Case report

Adult-onset Still's disease presenting with aseptic meningitis as the first symptom in an elderly patient

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ARTICLE INFO

Keywords:
Adult-onset Still's disease
Aseptic meningitis
Neutrophilic pleocytosis
Procalcitonin, hyperferritinemia, steroid therapy.

Dear Editor,

Adult-onset Still's disease (AOSD) is a systemic inflammatory disease characterized by the classic triad of persistent high spiking fever, arthralgia, and salmon-colored skin rash [1]. The most widely cited Yamaguchi criteria are shown to be most sensitive (93%). There are no specific biomarkers for AOSD, although liver dysfunction and hyperferritinemia are commonly observed [2]. Neurological complications including cranial nerve palsies, seizures, and peripheral neuropathy also occur in 7%-12% of patients with AOSD, particularly during the late stage [3-6]. Aseptic meningitis is one of the rare neurological symptoms of AOSD, and to our knowledge, 15 cases of AOSD-related aseptic meningitis have been reported to date. Almost all the reported cases included an onset at younger adult age, and all except two cases presented with meningitis during the course of AOSD [7-9]. Here, we report an AOSD case with meningitis as the first symptom in an elderly patient.

1. Case report

A 63-year-old Japanese male with a history of fever and headache was admitted to our hospital. He was previously healthy, except for experiencing hypertension, and was taking an antihypertensive drug. From 4 days before admission, he experienced a headache, at the back of his head to his neck, and fever of up to 40 °C. He was administered oral cefcapene pivoxil one day before admission, however, this had no effect. A physical examination upon admission showed a high body temperature of 39.3 °C and worsening or jolt accentuation of the headache. Nuchal rigidity, Kernig's sign, and other meningeal irritation were negative. His consciousness was clear and no other neurological focal symptoms existed. He had no skin rash, no arthralgia, and no organomegaly. A laboratory test on admission revealed C-reactive protein (CRP): 6.12 mg/dL, white blood cell (WBC) count: 11.8 × 10\textsuperscript{3} (79% neutrophils), aspartate aminotransferase (AST): 47 IU/L, alanine aminotransferase (ALT): 142 IU/L, and creatinine: 1.13 mg/dL.

Cerebrospinal fluid (CSF) analysis revealed a yellow and turbid appearance, with a high opening pressure (310 mmH\textsubscript{2}O), elevated WBC count (1194 per mm\textsuperscript{3}) with neutrophilic pleocytosis (68% neutrophils, 32% monocytes and lymphocytes), elevated protein levels (215 mg/dL), and normal glucose levels (52 mg/dL). Brain MRI revealed no abnormalities. Bacterial meningitis was suspected from the CSF findings and intravenous administration of dexamethasone (40 mg/day), meropenem (6 g/day), and vancomycin (3 g/day) was initiated (Fig. 1). On the second day, his fever and headache rapidly improved. On the fourth day, the steroid therapy was completed. Culture of the blood and CSF at admission was negative. On the fifth day, his liver enzymes levels increased (AST, 249 IU/L; ALT, 373 IU/L). We decreased the vancomycin dose from 3 g/day to 2 g/day as drug-induced hepatic injury was suspected. His fever increased up to 38 °C on the eighth day, and a non-
pruritic maculopapular skin rash was observed on his neck, chest, abdomen, and back on the ninth day. Arthralgia of limbs and pharyngeal pain appeared on the tenth day, and he developed anuria because of acute renal insufficiency that required hemodialysis. Repeated examinations of the CSF revealed improved acute renal insufficiency. An additional laboratory test showed increased ferritin (3080 ng/mL), procalcitonin (PCT; 11.2 ng/mL), negative antinuclear antibodies (ANA), and negative rheumatoid factor (RF). Two additional blood cultures and CSF cultures remained negative. Serological tests for Epstein–Barr virus, cytomegalovirus, herpes simplex virus, varicella zoster virus, Mycobacterium tuberculosis using QuantiFERON, and human immunodeficiency virus were all negative. Skin biopsy of the leg rash, performed on the twelfth day, showed a mild nonspecific perivascular inflammation (Supplementary Fig. 1). Computed tomography of the trunk, on the thirteenth day, showed cervical lymphadenopathy and splenomegaly.

He was diagnosed with AOSD with two major (typical rash and arthritis) and five minor criteria (sore throat, lymphadenopathy, splenomegaly, abnormal liver function tests, negative RF, and ANA) according to the diagnostic criteria of AOSD defined by Yamaguchi [2], with the exclusion of similar underlying diseases. After treatment with methylprednisolone (1000 mg/day) from the thirteenth to fifteenth day, his fever resolved immediately and his inflammatory conditions improved. Oral prednisolone (60 mg/day) was administered after initial steroid therapy administered for bacterial meningitis. Moreover, our patient showed meningitis as the first symptom of AOSD and was oldest of the reported AOSD-related aseptic meningitis patients, we cogitated whether the meningitis was AOSD-related or bacterial meningitis. However, the findings were not consistent with bacterial meningitis because of the following: (i) Gram staining and blood and CSF cultures at admission were negative despite only a one-day oral antibiotic administration before admission; (ii) the CSF glucose levels were higher than in typical bacterial meningitis; and (iii) improvement after initial therapy with antibiotics and steroids was extremely rapid.

In contrast, these findings are consistent with the characteristics of AOSD-related meningitis. A marked improvement in meningitis was observed with the initial steroid therapy administered for bacterial meningitis. Moreover, a high serum concentration of PCT during febrile spikes in the absence of infection has also been reported in AOSD patients [10]. The negative results of all repeated blood and CSF cultures in the course of the disease are also concurrent with findings in AOSD-related meningitis.

In conclusion, AOSD-related aseptic meningitis is one of the differential diagnosis of neutrophilic meningitis and could be a first symptom of AOSD even in elderly patients. Although a differential diagnosis, from bacterial meningitis, may be difficult because of the similarities of CSF findings and improvement with initial steroid therapy for bacterial meningitis, hyperferritinemia could be a clue to the diagnosis as AOSD-related aseptic meningitis.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ensci.2019.100202.

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