

CHRONIC LYMPHOCYTIC INFLAMMATION WITH PONTINE PERIVASCULAR ENHANCEMENT RESPONSIVE TO STEROIDS (CLIPPERS SYNDROME)-CASE REPORT OF A RARE DISORDER

Waseem Mehmood Nizamani,¹ Ameet Jesrani,² Mujtaba Khan,¹ Kalthoum Tlili,¹ Nader Al Khuraish,¹ Majid Shaikh²

¹ Department of Radiology, Prince Sultan Military Medical City Riyadh, Kingdom of Saudi Arabia (KSA).

² Department of Radiology, Sindh Institute of Urology and Transplantation (SIUT), Karachi, Pakistan.

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ABSTRACT

It is an uncommon central nervous system inflammatory syndrome characterized by infiltration of the brain by inflammatory cells. It is predominantly affecting the pons, with characteristic punctuate and curvilinear regions of post contrast enhancement on MRI. Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) was first described in 2010 by Pittock and colleagues. The patient described here is a 57-year-old man with no co morbid presented with ataxia, diplopia, hearing and taste disturbances. His GCS was significantly decreased so that the patient required intubation and was admitted in intensive care unit. Other accompanying symptoms of seizures and central pyrexia seen, which has not been previously described in case reports of CLIPPERS. The patient had a good outcome with intravenous glucocorticosteroids. The importance of recognition of atypical radiological findings and rapid treatment cannot be overemphasized in improving patient's long-term outcomes. Early recognition on MRI and radiological follow up are also important to optimize the treatment.

Keywords: Chronic Lymphocytic Inflammation, Pontine Perivascular Enhancement, Steroids, Clipper syndrome

Introduction

Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) was initially defined as a syndrome with similar clinical and neuroradiological findings by Pittock et al in 2010.¹ The underlying pathogenesis of CLIPPERS has not been fully elucidated; however the common symptoms and magnetic resonance imaging (MRI) findings include double vision, uncoordinated walking (gait ataxia), dysarthria and pontine lesions. Most Patients with CLIPPERS recovers significantly to glucocorticosteroids therapy.¹ The diagnosis of CLIPPERS tends to be exclusion because most of the patients often initially treated for stroke, encephalitis, multiple sclerosis or Wernicke's encephalo-

pathy.² CLIPPERS constitute a treatable condition and that patient may benefit from an early introduction of glucocorticosteroids may reduce the need for long-term immunosuppressant therapy, although others argue that CLIPPERS is by its nature relapsing remitting and therefore lifelong treatment is required.³⁻⁵ There are multiple cases of CLIPPERS which have been fatal.⁶ CLIPPERS may mimic CNS lymphoma, and several cases to CNS lymphoma have been reported as misdiagnosis of the initial presentation.⁷ New case of CLIPPERS is presented to increase acknowledgement of the condition so that in future patients may receive appropriate and effective treatment in a convenient time. Seizure and central pyrexia is less commonly described in the literature which is noticed in this patient.

Correspondence : Dr. Ameet Jesrani
Department of Radiology,
Sindh Institute of Urology and Transplantation (SIUT),
Karachi, Pakistan.
Email: ameer.jesrani@yahoo.com

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Case Report

A 57-year-old male presented to the emergency department with a complain of 10-days history of vomiting and feeling generally unwell. During this time, he had also developed dizziness, ataxia and diplopia. Patient also described taste and hearing disturbances. On examination, he had bilateral nystagmus and marked gait ataxia. Within 24 hrs admission, he had developed right-sided weakness and became less responsive and GCS decreased to 8 (E2, V3, M3), at which point the patient was shifted to the intensive care unit. On examination downgoing plantar reflexes and myoclonic jerks were noted.

