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# A case of cerebral amyloid angiopathy related inflammation after vaccination against SARS-CoV-2

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ABSTRACT

*Background:* Cerebral amyloid angiopathy related inflammation (CAA-RI) is a neuroinflammatory disease that is associated with perivascular amyloid- deposition.
*Case presentation:* A middle-aged woman with a remote history of autoimmune disorders presented with unilateral migraine headaches, dizziness, unsteadiness, and fogginess 36 hours after administration of mRNA vaccine against SARS-CoV-2. Initially, unilateral leptomeningeal enhancement on MRI on the same side of headaches raised suspicion for leptomeningeal involvement of her known cutaneous T-cell lymphoma in remission. After two relatively unremarkable CSF analyses, she underwent a brain biopsy which showed amyloid deposits in vessels instead of lymphomatous infiltration. She was diagnosed with CAA-RI, and the headache and cognitive symptoms responded well to high-dose corticosteroids with a slow taper.
*Discussion/conclusion:* We review the clinical literature of CAA-RI and its potential association with amyloid-related imaging abnormalities (ARIA) after administration of immunotherapy against amyloid.

## Present illness

A 57-year-old Caucasian female was admitted for a 3-week history of new-onset headaches. The headaches started within 36 hours after the first dose of the Moderna SARS-CoV2 vaccine. The key headache features included right temporal throbbing sensation associated with scintillating scotomas in the right eye, dizziness, unsteadiness, and fogginess. Before her presentation to the hospital, she went to an urgent care clinic with personal concerns for temporal arteritis and took one tablet of 20 mg prednisone which briefly alleviated her headaches. She now reported several episodes of numbness that started in the left finger that progressed to the arm and then the left leg lasting several minutes.

## Past illnesses

Past medical history was significant for immune thrombocytopenic purpura in childhood and cutaneous T-cell lymphoma status post multiple local resections that is in remission.

## Relevant physical/neurological exam findings

Gross examination and neurological exam were normal without focal neurological deficits.

## Notable negative history/exam findings

She denied any persistent weakness, numbness, tingling, dysarthria, gait disturbance, fever, chills, or weight loss.

## Imaging

MRI head with and without contrast showed leptomeningeal enhancement and sulcal edema more prominent on the right (Fig. 1A, Fig. 1B). She also had a cortical microhemorrhage in the right hemisphere (Fig. 1C).

## Laboratory

First lumbar puncture: 0/$\mu$L white cells, protein 40 mg/dL. Second lumbar puncture: 6/$\mu$L white cells with 100% lymphocytes, protein 47 mg/dL. Both with normal opening pressure and negative cytology and flow cytometry. Dura and brain biopsy: negative for T-cell lymphoma, positive for meningothelial hyperplasia, and vascular amyloid-$\beta$ deposits (Fig. 1D). There was no perivascular or destructive vasculitis with the vessels positive for amyloid-$\beta$ deposits observed in the pathology.

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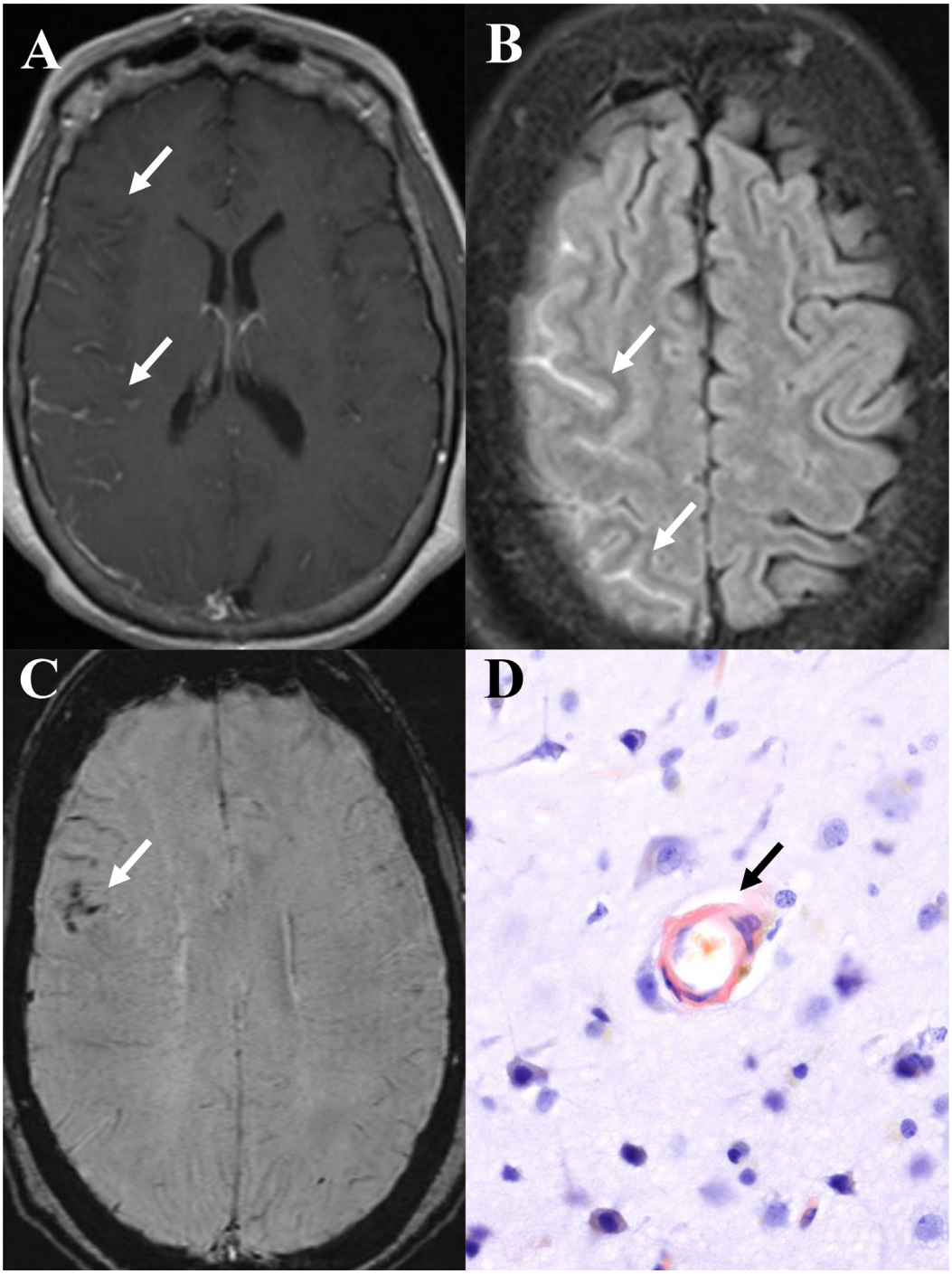


