

BEYOND THE PONS: LONG TERM FOLLOW-UP OF TWO CASES WITH TYPICAL AND ATYPICAL CHRONIC LYMPHOCYTIC INFLAMMATION WITH PONTINE PERIVASCULAR ENHANCEMENT RESPONSIVE TO STEROIDS (CLIPPERS)

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Background: CLIPPERS is a recently described and increasingly recognized inflammatory disorder of the central nervous system (CNS) characterized by recurrent brainstem symptoms and a typical appearance on brain imaging with punctate foci of contrast enhancement, usually peppering the pons (1).

Objective:

We report two cases of CLIPPERS patients presenting with typical and atypical MRI findings and long term follow up.

Subject 1

A 71 year old man was admitted in our Department in 2013 for sub-acute onset of gait instability. Neurological examination showed ataxia, right brachioradial weakness, dysphonia, and lower right facial nerve deficit.

3T brain magnetic resonance imaging (MRI) revealed an extensive lesion hyperintense in FLAIR involving the brainstem, extending until the left internal capsule with an irregular uptake of gadolinium and a striking pattern of a perivascular distribution. The spectroscopy was normal (fig. 1).

Subject 2

A 65 year old woman was admitted in 2009 for sub-acute onset of confusion, verbal expression difficulties and decrease in visual acuity in the right eye.

A 1,5 T brain MRI showed a large lesion involving the left cerebral peduncle, the midbrain-diencephalic junction, the left thalamus, the left basal ganglia and the left optic tract, with patchy contrast enhancement; the spectroscopy was normal.

Methods:

- Lumbar punctures: normal, with negative cultural and virological tests, no oligoclonal bands and no neoplastic cells.
- Laboratory screening: autoimmune, virological and bacteriological investigations were normal, except for an already known HCV positivity in subject 1
- Spinal Cord MRI, contrast-enhanced chest and abdominal TC, total body 18-FDG-PET: normal
- Cerebral angiography (only subject 2): normal.

Clinical management and follow up:

- Five days methylprednisolone (1 g/die): resolution of the neurological symptoms and improvement of MRI alterations.
- Long term radiological and clinical follow up (respectively of 3 and 7 years): every attempt to reduce corticosteroids until withdrawal led to reappearance of symptoms and relapse of brain lesions on MRI.
- After each relapse a new high-dose corticosteroids cycle resulted in subsequent clinical and radiological benefit (fig. 2).

Discussion and conclusions

We describe two cases of CLIPPERS, the former with all the typical characteristics of the disease, and the second one with an atypical brain distribution of lesions sparing the pons, but presenting the classical and core diagnostic feature of steroids responsiveness, due to the putative inflammatory aetiopathogenesis of CLIPPERS (2).

CLIPPERS is a rare disease characterized by a spectrum of possible lesions not only localized in pons, but which may involve all the CNS with a pattern of perivascular distribution. Follow up must be very accurate and steroids reduction must be careful to prevent relapses (3).

Fig. 1: 3 T brain MRI scan with Gadolinium of patient 1 at initial presentation of symptoms (08/2013).

