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Case Report

Supratentorial lymphocytic inflammation with parenchymal perivascular enhancement responsive to steroids: A case report and literature review

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Received : 11 April 2021
Accepted : 11 June 2021
Published : 06 July 2021

DOI
10.25259/SNI_355_2021

Quick Response Code:

ABSTRACT

Background: Chronic Lymphocytic Inflammation with Pontine Perivascular Enhancement Responsive to Steroids is a rare disorder that presents with subacute brainstem symptoms such as ataxia, facial paresthesias, and episodic diplopia, thought to be due to a T-cell medicated perivascular inflammatory process. A supratentorial variant, Supratentorial Lymphocytic Inflammation with Parenchymal Perivascular Enhancement Responsive to Steroids (SLIPPERS), has been described in only three patients.

Case Description: A 71-year-old male presented with word-finding difficulties, confusion, and left leg weakness. Radiographic workup demonstrated multiple supratentorial ring-enhancing lesions. PET/CT demonstrated hypermetabolism and susceptibility-weighted imaging demonstrated a hemorrhagic component. Frozen pathology revealed a predominately T-cell and monocyte inflammatory infiltrate. He demonstrated interval improvement to dexamethasone therapy, but then demonstrated worsening of his symptoms following discontinuation.

Conclusion: Given his dramatic response to corticosteroids, he was diagnosed with SLIPPERS. SLIPPERS is an underrecognized diagnostic entity to consider in patients with ring-enhancing lesions and can present with hypermetabolic lesions on PET/CT.

Keywords: CLIPPERS, CNS lymphoma, Neuroimmunology, SLIPPERS

INTRODUCTION

Chronic Lymphocytic Inflammation with Pontine Perivascular Enhancement Responsive to Steroids (CLIPPERS) was first described by Pittock *et al.* in eight patients who presented with various brainstem symptoms such as episodic diplopia, ataxia, and facial paresthesias.[3] Radiographically, these patients exhibited scattered gadolinium enhancement throughout the pons with histology demonstrating perivascular white matter infiltration of predominately T lymphocytes. Supratentorial Lymphocytic Inflammation with Parenchymal Perivascular Enhancement Responsive to Steroids (SLIPPERS) is a supratentorial variant of CLIPPERS first described by Armand *et al.* in two patients.[1] Here, we present a novel presentation of SLIPPERS with unique radiographic and clinical findings.

CASE DESCRIPTION

History, physical examination, and baseline imaging

A 71-year-old male presented with a 3-month history of word-finding difficulties, confusion, and left leg weakness. CT head demonstrated several ill-defined hypodense areas within the right parietal and occipital subcortical white matter. MRI of the brain demonstrated a contrast-enhancing 3.2 cm lesion in the right occipital lobe, a 1.8 cm enhancing lesion in the right precentral gyrus, and multiple smaller enhancing lesions in the right periventricular region with associated vasogenic edema but no mass effect [Figure 1a]. PET/CT showed no evidence of systemic malignancy but visualized right posterior temporal, occipital and parietal lobe lesions [Figure 1b and c]. Susceptibility-weighted angiography (SWAN) imaging demonstrated a hemorrhagic component of the right occipital lobe lesion [Figure 1d].

Surgical core biopsy

A needle core biopsy was obtained of the right occipital lesion, and intraoperative frozen pathology was thought to be consistent with a lymphoma. Formal pathology, however, only showed an intense inflammatory process [Figure 2a and b] comprised foamy macrophages and T-cells with scattered small B-cells. These cells were CD3 [Figure 2c], CD163, Iba1, and CD68 positive. B cell immunohistochemistry was scantly positive [Figure 2d]. The T-cell population was found to be composed of more CD4+ than CD8+ cells.

Postoperatively, he was started on high-dose dexamethasone. However, this was discontinued once the formal pathology was available. A follow-up brain MRI after 1 month demonstrated a decrease in the size of all enhancing lesions. MRI of the total spine was without evidence of disease. Dexamethasone was subsequently tapered off given initial concern for sentinel lymphomatous lesions.

CSF studies, ordered 2 months after the patient's biopsy, were unremarkable for autoimmune, bacterial, viral, fungal, parasitic, or inflammatory etiologies. CSF flow cytometry was limited by the low cellularity of the specimen but revealed a predominance of CD5+ T cells. Repeat MRI brain off of corticosteroids demonstrated an interval increase in size and conspicuity of all previously observed enhancing lesions, and the decision was made to perform an excisional biopsy of the right occipital lesion.