A CT head on day 1 was done that showed no definite evidence of intracranial pathology. Elevated leucocytes count of $17 \times 10^9/L$ was noted in complete blood count. Cerebrospinal fluid taken on day 2 showed a leucocytes count of 96 (40% polymorphs and 60% lymphocytes). Culture, viral PCR and cryptococcal antigens were negative. All blood, urine, sputum and cerebrospinal fluid cultures and viral screens were negative. The patient was treated as a potential encephalitis and commenced amoxicillin, ceftriaxone and acyclovir.

Seizure activity was observed such as dilatation and constriction of pupils, tonic-clonic movements of lower limbs and spasticity of both upper and lower limbs. Seizures occurred on a daily basis and were terminated with intravenous administration of lorazepam as required. EEG confirmed seizure activity. Intravenous phenytoin was successfully used to prevent further seizures.

Although the initial CT head had been inconclusive, an MRI head was performed on day 3, which showed multiple patchy abnormal areas of contrast enhancement in pons, in temporal lobes and in right cerebellar hemisphere and CLIPPERS was suggested as a differential diagnosis. No significant perilesional edema was noted (Fig. 1).

Following this, treatment was commenced with methylprednisolone 1g intravenously. An almost immediate improvement was seen in the patient's clinical condition. Patient was alert and able to follow commands within several days, he had no further spasticity. A follow-up MRI was done which showed complete disappearance of abnormal areas of postcontrast enhancement in pontine and extra pontine areas (Fig. 2).

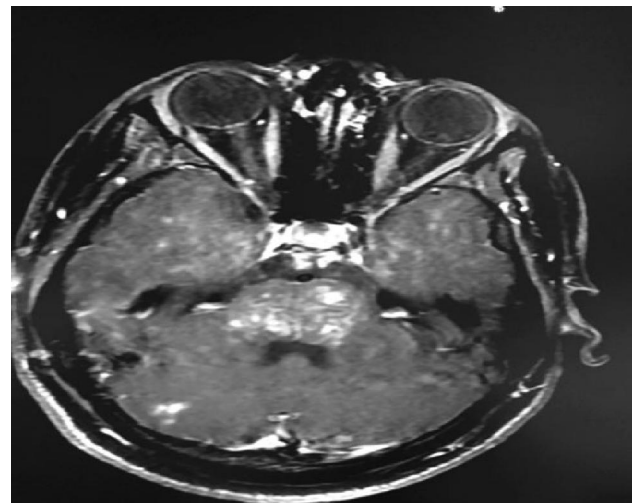
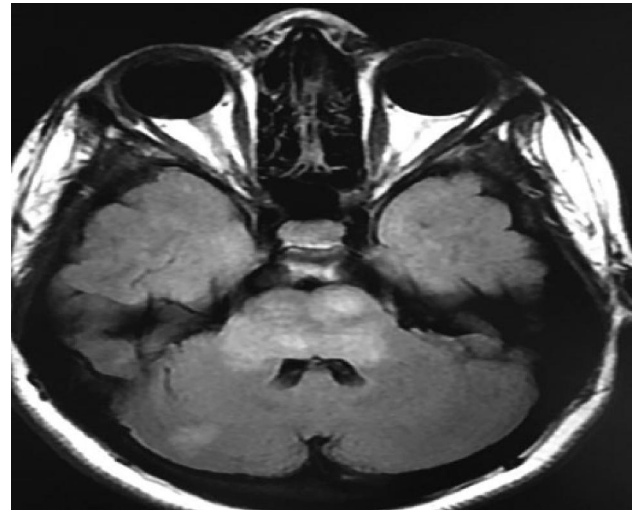


Figure 1: Pre and postcontrast axial images of MRI scan, showing patchy areas of abnormal enhancement in pons, temporal lobes and right cerebellar hemisphere

