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Encephalitis an extra-articular manifestation of rheumatoid arthritis complicated by a takotsubo cardiomyopathy: A case report

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Abstract

We describe the case of a 68-year-old woman with encephalitis as a rare extra-articular manifestation of rheumatoid arthritis associated with Takotsubo cardiomyopathy. The patient presented to the emergency department with several neurological deficits, electrocardiographic findings of ST-segment elevation in all precordial leads and an elevated troponin level (4.293 µg/L). Magnetic resonance imaging (MRI) confirmed encephalitis with cortico-subcortical edema in the right frontal area, whereas echocardiography showed typical changes associated with takotsubo cardiomyopathy. Lumbar puncture revealed purulent cerebrospinal fluid with elevated protein content and white blood cells; however, no bacterial or viral microorganisms were detected. The patient was treated with antibiotics, antiviral agents, and corticosteroids. Subsequent investigations, including electroencephalogram, MRI, and autoimmune tests, supported the diagnosis of rheumatoid arthritis complicated by encephalitis and tako-tsubo syndrome. The patient's condition improved with treatment, and was discharged after one month of prednisolone therapy and scheduled for follow-up at the rheumatology clinic.

Introduction

This case highlights the rare occurrence of encephalitis as an extra-articular manifestation of rheumatoid arthritis associated with stress cardiomyopathy, emphasizing the importance of a comprehensive diagnostic approach and appropriate management of such complex clinical presentations. To our knowledge, there are no reported cases of rheumatoid encephalitis associated with stress cardiomyopathy described in the literature.

Case presentation

A 68-year-old woman with a history of rheumatoid arthritis treated with leflunomide for 15 years, complicated by a pulmonary rheumatoid nodule, gastric ring, hiatal hernia, and asthma, was brought to the emergency department by the prehospital medical team. The patient was discovered lying on the floor with a Glasgow coma scale score of 14 and exhibited vomiting. In the emergency department, the patient had a National Institutes of Health Stroke Scale (NIHSS) score of 15 (facial palsy, left hemiparesis, dysarthria, and total hemianopsia). The patient also developed partial seizures with spontaneous resolution. The contrast CT brain scan performed on admission was not suggestive of any vascular abnormality but showed parieto-temporal and temporo-occipital hypodensity in the white matter. Magnetic resonance imaging (MRI) confirmed that no vascular disease was involved but revealed encephalitis with cortico-subcortical edema in the right frontal area. Blood tests revealed elevated inflammatory markers with a white blood count of 11.5×10^9 /L and C-reactive protein level of 133 mg/ml with an initial rise in troponin level (4.293 µg/L) associated with ST elevation in all precordial leads. The cardiology team confirmed the presence of typical echocardiographic changes associated with takotsubo cardiomyopathy. This patient fulfilled all four criteria proposed by the Mayo Clinic for tako-tsubo diagnosis [1].

Despite these findings, a coronary angiography was performed in this patient with no cardiovascular risk factors and ultrasound findings of takotsubo cardiomyopathy. The patient initially refused consent and agreed 3 weeks later. Coronary angiography revealed diffuse atherosclerosis without significant lesions in the right coronary artery, with a left ventricular ejection fraction > 50 percent. These findings ruled out myocardial infarction and myocarditis but confirmed stress cardiomyopathy. Lumbar puncture revealed purulent cerebrospinal fluid (CSF), a high protein content (2.96 g/L) an elevated white blood cell count (802/mm^3) with 95 percent of neutrophils. Bacterial cells were not detected.

The patient was admitted to the Neurology Department of our hospital. The suspected diagnosis was bacterial or viral meningoencephalitis complicated by takotsubo cardiomyopathy, which was initially treated with a combination of ceftriaxone 300 mg/kg (4 days), amoxicilline 200 mg/kg (21 ds), gentamicine 5 mg/kg (one day), aciclovir 500 mg (every 8h for 4 days), 10 mg of dexamethasone (once), and leviteracetam 500 mg (twice a day after the patient had a partial seizure).

EEG repeated 10 days after admission showed a moderately slow background rhythm in the right hemisphere. Another EEG repeated one week later did not show any abnormalities. After 2 weeks, repeat MRI revealed stable encephalitis. A decrease in C-reactive protein

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levels was observed after 4 days of treatment. The patient had been treated with leflunomide for more than 10 years; however, we decided to discontinue the medication. We proceeded with 2 lumbar punctures: The first at 1 week of admission and the second at 2 weeks. The first revealed a significant decrease in white blood cell count (27 /mm^3 with 95 percent of them being lymphocytes) and a CSF protein content of 0.61 g/L and no bacterial or viral microorganisms. The second was similar to the first, but the autoimmune tests were positive for anti CCP (Cyclic Citrullinated Peptide) and anti-RF (Rheumatoid Factor) antibodies in the CSF associated with IL6 level and a ratio of Il10/Il6 inferior to 1, suggesting an inflammatory process. Blood culture results were negative. The patient also tested negative for HIV, VHC, VHB, syphilis, Lyme disease, HSV, arboreal viruses, and Mycoplasma pneumoniae. Serum protein electrophoresis revealed no qualitative abnormalities. Vitamin B9 and B12 levels were within normal limits. A computed tomography (CT) revealed an increase in the size of known rheumatoid pulmonary nodules and two new rheumatoid nodules. Based on the imaging findings, anti-CCP and anti-RF positivity, and no other differential diagnosis, we concluded that rheumatoid arthritis complicated by encephalitis was associated with takotsubo cardiomyopathy.

The patient was discharged 1 month later and prescribed prednisolone 50 mg/day. The patient regained all motor functions, and the troponin level decreased. An outpatient follow-up in a rheumatology clinic was conducted to adjust the patient's treatment and to start methotrexate as a new treatment for rheumatoid arthritis. A lung function test was performed as a pretherapeutic workup.

Discussion

Rheumatoid arthritis-associated meningoencephalitis is a rare extra-articular manifestation with an unknown frequency, as described in the literature. Indeed, there are no reported cases of rheumatoid arthritis causing encephalopathy associated with takotsubo cardiomyopathy. A case report published in 2018 described autoimmune encephalitis as an extra-articular manifestation of rheumatoid arthritis [2]. The report described encephalitis in a 57-year-old woman who presented with memory loss, depression, anorexia and headache for 7 months. There is no specific treatment for stress cardiomyopathy other than etiologic treatment of the underlying condition and cardiovascular control of risk factors.

Aseptic meningitis caused by leflunomide is extremely rare and has been described twice in the literature, in two case reports. The first case was reported in 2004 and the second in 2021 [3,4]. In our case report, the chronological occurrence was not suggestive of a direct complication of the medication, but we cannot rule it out completely.

Conclusion

This case highlights a rare presentation of rheumatoid encephalitis associated with Takotsubo cardiomyopathy and underscores the importance of a comprehensive diagnostic approach when evaluating patients with rheumatoid arthritis who develop unexplained neurological symptoms, emphasizing the importance of a comprehensive diagnostic approach and appropriate management of such complex clinical presentations.

Conflicts of interest

The authors declare no conflict of interest.

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