**Fig. 1.** MRI head and pathology finding. (A) MRI head, T1 post-contrast and (B) fluid attenuation inversion recovery; arrows represent asymmetric sulcal hyperintensity in the right hemisphere. (C)MRI head, susceptibility weighted imaging; arrow represents cortical microbleeds. (D) brain biopthy, Congo-red staining; arrow represents perivascular deposition of amyloid-$\beta$.

## Discussion

Initially, unilateral leptomeningeal enhancement on the same side of headaches raised suspicion for leptomeningeal involvement of her known cutaneous T-cell lymphoma in remission. After two relatively unremarkable CSF analyses, she underwent a brain biopsy which showed amyloid deposits in vessels instead of lymphomatous infiltration. Clinical diagnosis of cerebral amyloid angiopathy (CAA) – related inflammation (CAA-RI) with amyloid spells was made, and she was treated with high dose steroids (1 g intravenous methylprednisolone with a prednisone taper; 80 mg for 10 days, then decrease by 20 mg every 3 days until off) with subsequent resolution of her headaches and cognitive symptoms.

CAA could be associated with perivascular inflammation in histopathological analysis (CAA-RI); if there is angiodestructive component, the condition is often called amyloid related angiitis (ABRA). CAA-RI is a rare cause of subacute inflammatory cognitive decline, headaches, and seizures (Corovic et al., 2018). A systematic review of 214 published cases in 2018 reported that the mean age at presentation of pathologically proven CAA-RI was 67 years (range: 42-87) with

slight male predominance (55%) (Corovic et al., 2018). The most common presentation was cognitive decline (48%), followed by headaches and seizures (32% respectively). The duration of symptoms varied: 24 % with acute course ≤ 2 days, 17% with subacute course ranging 3-29 days, and 61% had a chronic course ≥ 30 days. The mean duration of symptoms up to presentation was 21 weeks suggestive of diagnostic delay. More recently, a prospective cohort study of 113 patients with CAA-RI followed for 2 years revealed similar characteristics of the patient population with clinical recovery in 84.1% at the 12-month follow-up (Antolini et al., 2021). Radiographic findings typically include asymmetric T2 hyperintensities involving juxtacortical regions, leptomeningeal enhancement, and microhemorrhages in susceptibility-weighted images (Corovic et al., 2018, Antolini et al., 2021, Cho and vasculopathies, 2020, Salvarani et al., 2016). CSF commonly shows elevated protein of > 45 mg/dL in 83% of cases and elevated white cell count of >5 cells/$mm^3$ could be seen (44%) (Corovic et al., 2018). Corticosteroids are used most commonly for treatment in up to 81% of cases, followed by cyclophosphamide, azathioprine, and intravenous immunoglobulin. Recurrence occurred in 38.3% of the cases which was more likely with abrupt cessation of corticosteroids after high-dose corticosteroid treatment (hazard ratio 4.68, 95% confidence interval: 1.57-13.93) (Antolini et al., 2021). Radiographic and pathological findings of CAA-RI can be similar to those of amyloid-related imaging abnormalities (ARIA) after administration of immunotherapy against amyloid-$\beta$. The number of microbleeds at baseline and an *APOE*$\varepsilon$4 allele are risk factors for both ARIA and CAA with and without inflammation, suggesting that there may be a link between the pathogenesis of ARIA and CAA-RI (Antolini et al., 2021, Greenberg et al., 2020).

It is difficult to prove causation rather than a chronological association of preceding SARS-CoV2 vaccination as with any vaccine-related adverse events. CAA-RI in general has not been described in the setting of preceding infection or vaccination. In 2021, an abstract described a case of CAA-RI after SARS-CoV2 vaccination (Tozinameran from Pfizer) who presented with refractory status epilepticus that responded to corticosteroids, and IgG against the spike protein of SARS-CoV2 was found in CSF deemed to be secondary to the vaccination (Rossato et al., 2021). Further study is needed to investigate true associations between vaccinations and CAA-RI.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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