta 2, Noritaka Katagiri 3, Naho Yoshioka 3, Fumiko Yamane 3, Chiaki Sano 4

1. Medicine, Shimane University Faculty of Medicine, Izumo, JPN 2. Community Care, Unnan City Hospital, Unnan, JPN 3. Family Medicine, Shimane University Faculty of Medicine, Izumo, JPN 4. Community Medicine Management, Shimane University Faculty of Medicine, Izumo, JPN

Corresponding author: Ryuichi Ohta, ryuichohta0120@gmail.com

Abstract

Autoimmune vasculitis is an autoimmune disease that causes various systemic symptoms, such as fever, fatigue, joint pain, and night sweats. Its clinical course depends on the severity of the inflammation, which can cause acute clinical progression of symptoms. Moreover, when the inflammation of the arteries occurs in the deeper parts of the body, a biopsy may be difficult to perform. Here, we report a case of autoimmune vasculitis in an elderly man who visited our hospital with a chief complaint of muscle pain and fever triggered by a rapid paralysis of both lower limbs. Autoimmune vasculitis can cause a variety of systemic symptoms depending on the size of involved arteries, and its clinical course depends on the severity of the inflammation. Prompt diagnosis and simultaneous treatment of symptoms, excluding other likely diseases, prevent the development of severe and long-term complications of autoimmune vasculitis.

Introduction

Autoimmune vasculitis is an autoimmune disease that causes various systemic symptoms, such as fever, fatigue, joint pain, and night sweats [1,2]. There are several types of autoimmune vasculitis based on the size of involved arteries [1]. Inflammation of the small or middle arteries can cause various systemic symptoms, such as nephritis, hepatitis, neuropathy, and interstitial pneumonia [3]. The four major autoimmune vasculitis types are microscopic polyangiitis, granulomatosis with polyangiitis (GPA), eosinophilic GPA, and polyarteritis nodosa [4]. Vasculitis can be diagnosed based on symptoms and pathological findings of necrotic or granulomatous inflammation on the arterial walls via biopsy [2,3]. Treatment with steroids and immunosuppressive drugs can prevent the development of severe complications of vasculitis [5].

The clinical course of autoimmune vasculitis depends on the severity of the inflammation, which can cause acute clinical progression of symptoms [6]. Ideally, pathological examinations are performed to diagnose vasculitis; however, autoimmune vasculitis with a very acute clinical course cannot be diagnosed by such examinations [7]. Moreover, when the inflammation of the arteries occurs in the deeper parts of the body, biopsy itself can be challenging [3]. Here, we report a case of autoimmune vasculitis in an elderly man with a chief complaint of muscle pain and fever. Acute bilateral lower limb paralysis was observed during the clinical course. He was diagnosed with small-to-medium-sized vasculitis based on the clinical symptoms and inflammatory changes in the arterial walls on computed tomography with contrast and laboratory tests. The patient was eventually diagnosed with GPA based on the serological results. He was successfully treated with intravenous prednisolone pulse, cyclophosphamide, and rituximab and partially recovered from lower leg paralysis. This case highlights the importance of promptly diagnosing autoimmune vasculitis by excluding various critical diseases and providing related treatments to prevent developing severe and long-term complications of vasculitis.

Case Presentation

An 82-year-old man who can independently perform activities of daily living (ADL) presented to our hospital with a chief complaint of fever, fatigue, and muscle pain while walking. He was admitted to the hospital for further investigation of the fever with a high inflammatory response. He had a history of prostate cancer at the age of 60 years, treated with radical prostatectomy and other comorbidities, including bronchial asthma, Barrett’s esophagus, hyperlipidemia, and chronic obstructive pulmonary disease. He has been a smoker until the age of 60 years. His medications include pravastatin sodium (10 mg), budesonide formoterol fumarate hydrate, and tipepidine hibenzate.

