Reviewer’s report

Title: Monitoring Chronic Hepatitis B infection in Chronic Lymphocytic Inflammation with Pontine Perivascular Enhancement Responsive to Steroids (CLIPPERS)

Version: 3 Date: 21 October 2015

Reviewer: Guillaume Taieb

Which of the following best describes what type of case report this is?: New associations or variations in disease processes

Do you believe the case report is authentic?:
Yes, however I don’t understand why the patient had anti-HBe antibodies together with elevated HBV viral load. The HBV is a mutant?
The authors did not mention the HBs antigen / anti-HBs status. Why?
Because radiological features of CLIPPERS could be found in vasculitis, the results of MRA, or cerebral angiography should be added, especially in the setting of chronic HBV with the risk of polyarteritis nodosa. The characteristics punctate and curvilinear enhancements are not well seen on the figure. Perhaps you should add another MRI sections.

Do you have any ethical concerns?:
Yes.

Is the Abstract representative of the case presented?:
Yes

Does the Introduction explain the relevance of the case to the medical literature?:
Not really. The diagnosis of CLIPPERS is very complicate.
Several diseases could show radiological features of CLIPPERS: glioma, primary CNS lymphoma, lymphomatoid granulomatosis, mantle cell lymphoma, primary CNS vasculitis, multiple sclerosis and more recently MOG-opathy.
Therefore radiological features of CLIPPERS (i.e. brainstem punctate and curvilinear gadolinium enhancement which could spread rostrally up to juxta-cortical areas, and caudally up to the conus) are not really specific. In addition, except glioma, all these diseases respond well to corticosteroid therapy, and could show lymphocytic perivascular infiltrates on brain biopsy. In absence of steroid therapy (or below 20 mg/d of steroids), the natural history of
CLIPPERS is a relapsing remitting course including relapses that remain concentrate in the pons and/or middle cerebellar peduncles. For these reasons, the diagnosis in the present case is not certain.

References:


Does the article report relevant patient information?: Yes

Does the article report relevant physical examination findings?: Yes

Does the article report important dates and times in this case?: Yes

Does the article report the diagnostic assessments?: No

Does the article report the types of intervention?: Yes

Does the article report a summary of the clinical course of all follow-up visits?: Yes

If any information is missing from the reporting, please detail it here.: The authors present a case of chronic HBV complicated by clinical and radiological features of CLIPPERS.

I don’t understand why the patient had anti-HBe antibodies together with elevated HBV viral load. The HBV is a mutant?

The authors did not mention the HBs antigen / anti-HBs status. Why?

What are the serum alpha-fetoprotein levels?

What is the hepatitis D status?

Because radiological features of CLIPPERS could be found in vasculitis, the results of MRA, or cerebral angiography should be added, especially in the setting of chronic HBV with the risk of polyarteritis nodosa.

In addition, because CLIPPERS is suspected, it could be interesting to add the
dosage of IgE levels and anti-MOG antibody.
The characteristics punctate and curvilinear enhancements are not well seen on the figure. Perhaps you should add another MRI sections.

**Is the interpretation (discussion and conclusion) well balanced and supported by the case presented?**

In the discussion: if the HBV viral load is correlated with the presence of Treg, I don’t understand why this situation favoured the emergence of CLIPPERS, which is probably a Th1/Th17 polarization disorder.
In addition chronic hepatitis B seems to be associated with a higher risk to develop a primary CNS lymphoma.

**Does the case represent a useful contribution to the medical literature?**

Yes, but the case is poorly discussed.

**Was written informed consent to publish this case obtained?**: Yes

**Is the anonymity of the patient protected?**:

Yes

**Additional comments to authors?**:

No

**Level of interest**: An article of importance in its field

**Quality of written English**: Needs some language corrections before being published

**Declaration of competing interests**: I declare that I have no competing interests