Surgical excisional biopsy

The patient was brought to the operating room for excisional biopsy of the right occipital lesion. He was positioned supine

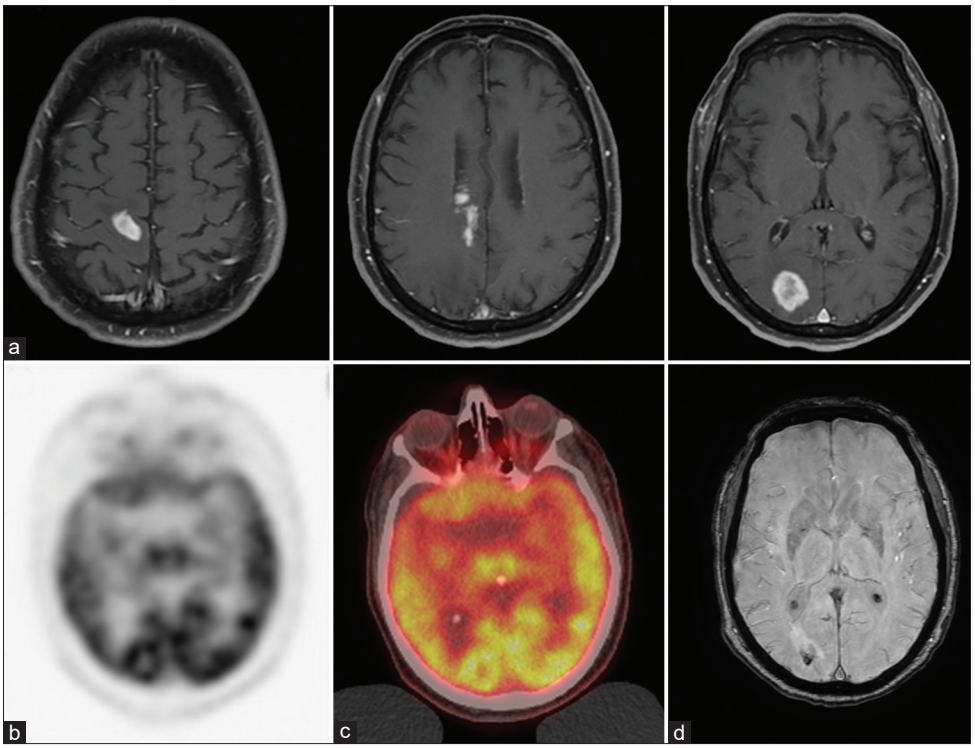

Figure 1: Initial pre-operative radiographic appearance of mass lesion. (a) Pre-operative axial T1 MRI with contrast demonstrating contrast-enhancing lesions in the right occipital lobe, right precentral gyrus, and within the right periventricular region. (b) Axial PET imaging and (c) PET/CT demonstrating a hypermetabolic lesion in the right posterior occipital lobe. (d) Axial SWAN imaging demonstrates a hemorrhagic component of the right occipital lesion.

with his head placed in the Mayfield head holder. The field was prepped and draped, and an incision was made down to the bone. A burr hole was made, and a craniotomy was turned over the lesion as confirmed with image-guidance. There was a pale tan pink discoloration of the brain. Several biopsies were obtained, and then the lesion was resected under the microscope and sent for pathology.

Pathology

Further histological analysis demonstrated areas of macrophages/lymphocytes with markedly reactive astrocytes that showed quick transition to reactive less inflamed cortex. The lymphocytic population appeared small, but polymorphous, containing scattered plasma cells. There was marked perivascular inflammation but no fibrinoid necrosis. Flow cytometric and immunohistochemical workup failed to demonstrate a definitely clonal lymphocyte population. There was no evidence of demarcated myelin loss or a vasculitic process.

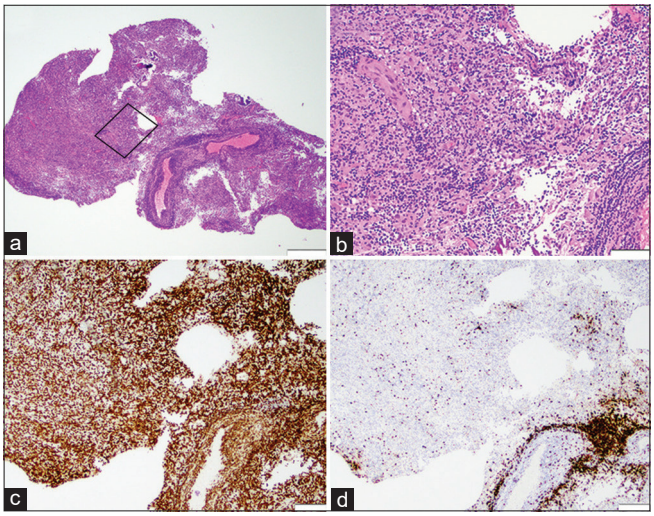

Figure 2: Histologic characterization of frozen biopsy sample. (a) ×2 and (b) ×10 H and E demonstrating brisk parenchymal and perivascular infiltrate of small lymphocytes in a background of marked reactive astrocytosis. (c) CD20 immunohistochemistry highlights many small B-cells in a predominantly perivascular distribution. (d) CD3 immunohistochemistry highlights numerous small T-cells. Scale bars: 500 μm for (a), 100 μm for (b), 200 μm for (c) and (d).

