Learning objectives

- To understand the imaging features of CLIPPERS
- How imaging influences the management and treatment response in CLIPPERS
Background

CLIPPERS is a rare inflammatory disorder primarily involving the brainstem. The disease shows clinical and radiological response to corticosteroids. It is often encountered in older males. The clinical presentation is quite variable and can include ataxia, diplopia, facial parasthesias, nystagmus and in few cases spastic paralysis. Laboratory findings are nonspecific, and no diagnostic marker is available for this disease. Elevated serum IgE and CSF protein are usually found. Biopsy of the lesion reveals diffuse lymphocytic infiltration of the brain parenchyma. There is usually no myelin loss in contrast to major demyelinating disorders like multiple sclerosis (MS) and Neuromyelitis Optica (NMO). The predominant cell types encountered are CD3 T lymphocytes. The disease usually shows good response to IV Methylprednisolone, however oral dexamethasone and cyclophosphamide have also been shown to be effective.\(^1,2\)

There is currently a proposed diagnostic criterion for CLIPPERS which includes a combination of clinical, neuropathological and MRI findings. Patients that satisfy all the criteria are considered to have a definite diagnosis, while those without neuropathological findings can only have a probable diagnosis of CLIPPERS.\(^3\)

Case

A 58-year-old gentleman presented to the Emergency Department with gait disturbance lasting for over two years associated with intermittent attacks of vertigo, facial paresthesia and hearing loss. He had no other significant history. On examination, he had a high stepping gait, dysdiadochokinesia, hyperreflexia and upgoing plantar reflexes in the lower limbs. He had an MRI of the brain for further evaluation. A Lumbar Puncture (LP) was performed which showed low counts of WCCs and no oligoclonal bands. NMO and MOG testing were negative. Biopsy of the lesion was not performed due to patient preference.

He was commenced on IV methylprednisolone as an inpatient and discharged on oral prednisolone. Imaging was performed after 2 months of commencement of steroids which resulted in improvement of the patient's symptoms and the size of the lesion on MRI. Steroids were ceased 4 months since symptom commencement. Repeat imaging was performed 6 months after symptom commencement (2 months after ceasing steroids) which showed a progressive increase in size of the pontine lesion.

He was recommenced on high dose steroids and imaging was performed at 12 months post symptom commencement (6 months after the previous MRI) which showed a near complete resolution of symptoms and the pontine lesion on MRI.
Imaging findings OR Procedure details

On initial imaging, T2 and FLAIR images demonstrated a longitudinal hyperintense lesion in the mid pons extending to the medulla and patchy enhancement in the left midbrain. There was restricted diffusion on DWI extending bilaterally involving the cerebellar peduncles. Post contrast T1 w images showed focal areas of enhancement. (Fig 1 and 2)

Follow up imaging in 2 months demonstrated a significant improvement in the T2 signal in the medulla extending into the cerebellar peduncles with mild residual T2 signal in the left middle, inferior cerebellar peduncles and left aspect of the medulla. There was also improvement in patchy enhancement.(Fig 3)

Further imaging performed in six months showed an interval increase in the size of the pontine lesion, hence patient was commenced on long term high dose corticosteroids. (Fig 4) At 12 months, near total interval resolution of signal changes in the left side of the pons was seen with remaining mild residual stippled enhancement. (Fig 5)

Discussion

After the diagnosis of CLIPPERs is made, patients are usually commenced on IV methylprednisolone 1g for 5 days followed by oral corticosteroids. Patients often experience improvement in symptoms at day 2-4 following IV methylprednisolone. Long term immunosuppression is required to prevent relapse in patients.

In our case, the patient responded well to steroids for the first two months. Since steroids were ceased at the four month mark due to improvement in the patient's symptoms, the patient experienced worsening of his symptoms over the next two months and MRI showed worsening of the patient's pontine lesion. This is a common theme seen in literature, where immunosuppressive therapy is ceased, and the patient experiences a worsening of symptoms.

There is no consensus in literature regarding how long steroids must be continued. Patients almost always relapse after ceasing corticosteroids. The time to relapse varies between 2 weeks to 10 months. Steroids and/or other immunosuppressive agents like azathioprine and methotrexate were used for many years to maintain suppression.4,5
Fig. 2: Sagittal T2WI (a) shows a patchy hyperintense lesion in the dorsal pons. This lesion also shows stippled gadolinium enhancement (b)

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Fig. 4: MRI performed at 2 months from symptom onset. The lesion has reduced in size as seen on T2WI (a), FLAIR (b) with decreased enhancement on postcontrast sequence suggestive of improvement (c).

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**Fig. 3:** Imaging at 6 months (2 months after ceasing steroids) shows increase in size of lesion as seen on T1 WI (a), T2 WI (B), FLAIR (c) and starts showing enhancement again on post contrast (d) imaging.

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Fig. 5: Imaging at 12 months post symptom onset. The patient was put on oral steroids for 6 months. T1 WI (a), T2 (b), FLAIR (c) show complete resolution of high signal and on post contrast (d) imaging minor residual stippled enhancement is present.

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Conclusion

- CLIPPERS is a subacute disorder of the CNS which shows rapid clinical and radiological response to steroids.

- The MRI findings in this disease are quite characteristic and often guide management in the absence of neuropathological findings.
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References


