CASE STUDY

Burkholderia sepsis mimicking flare of ANCA-associated vasculitis: A rare presentation

Mayank Gupta[1], Lalit Duggal[1], Neeraj Jain[1], Chintala Bhavya[1]*

[1]Department of Rheumatology, Sir Gangaram Hospital, New Delhi, India

Abstract

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis is an autoimmune condition that primarily targets small to medium sized vessels in multiple organ systems, with sinonasal, pulmonary and renal involvement being common. The present case study discusses a known case of ANCA associated vasculitis, type 2 diabetes and hypertension, who presented with altered sensorium and weakness of the left side of the body. Few months before the onset of symptoms, the patient received rituximab injection for treating cutaneous panniculitis and high pANCA titers. MRI of brain and CECT of chest were suggestive of vasculitis and blood culture showed the growth of *Burkholderia cepacia*. She was treated with broad spectrum antibiotics and other supportive treatment. Despite all the efforts including ionotropic and ventilator supports, the patient succumbed to the infection.

Keywords: ANCA, *Burkholderia*, Crow-Fukase, vasculitis

Introuction

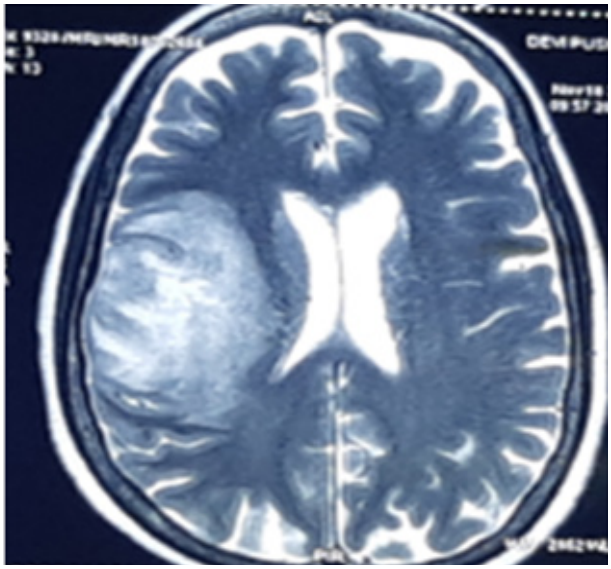
Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis is an autoimmune inflammatory condition affecting the small blood vessels of various organs.[1] *Burkholderia pseudomallei* is a gram negative, bipolar, aerobic, motile, rod shaped bacterium responsible for causing melioidosis.[2] The variable symptoms include respiratory distress, severe headache, fever, diarrhea, disorientation, and pus-filled lesions of skin and muscles.[3,4] The infection is typically of shorter duration and the abscess can be found throughout the body.[5] Neurological melioidosis is a very rare entity, and >50 cases have been reported so far globally.[6] The present study discusses a rare case of *Burkholderia* infection, which mimicked a flare of ANCA vasculitis. The disease would have got activated following rituximab injection.

Case report

A 54-year-old female presented with complaints of slurring of speech and deviation of angle of mouth towards right for 6 days, and weakness of left upper and lower limbs for 3 days. She was on medications for diabetes mellitus (15 years), hypertension (10 years), and hypothyroidism (5 years). Her medication history revealed that she had received azathioprine and oral glucocorticoids (off treatment since 8 months) for neutrophil cytoplasmic antibody (ANCA) vasculitis diagnosed around two years back. The patient had a history of hospitalization around 2 months ago with complaints of multiple tender nodular skin lesions along with high pANCA titer not responding to steroids and immunosuppressive medications. Her skin biopsy was suggestive of cutaneous panniculitis. At that time of flare, ANCA vasculitis was suspected and rituximab (1gm) injection was administered. Three days after receiving rituximab injection, the patient developed bilateral lower limb weakness. MRI of spine revealed paraspinal abscess, and the drainage culture revealed *Burkholderia cepacia.* Her history showed that the condition improved following IV antibiotics and she was discharged. The patient was readmitted in the same hospital after 4 days with complaints of slurring of speech and left-side weakness. MRI of brain showed hyperintense lesions in frontotemporal lobe (Fig.1). Contrast-enhanced computed tomography (CECT) showed multiple, small, randomly distributed, angiocentric, multiple cavitary and non-cavitary nodules. Both the findings were suggestive of ANCA vasculitis. Whereas, blood culture and pus culture of brain lesions, and paraspinal abscess concluded *Burkholderia* infection.