Post-operative course

Two weeks postoperatively, he had worsening behavioral outbursts, frequent mood fluctuations, poor comprehension, and worsening balance. Given the clinical deterioration, he was restarted on high-dose dexamethasone. The following MRI demonstrated post-surgical changes with significant decrease in the size of the right occipital lesion [Figure 3]. His steroids were changed to a Prednisone taper starting at 60 mg that was tapered to 20 mg over the course of 6 weeks. Upon follow-up, he was noted to have improved cognitive processing and improved left-sided weakness. Given the clinical and radiographic responsiveness to steroids in the absence of infectious, inflammatory, or neoplastic etiologies, the diagnosis of SLIPPERS was made.

DISCUSSION

In the two cases described by Armand *et al*., inflammatory ring-enhancing lesions were observed that were confined to the supratentorial space.[1] Both patients presented with enhancing supratentorial lesions and improved with steroid therapy. One presented with repeated seizure episodes and underwent a biopsy that revealed perivascular infiltrates of CD4/CD8 lymphocytes. The second patient presented with hemiparesis and headaches and underwent a biopsy that revealed infiltrative CD3 T lymphocytes. A third case was described by Horng *et al*. in 2017,[2] in a patient that presented with isolated cognitive dysfunction. Imaging demonstrated bilateral periventricular deep white matter, amygdala, and hippocampal lesions that demonstrated "peppery" appearing perivascular contrast enhancement. Brain biopsy demonstrated perivascular CD4/

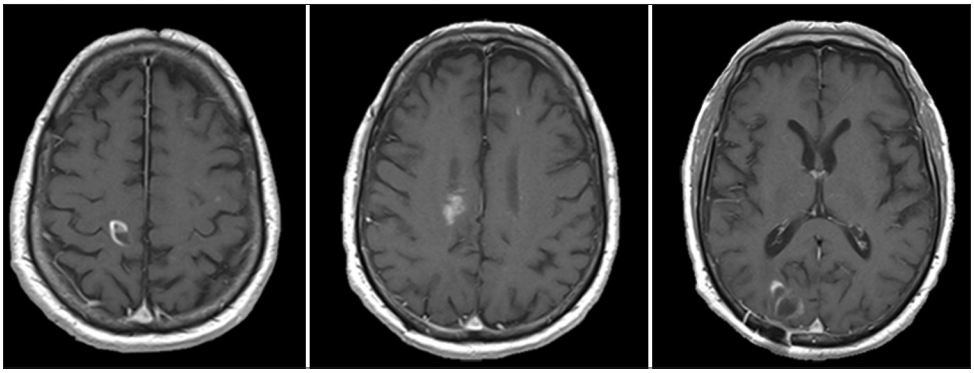

Figure 3: Post-operative MRI demonstrating decrease in size of enhancing lesions. Radiographic improvement in contrast-enhancing regions following surgical excision and prolonged high-dose dexamethasone therapy.

CD8 cells with reactive CD68 microglia. The rarity of this pathological phenomenon makes it an overlooked diagnosis in a patient who presents with focal neurologic deficits and ring-enhancing lesions, especially if they are responsive to steroids.

CONCLUSION

This case demonstrates similarities with previously described SLIPPERS cases while also expanding the pathological phenotype. Our patient is the first report of pathologic lesions showing hypermetabolism on PET/CT. SLIPPERS, as a mimic of primary CNS lymphoma with FDG avidity on PET imaging, is important for neurologists to recognize as it is highly steroid responsive. Further characterization of the cerebral perivascular inflammatory infiltrate is needed to guide diagnosis and whether patients that have disease that has relapsed or become refractory to steroids would respond to an anti-CD3 antibody in the event of corticosteroid failure or relapse.

Acknowledgments

The authors would like to thank our patient for allowing the details of his case to be shared.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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How to cite this article: Sudhakar V, Gersey Z, Polster SP, Mantica M, Zenonos G. Supratentorial lymphocytic inflammation with parenchymal perivascular enhancement responsive to steroids: A case report and literature review. Surg Neurol Int 2021;12:327.