

## Case report

# Comparison of costs and outcomes of patients presenting with a rare brainstem syndrome

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## ABSTRACT

In this case report we compare two patients presenting with similar symptoms of a brainstem syndrome including ataxia, dysarthria, and diplopia. Their MRIs showed hyperintense FLAIR signal changes with patchy areas of contrast enhancement within the brainstem particularly the pons and cerebellum. The broad differential diagnosis of this brainstem pathology included rhomboencephalitis, neurosarcoidosis, lymphoma, vasculitis, infection, and paraneoplastic or autoimmune process. Patient 1 had an extensive work up including CSF cytology, MRI brain spectroscopy, full body CT, cerebral angiogram, and ultimately brainstem biopsy. None of these studies were diagnostic of a specific etiology and total cost was \$176,069. After months of declining medical condition without a clear diagnosis, chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) was considered and the patient began steroid therapy resulting in clinical and radiographic improvement. Patient 2 had serum and CSF studies that were negative for infectious, paraneoplastic, and other inflammatory processes. The team diagnosed CLIPPERS and initiated steroid therapy within days resulting in dramatic clinical and radiographic resolution. The workup cost \$12,905. Comparison of these cases shows how early awareness of CLIPPERS and a directed diagnostic work up can limit invasive diagnostic testing, expedite initiation of effective therapy, improve patient outcomes, and reduce cost

## 1. Introduction

First described in 2010, chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) is a rare inflammatory syndrome affecting the brainstem and adjacent structures such as the cerebellum that has classic MRI findings of post-gadolinium enhancing punctate, curvilinear lesions in these areas and shows dramatic clinical and radiographic response to steroids. The diagnosis of CLIPPERS is based on clinical presentation, radiographic findings, response to steroids, and exclusion of other diagnoses with imaging, serum and CSF laboratory testing [1]. In this case report, we demonstrate that early recognition of this syndrome and a directed diagnostic approach may expedite treatment, improve patient outcomes, and limit unnecessary cost.

In June 2013, a 72 year old female presented with a one week history of dizziness, gait imbalance, bifrontal headache, blurred vision, diplopia, and dysarthria. On examination, she had mild dysarthria and impaired tandem gait. MRI brain (Fig. 1) showed right cerebellar peduncle and brainstem lesions with enhancement and mass effect. She

had an extensive work up including CSF cytology, MRI brain spectroscopy, full body CT, conventional cerebral angiogram, and ultimately brainstem biopsy. None of these studies aided in diagnosis of a specific etiology and ultimately cost \$176,429 (see Table 1 in supplementary data for complete diagnostic work up and associated costs). Without a certain diagnosis, her condition declined over the subsequent months and caused psychological distress to the patient and family. At this time, a diagnosis of CLIPPERS was considered and the patient began steroid therapy. There was clinical and radiographic improvement following this. The patient met all clinical, MRI, and neuropathology criteria for a definite diagnosis of CLIPPERS based on proposed criteria by Tobin et al. [2]

In April 2017, 59 year old inmate with a past medical history of diabetes, asthma, schizophrenia and hypertension presented to the intensive care unit of the same hospital with progressive symptoms of gait imbalance, dysphagia, and altered mental status. On the day of admission, he had a generalized tonic clonic seizure, become less responsive, and was intubated for airway protection. After the patient was extubated and weaned off sedation, he was noted on examination