She was referred to the current institute for further management. Slurring of speech and weakness of left upper and lower limb were sudden in onset and progressive. The weakness started with left side lower

Fig. 1: MRI of brain showing hyperintense lesions in right frontal and medioparietal temporal lobe



limb, followed by upper limb. There was no history of fever, cough, loss of consciousness, seizures, chest pain and headache. The patient was admitted in ICU with altered sensorium. General examination revealed blood pressure 134/82 mm Hg, tachycardia, tachypnea, sluggish reaction of pupils to light, neck rigidity and negative Kerning sign. Systemic examination showed the presence of bilateral fine crepts in chest. Central nervous system examination indicated that the patient was drowsy, with upper motor neuron palsy of 7th cranial nerve. Decrease in muscle tone and power was noted in left upper and lower limbs with left plantar extension. On routine investigations, hemogram showed anemia (8.8 gm/dl), leukocytosis (21000/mm^3), thrombocytopenia (11000/uL), normal liver function test, raised serum procalcitonin (29.8 ng/ml), creatinine, and p-ANCA titer (24 AU/ml), negative c-ANCA, and urine PC ratio 2.63. Blood culture showed *Burkholderia Pseudomallei* sensitive to meropenem and minocycline, while the urine culture was sterile. She was kept on non-invasive ventilation. In view of increase in size of lesion in CECT in right frontoparietotemporal region and right hippocampus region with enhancement along the sulci and periphery of these hypodensities (Fig 1), craniotomy was done along with corticectomy over frontal gyrus. Brain pus culture and brain biopsy of necrosed brain tissue also revealed Burkholderia infection. The patient gradually developed hypotension, which was not responding to fluids and vasopressor support and she was shifted to mechanical ventilation due to fall in oxygen saturation. Despite all the possible efforts, she succumbed to infection.

Discussion

Many conditions can mimic ANCA-associated vasculitis (AAV), a subtype of vasculitis due to the raised ANCA titers. Infection is a major concern in the management of AAV and it is the most common cause of death, especially in patients with malnutrition or immunosuppressive therapy.[7] In a single-centre cohort study involving 248 Chinese patients with AAV, major infections were reported in 34.6% of the subjects.[8] Approximately 64.1% of these infections developed in the first three months of induction therapy. According to the literature, bacteria such as *Streptococcus pneumonia* and *Hemophilus influenza* are the most common causative pathogens.[9] The corresponding 1-, 2-, and 5-year cumulative incidences of infection noted in a retrospective study involving 489 patients with biopsy-proven AAV were 51%, 58%, and 65%, and severe infections were 22%, 23%, and 26%.[10]

It is highly challenging to differentiate between underlying infection and flare of vasculitis. There is no serological or imaging biomarker that can accurately differentiate between infection and vasculitis. Early identification of organisms in culture and tissue specimen is the gold standard for diagnosis. Koo *et al.* have reported that treating Burkholderia infection is highly complex, as it demonstrates multidrug resistance through various innate and acquired mechanisms such as biofilm formation, adherence to epithelial cells, and secretion of factors that assist in host evasion. Moreover, there is no trial-based evidence to decide the optimal antibiotic regimen to be

followed for managing *B. cepacia* complex infections. Hence antibiotic susceptibility profile and early recognition are keys to decide the appropriate therapy.[11]

In the current case, the *Burkholderia* sepsis infection mimicked as a flare of a known case of ANCA vasculitis.[12,13] After receiving rituximab, the infection aggravated and the patient developed neurological manifestation. Diagnosis of neurological melioidosis was made on the basis of culture reports from affected tissue (brain and spinal cord) and tissue specimen (brain biopsy). To the best of our knowledge, this is the first reported case of patient who developed neurological melioidosis after receiving rituximab injection, which mimicked as a flare of ANCA associated vasculitis.

Conclusion

Burkholderia infection can complicate vasculitis course, particularly in immunocompromised individuals. It can lead to multiorgan dysfunction with involvement of lung and rarely CNS (as in our case). Immunosuppressive agents like rituximab should be judiciously used after proper screening for underlying infection. Prompt treatment with 3rd generation cephalosporins/ carbapenem is key to patient management.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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*Correspondence: Dr Chintala Bhavya, Sir Gangaram Hospital, SSRB Building, 2nd floor, Old Rajender nagar, New Delhi, India
bhavya.chintala1990@gmail.com

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