



Letter to Editor: Is Hemorrhagic Demyelinating Lesions of Central Nervous System a Spectrum?



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Running Title Hemorrhagic Demyelinating Lesions in CNS

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Highlights

- In recent years, there have been reports of hemorrhage in other demyelinating diseases of the CNS. A look at these cases can help us understand the less known symptoms of the demyelinating diseases of the CNS.
- HDLC can be defined as hemorrhagic lesions that have a hemorrhagic mechanism due to CNS tissue demyelination.
- Recognition of HDLC as a separate spectrum disorder makes it necessary to investigate the immunological basis of this new entity.

Dear Editor,

A Small number of demyelinating diseases of the central nervous system (CNS) are associated with hemorrhage in the neural tissue, among which, the most well-recognized is acute hemorrhagic leukoencephalitis (AHL). There have been reports of hemorrhage in other demyelinating diseases of the CNS. Investigating these cases can help us understand the less recognized

symptoms of the demyelinating diseases of the CNS. hemorrhagic demyelinating lesions of CNS (HDLC) can be defined as per the following criteria: 1. Hemorrhage should be definitely revealed by imaging; 2. Hemorrhagic lesions must have a hemorrhagic mechanism due to CNS tissue demyelination; 3. Other possible differential diagnoses such as autoimmune encephalitis, vasculitis, and vasculopathy should be evaluated and ruled out.

This definition can provide a clear and pathological understanding of these lesions. In addition, the recogni-

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tion of HDLC as a separate spectrum disorder necessitates investigating the immunological basis of this new entity. A comprehensive literature research has been conducted on PubMed, Scopus, Web of Science, and Google Scholar in this regard; however, there were few cases compatible with HDLC definition. Although the reports consistent with this definition are scarce, attention must be paid to better understand and consequently better treat this rare symptom.

Multiple Sclerosis

Multiple sclerosis (MS) is the most recognized CNS demyelinating disease. However, there are very few reports of hemorrhage in this disease; to our knowledge, some of those reports meet the definition of HDLC. The studied patient was a 43-year-old woman who referred to the emergency department with a decreased consciousness and seizure. In magnetic resonance imaging (MRI), besides a tumefactive hemorrhagic lesion, there were periventricular plaques. Moreover, tumefactive lesion biopsy revealed a tumefactive hemorrhagic demyelinating lesion. The patient responded well to steroid treatment [1].

As mentioned above, there are limited reports of hemorrhage in MS disease. The demyelination mechanism is irresponsible for such hemorrhage; the use of anticoagulants, tobacco [2], MS medicines [3], or some vascular lesions [4] are associated with it. However, in one of these cases, an MS patient treated with natalizumab had a hemorrhage in the former site of the tumefactive demyelinating lesion. The authors correctly referred to the role of natalizumab in preventing angiogenesis; thus, facilitating hemorrhage, since hemorrhage occurred in the former site of the tumefactive lesion, can highlight the role of demyelination mechanism in causing this hemorrhage [5].

Myelitis

Another CNS demyelinating disease is the involvement of the spinal cord by the demyelinating process, recognized as isolated transverse myelitis. Hemorrhage in myelitis caused by the demyelinating mechanism is quite rare; spinal cord hemorrhage mainly occurs due to tumors, vascular malformations, or infections like varicella-zoster virus (VZV). In a case report, a 33-year-old Japanese woman was discussed who presented with paraparesis. A longitudinal extensive transverse myelitis (LETM) with hemorrhage was observed in her MRI. There was no pathology sample available. Furthermore, all possible causes in this patient were examined and re-

jected; therefore, the most important cause was the demyelinating involvement of the spinal cord [6].

Acute Hemorrhagic Leukoencephalitis

As mentioned above, AHL is the most well-recognized CNS demyelinating disease, diagnosed by hemorrhage. It is a rare, yet deadly disease, which is a subset of acute disseminated encephalomyelitis (ADEM). Unlike that, AHL is most commonly observed in adults. It is clinically recognized with a rapid progressive trend that can lead to death within a few days. In scanning, the disease is diagnosed with large bilateral lesions and edematous with hemorrhage [7].

Acute Necrotizing Encephalopathy

This rare disease was first introduced by Mizuguchi et al. in 1995 [8]. Clinically, the disease is also recognized with a rapidly progressive and fatal trend. Unlike AHL, it is mainly observed in children. The majority of reported cases are related to infectious diseases, especially influenza. Radiologically, bilateral hemorrhagic lesions may also be observed in the white matter of the cerebellum, brain stem, and thalamus [9, 10]. Its primary distinguishing feature from AHL is the lack of demyelinating characteristics in biopsy [8]. The lack of demyelination in the pathology contradicts our definition of HDLC; however, concerning that, it is similar to AHL in terms of progression and radiological features, it was reviewed here, and it needs further attention.

Conclusion

In addition to AHL, HDLC can occur in other CNS demyelination diseases like MS or myelitis. Thus, HDLC should be considered as a spectrum disorder. Although the number of reported cases in this regard is minimal, taking into account the increased incidence of CNS demyelination worldwide, calls for paying more attention to this issue.

Ethical Considerations

Compliance with ethical guidelines

All the study procedures complied with the ethical guidelines of the Declaration of Helsinki 2013.

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Conflict of interest

There are no conflicts of interests to be declared.

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