His vital signs on admission were as follows: temperature was 36.8 °C, blood pressure was 117/62 mmHg, pulse rate was 95 beats/min, respiratory rate was 16 times/min, and SpO₂ was 98% (room air). Physical examination revealed tenderness in the deep lower right abdomen and right dominant lateral
abdomen. A manual muscle test (MMT) results were as follows: iliopsoas muscle, 4+/5; quadriceps muscle, 5/5; biceps femoris muscle, 5/5; triceps femoris muscle, 5/5; and tibialis anterior muscle, 5/5. During the examination, the patient experienced pain induced by hip flexion. After admission, the patient developed a fever (temperature > 39°C) and tachypnea. The laboratory showed high inflammatory condition (Table 1).

| Marker                 | Level | Reference                          |
|------------------------|-------|------------------------------------|
| White blood cells      | 4.00  | 3.5-9.1 × 10^3/μL                  |
| Neutrophils            | 77.9  | 44.0-72.0%                         |
| Lymphocytes            | 10.2  | 18.0-30.0%                         |
| Monocytes              | 10.7  | 0.0-12.0%                          |
| Eosinophils            | 0.8   | 0.0-10.0%                          |
| Basophils              | 0.4   | 0.0-3.0%                           |
| Red blood cells        | 3.98  | 3.78-5.50 × 10^6/μL                |
| Hemoglobin             | 11.7  | 11.3-15.2 g/dL                     |
| Hematocrit             | 36.5  | 33.4-44.9%                         |
| Mean corpuscular volume| 91.5  | 79.0-100.0 μL                      |
| Platelets              | 28.5  | 13.0-36.9 × 10^4/μL                |
| Erythrocyte sedimentation rate | 89    | 3-10 mm/h                           |
| Total protein          | 5.9   | 6.5-8.3 g/dL                       |
| Albumin                | 3.0   | 3.8-5.3 g/dL                       |
| Total bilirubin        | 0.2   | 0.2-1.2 mg/dL                      |
| Aspartate aminotransferase | 41  | 8-20 U/L                           |
| Alanine aminotransferase | 25   | 4-43 U/L                           |
| Alkaline phosphatase   | 118   | 100-222 U/L                        |
| y-Glutamyl transpeptidase | 72    | <48 U/L                            |
| Lactate dehydrogenase  | 366   | 121-245 U/L                        |
| Blood urea nitrogen    | 11.3  | 9-20 mg/dL                         |
| Creatinine             | 0.66  | 0.40-1.10 mg/dL                    |
| eGFR                   | 66.2  | <90.0 mL/min                      |
| Serum Na               | 137   | 135-150 mEq/L                      |
| Serum K                | 4.1   | 3.5-5.3 mEq/L                      |
| Serum Cl               | 101   | 88-110 mEq/L                       |
| Ferritin               | 361.7 | 14.4-303.7 ng/mL                   |
| CK                     | 27    | 50-244 U/L                         |
| C-reactive protein     | 13.16 | <3.30 mg/dL                       |
| TSH                    | 0.35  | 0.35-4.94 μIU/mL                   |
| Free T4                | 0.9   | 0.70-1.40 ng/dL                    |
| IgG                    | 1048  | 870-1730 ng/dL                     |
| IgM                    | 19    | 35-220 mg/dL                       |
| IgA                    | 188   | 110-410 mg/dL                      |
| Hbs antigen            | 0.0   | 8 μL                              |
HBs antibody  0.0  mIU/mL
HBc antibody  0.0  S/CO
HCV antibody  0.0  S/CO
Syphilis treponema antibody  0.0  S/CO
SARS-CoV-2 antigen  Negative  -

Urine test
Leukocyte  Negative  -
Nitrite  Negative  -
Protein  Negative  -
Glucose  Negative  -
Urobilinogen  Negative  -
Bilirubin  Negative  -
Ketone  Negative  -
Blood  Negative  -
pH  6.0  -
Specific gravity  1.024  -

TABLE 1: Initial laboratory data of the patient.

We considered the possibility of bacterial translocation from the gastrointestinal tract based on shaking chill and persistent fever and initiated intravenous cefmetazole treatment. The urine and blood culture results were negative.