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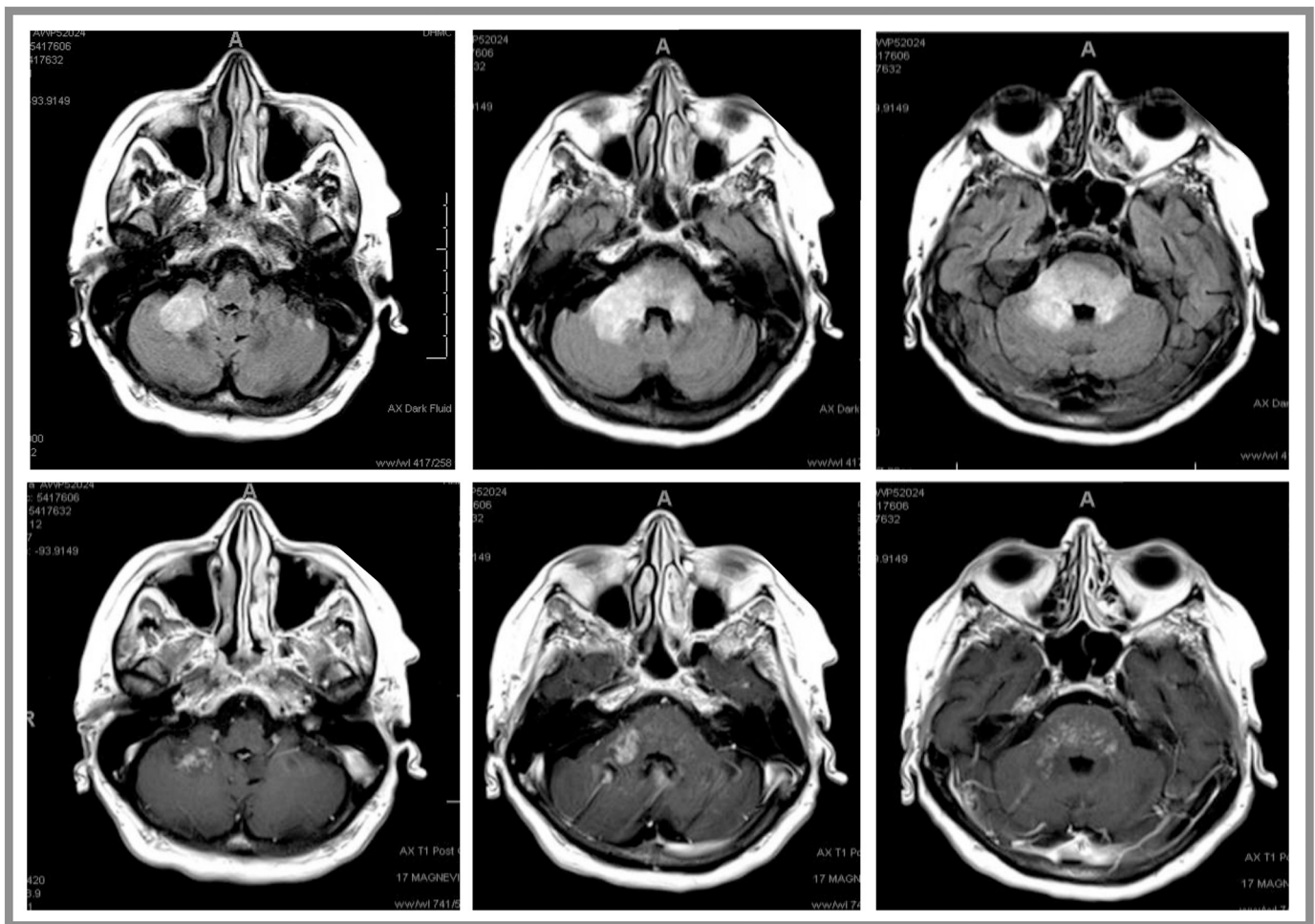
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**Fig. 1.** : Patient 1 axial FLARE and T1 post contrast MRI slices in June 2013<sup>a</sup>.  
<sup>a</sup>Top images are axial FLARE sequence, bottom are axial T1 post gadolinium enhancing.

to have dysarthria, impaired saccadic eye movements, left facial droop, ataxia on left finger to nose testing. MRI (Fig. 2) showed rhombencephalitis with patchy enhancement involving the lower brainstem and bilateral middle cerebellar peduncles. Serum and CSF studies were negative for infectious, paraneoplastic, and other inflammatory processes. The team diagnosed CLIPPERS and initiated steroid treatment within days of presentation resulting in dramatic clinical and radiographic resolution. The workup cost \$12,905 (see Table 2 in supplementary data for a complete diagnostic work up and associated costs). The patient did not have a brainstem biopsy for neuropathological diagnosis, but met all the clinical and MRI criteria for a probable diagnosis of CLIPPERS as proposed by Tobin et al. [2]

## 2. Discussion

CLIPPERS is a rare and treatable condition causing debilitating symptoms and classic MRI findings. The diagnosis of CLIPPERS remains challenging as there is no serum or CSF biomarker for the disease, histopathological findings are non-specific, and clinical findings may mimic other inflammatory and neoplastic disease. Therefore, when the

diagnosis is unclear because a patient does not meet the clinical, radiographic, and steroid response criteria for a diagnosis, more invasive and expensive testing such as conventional angiography and brainstem biopsy is warranted to rule out alternative diagnoses such as CNS vasculitis, infection, lymphoma, or glioma [3]. Patients 1 and 2 had clear criteria for CLIPPERS including subacute progressive ataxia and other brainstem symptoms; punctate enhancing lesions bilaterally within the pons and cerebellum; and absence of red flags such as infectious or systemic symptoms, markedly elevated CSF cell count and malignant cells, and lack of response to steroids. Ultimately, both of these patients received high dose steroid treatment, slowly tapered over time, which resulted in dramatic symptom improvement and resolution of enhancing MRI lesions. However, early recognition of CLIPPERS as a differential diagnosis and a focused diagnostic work up in the case of patient two lead to initiation of effective therapy within days as opposed to several months and reduced associated expenses by over \$150,000 as compared to patient one. Therefore, this case comparison demonstrates that early awareness of CLIPPERS as a differential diagnosis can have a significant impact on the treatment, patient outcomes, and expenses.