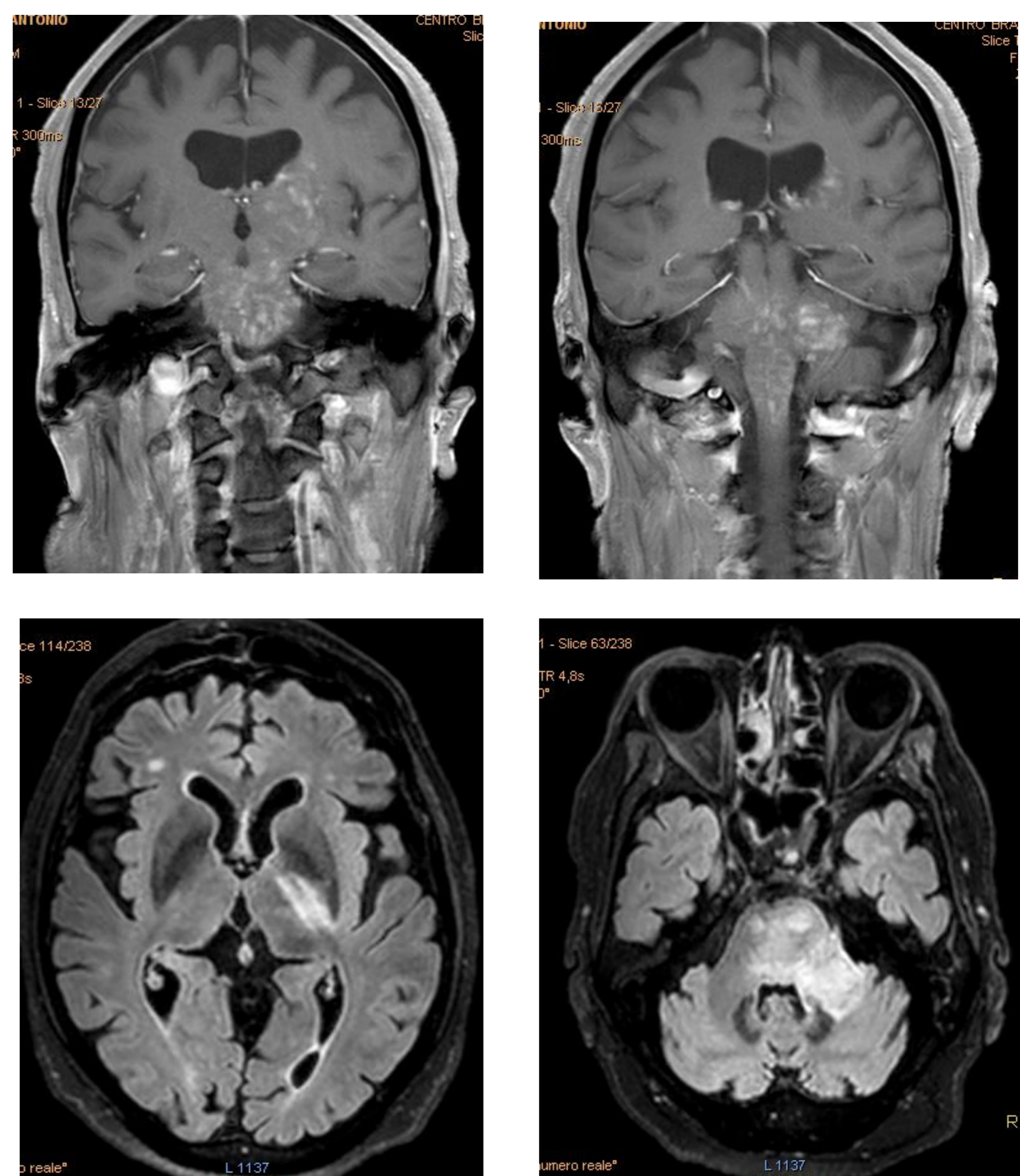
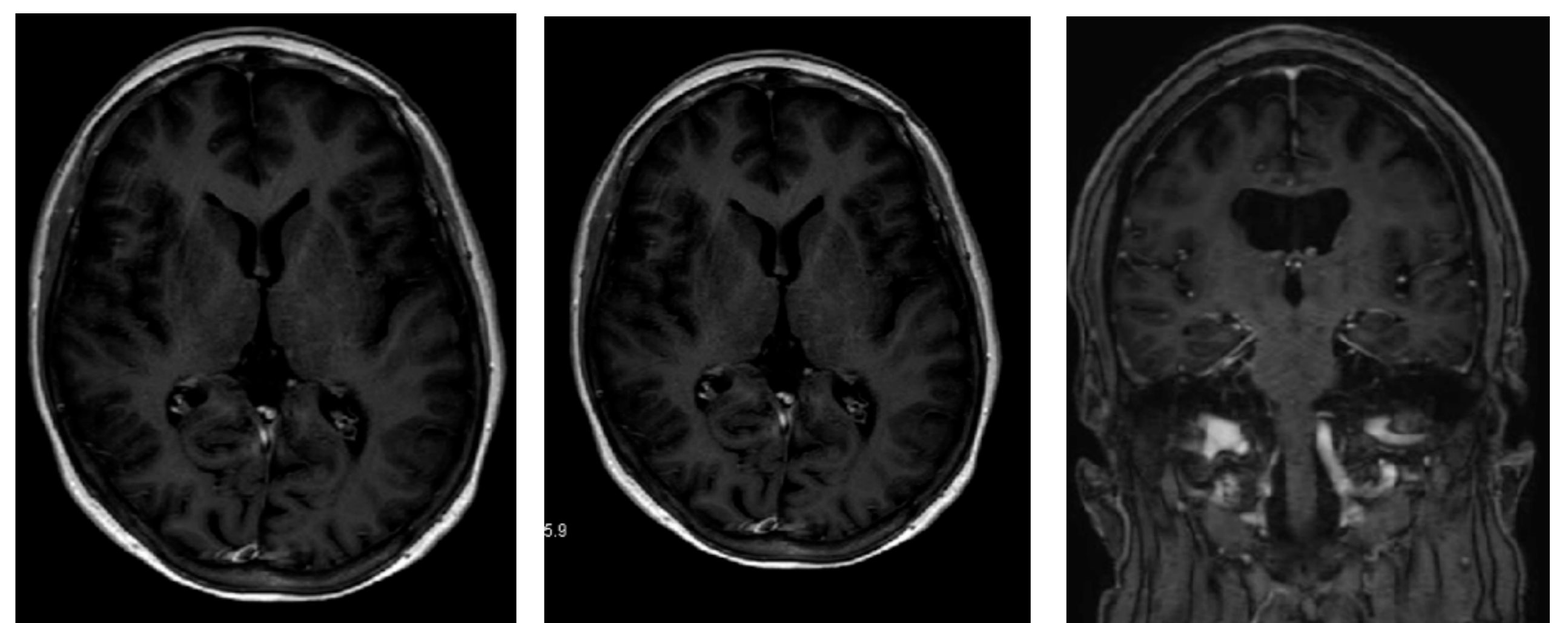


Fig. 2: 1,5 T brain MRI scan with Gadolinium of patient 2 after steroids therapy for a relapse (05/2015) and 3 T brain MRI scan during follow up of patient 1 (01/2016).



References

1. Pittock SJ, et al. Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS). *Brain* 2010;133(9):2626-34.
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3. Taieb G, et al. Long-term outcomes of CLIPPERS (chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids) in a consecutive series of 12 patients. *Arch Neurol.* 2012;69(7):847-55.