His fever continued (38°C) along with muscle pain; etodolac tablets (200 mg) were started to mitigate these. Additional tests were negative for antinuclear and antiphospholipid antibodies and revealed mildly elevated aldolase levels. Short tau inversion recovery magnetic resonance imaging (MRI) of the thighs revealed high signals in the bilateral gluteal and thigh musculatures (Figure 1).
FIGURE 1: A femoral magnetic resonance imaging scan (coronal plane) showing the bilateral hip and thigh muscles with a high signal (arrows).

A biopsy of the right semitendinosus muscle was performed, which showed negative findings for vasculitis and hematological malignancy. He was suspected of having polymyalgia rheumatica and was treated with 20 mg of prednisolone, which was increased to 30 mg two days later owing to persistent fever and exacerbated systemic muscle pain.

On day 18 of hospitalization, rapidly progressive paralysis of both the lower limbs appeared. Neurological examination revealed decreased tendon reflexes and a loss of rectoanal reflexes, and sensory loss in the lesions of L4 to S2. Cerebrospinal fluid analysis revealed protein–cell dissociation in the cerebrospinal fluid (protein, 117 mg/dL; cell counts: 21/μL). Lumbar and pelvic magnetic resonance imaging (MRI) showed high signals in the bilateral sciatic nerves without compression in spinal cord space from Th8 to L5 to induce paralysis (Figure 2).

FIGURE 2: A pelvic magnetic resonance imaging scan (coronal plane) showing high signals in the bilateral sciatic nerves (arrows)

His additional clinical history clarified proceeding epistaxis, cough, stomatitis, dyspnea, systemic edema, and hypertension. Repeat antibody tests were negative for perinuclear antineutrophil cytoplasmic antibodies (ANCA), but the cytoplasmic ANCA levels (C-ANCA) were mildly elevated (2.7 U/mL). Lumbar MRI did not reveal an obvious cauda equina syndrome. Computed tomography (CT) of the thoracic and pelvic regions showed generalized edema of the periarterial lesions around the superior and inferior mesenteric arteries (Figure 3) and effusions of pericardial and pleural fluids (Figure 4). There was no finding of the thrombosis of the artery of Adamkiewicz in the CT.
Based on the clinical course, the patient was presumed to have an acute progressive inflammatory condition caused by GPA. On day 19 of hospitalization, 1000 mg of methylprednisolone was administered for three days. Owing to the presence of protein-cell dissociation of the spinal fluid and acute progressive paralysis of the lower limbs, a diagnosis of Guillian-Barré syndrome was made; 4 mg/kg of intravenous immunoglobulin was administered for five days for the acute demyelinating condition. Ceftriaxone of 4 g per day and acyclovir of 1500 mg per day were administered to treat possible viral/bacterial meningitis. No obvious malignant findings were identified on muscle biopsy, spinal fluid analysis, or peripheral blood pathology; however, the patient’s symptoms progressed. Thus, 500 mg of cyclophosphamide pulse 500 was added for possible exacerbation of granulomatosis with polyangiitis. He also had urinary retention, was suspected of a neurogenic bladder, and was treated with a urinary catheter.

On day 29 of hospitalization, because of an inadequate response to cyclophosphamide pulse therapy, rituximab 500 mg was started. This caused marked relief of the abdominal pain. Moreover, the progression of muscle weakness in both lower limbs stopped, and symptoms in both lower limbs gradually improved with rehabilitation. The patient was treated with four weekly infusions of rituximab. The patient’s paralysis was alleviated, and we removed his urinary catheter on the 41st day. He was transferred to the
relationships or activities that could appear to have influenced the submitted work.