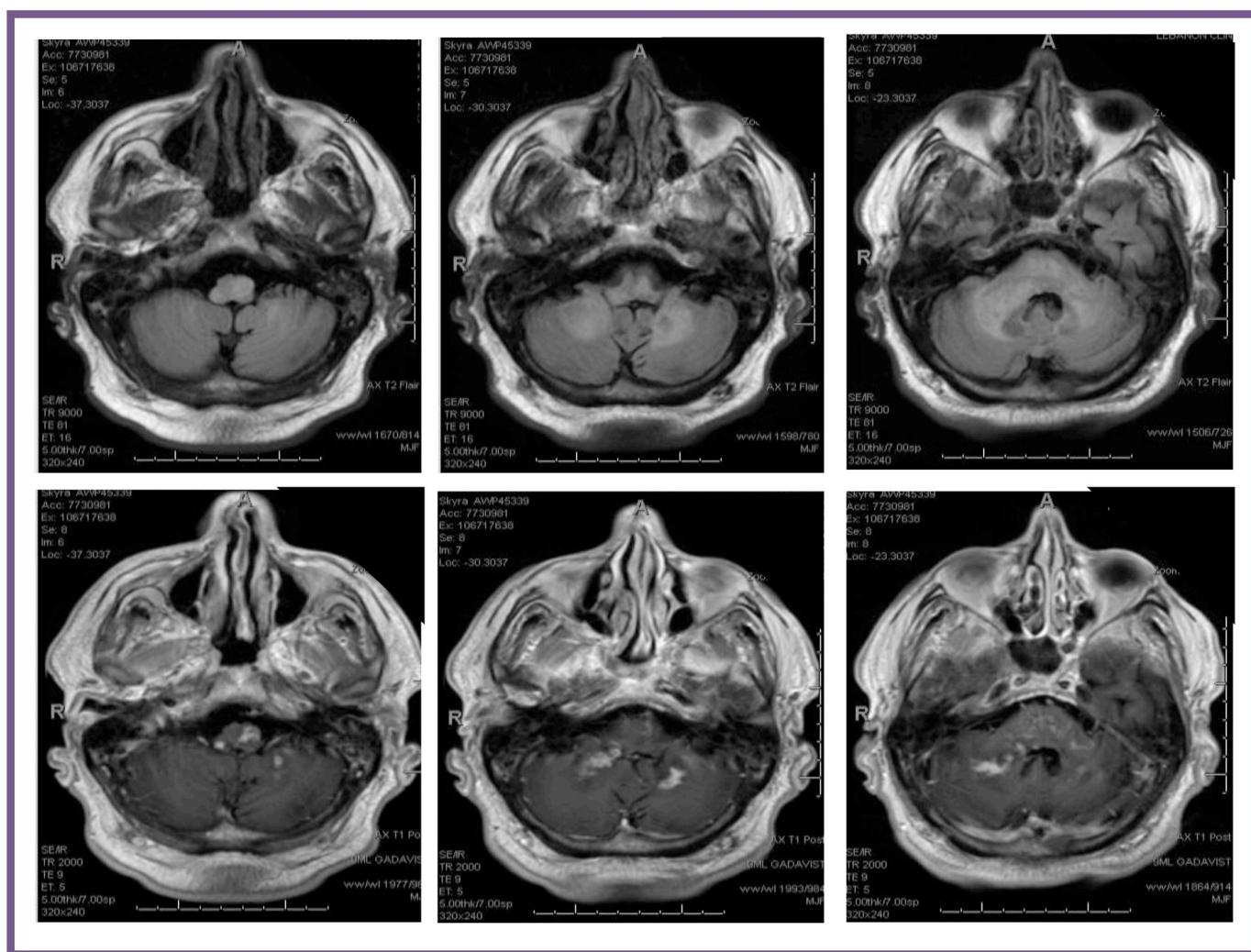


Fig. 2. Patient 2 axial FLARE and T1 post contrast MRI slices in April 2017<sup>a</sup>.

<sup>a</sup>Top images are axial FLARE sequence, bottom are axial T1 post gadolinium enhancing.

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## Declarations of interest

None.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jensci.2018.11.004>.

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