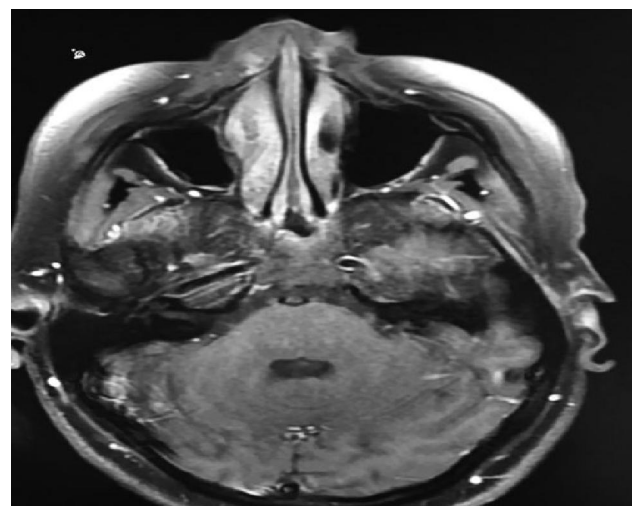


Figure 2: MRI axial postcontrast image show complete resolution of abnormally enhancing area in pons post treatment

Patient was shifted from the intensive care unit to the high-dependency unit, where his condition continued to improve. Intravenous methylprednisolone was shifted to oral prednisolone at 60 mg daily. This was reduced to 50 mg daily and the patient still continued to improve. Over the course of several months, oral steroids have been tapered down and discontinued. He continues to make progress, and it is thought that this will improve with ongoing rehab.

Discussion

The provisional diagnosis of CLIPPERS was made on day 3 after the exclusion of other differential diagnosis following the patient's MRI scan, and as well as failure to respond to other therapies.

Other case reports describe the history of allergies in patients with,⁸ pre-existing neurological conditions such as multiple sclerosis,⁹ or lymphoma;¹⁰ however, the previous complain of patients was lichen planus of the scalp.

Intravenous steroid therapy was successfully induced remission and it has been described in most of the literature. The evidence from the management of vasculitis, that the immunosuppression is recommended to continue for 2-5 years;^{11,12} however, this patient is not currently on immunosuppressive therapy. Patients remains under the care of a physician and is undergoing regular follow up.

The pathogenesis of CLIPPERS has so far has been an enigma. Cerebrospinal fluid analysis usually reveals increased protein levels, the absence of pleocytosis, contrast-enhancing MRI lesions and clinical good response to steroids suggest an immune-mediated pathogenesis of CLIPPERS. Pathologic studies (brain biopsy and a limited number of post-mortem examinations) have shown T-cell infiltration (predominance of CD4 cell) of the brainstem, with the pons being the mostly affected. On post-mortem, lesions were seen at different stages of evolution, suggesting a relapsing - remitting disease.¹³ Epstein-Barr virus also seen in several cases, one of them progressed to intracranial lymphoma. Some of the authors have hypothesized that CLIPPERS may be a pre-lymphoma condition and have emphasized the importance of continued follow-up to monitor long-term outcomes.¹⁴ The manifestation of bipolar disorder involving the

cerebral white matter, which may also cause seizure-like activity in the initial stage of the disease. However the mentioned lesions were located predominantly in the pons, brachium pontis, and cerebellum. Diffuse white matter may be involved in CLIPPERS in a recent study.¹⁵ Close attention should be paid to the clinical manifestations of lesions in other cerebral regions.

Conclusion

CLIPPERS is an immune mediated inflammatory disorder of the brainstem, which is increasingly being reported and new as well as less common features are still being described. Successful treatment of CLIPPERS involves the intravenous steroid use followed by maintenance dose. However, because of the rarity of CLIPPERS the other causes should be ruled out. MRI scan with and without contrast in this patient should be reviewed by specialized neuroradiologist with unusual clinical features or less-common radiological findings involving the pons. Most of the patients with CLIPPERS respond positively within five days, it may be worth trialing in patients with atypical neurological symptoms and radiological appearances, particularly if they are as unwell as the patient described above.

Conflict of Interest: None

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