Disclosures

All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Conclusions

We successfully treated a patient with rapidly progressive polyneuritis and paraplegia with steroid pulse, cyclophosphamide, and rituximab, although a diagnosis of GPA was not made based on biopsy results. It is important to initiate treatment for rapidly progressing vasculitis with neurological symptoms as early as possible. Elderly patients often present with undefined complaints, and general practitioners at community hospitals need to have a broad scope of practice to facilitate the diagnosis and treatment of such cases.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.
References

1. Saadoun D, Vautier M, Cacoub P: Medium- and large-vessel vasculitis. Circulation. 2021, 143:267-82.
2. Kitching AR, Anders HJ, Basu N, et al.: ANCA-associated vasculitis. Nat Rev Dis Primers. 2020, 6:10.1038/s41571-020-0204-y
3. Ferrario F, Vanzati A, Pagni F: Pathology of ANCA-associated vasculitis. Clin Exp Nephrol. 2015, 17:652-8.
4. Scott DG, Watts RA: Epidemiology and clinical features of systemic vasculitis. Clin Exp Nephrol. 2013, 17:607-10.
5. Greco A, Marinelli C, Fusconi M, et al.: Clinic manifestations in granulomatosis with polyangiitis. Int J Immunopathol Pharmacol. 2016, 29:151-9.
6. Zhang S, Yuan D, Tan G: Neurological involvement in primary systemic vasculitis. Front Neurol. 2019, 10:10.3389/fneur.2019.00450
7. James J, Jose J, Thulasendharan NK: Acute necrotizing vasculitic neuropathy due to polyarteritis nodosa. Oman Med J. 2018, 33:255-5.
8. Hur JH, Chun EJ, Kwag HJ, Yoo JY, Kim HY, Kim JJ, Lee KW: CT features of vasculitides based on the 2012 International Chapel Hill Consensus Conference Revised Classification. Korean J Radiol. 2017, 18:786-98.
9. Collins MP, Periquet MI: Isolated vasculitis of the peripheral nervous system. Clin Exp Rheumatol. 2008, 26:118-30.
10. Suresh E: Diagnostic approach to patients with suspected vasculitis. Postgrad Med J. 2006, 82:483-8.
11. Direskeneli H, Aydn EZ, Merkel PA: Assessment of disease activity and progression in Takayasu’s arteritis. Clin Exp Rheumatol. 2011, 29:86-91.
12. Robson JC, Jayne D, Merkel PA, Dawson J: Systemic vasculitis and patient-reported outcomes: how the assessment of patient preferences and perspectives could improve outcomes. Patient Rel Outcome Meas. 2019, 10:37-42. 10.2147/PROM.S163601
13. Hoganston DE, From AM, Michet CJ: ANCA vasculitis in the elderly. J Clin Rheumatol. 2008, 14:78-81. 10.1097/RHU.0b013e3181682bd
14. Ohta R, Rya Y, Sano C: Older people’s help-seeking behaviors in rural contexts: a systematic review. Int J Environ Res Public Health. 2022, 19, 10.3390/ijerph19106323
15. Ohta R, Rya Y, Sano C: Improvement in quality of life through self-management of mild symptoms during the COVID-19 pandemic: a prospective cohort study. Int J Environ Res Public Health. 2022, 19, 10.3390/ijerph19116652
16. Ohta R, Sato M, Kitayuguchi J, Maeno T, Sano C: The association between the self-management of mild symptoms and quality of life of elderly populations in rural communities: a cross-sectional study. Int J Environ Res Public Health. 2021, 18, 10.3390/ijerph18168857
17. Ohta R, Idea H, Kubota S, Sano C: Acute cholecystitis in an elderly patient With antineutrophil cytoplasmic antibody-associated vasculitis: a case report. Cureus. 2022, 14:10.7759/cureus.21877
18. Tokonami A, Ohta R, Tanaka Y, Amano S, Sano C: Pericarditis with cardiac tamponade mimicking yellow nail syndrome in a patient with rheumatoid arthritis and a paucity of joint symptoms. Cureus. 2022, 14:10.7759/cureus.21523
19. Ohta R, Rya Y, Kitayuguchi J, Sano C, Könings KD: Educational intervention to improve citizen’s healthcare participation perception in rural Japanese communities: a pilot study. Int J Environ Res Public Health. 2021, 18, 10.3390/ijerph18041782
20. Yamashita M, Ohta R, Mour N, Takizawa S, Sano C: Herpes simplex virus pneumonia mimicking Legionella pneumonia in an elderly patient with heart and liver failure. Cureus. 2022, 14:10.7759/cureus.21958