Hemophagocytic Lymphohistiocytosis (HLH) with Unusual Trigger

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Sir,

We read with much interest the article by Babu Raj et al., published in the recent (March, 2018) issue of your journal[1] but at the same time would like to make the following comments, which would benefit the general readers of JAPI.

The authors describe a 34 year old male with subarachnoid hemorrhage and left cerebellar contusion following an assault. He developed fever, skin rash, pancytopenia, splenomegaly, hepatitis, hypertriglyceridemia, hyperferritemia and evidence of hemophagocytes in the bone marrow. A diagnosis of Hemophagocytic Lymphohistiocytosis (HLH) was made and the patient was successfully managed with appropriate therapy.

Firstly, the authors state "Unusual trigger" for his HLH and though they suggest Epstein-Barr virus (although tested negative) and Phenytoin as the possible triggers they do not define any! We do agree with the authors partially. The patient had dysuria and his urine culture grew Enterococcus faecalis. Enterococcus being already known as a trigger for HLH,[2] the authors should have considered it as the most plausible of all probable triggers in this case.

Secondly, a possibility of parvoviral infection was considered on the basis of erythroblasts showing "large basophilic intranuclear inclusions and cytoplasmic budding" but the typical inclusion bodies seen in parvoviral infection are eosinophillic.[3] Moreover, with a strong suspicion of parvoviral infection they should have considered doing PCR based tests in this case to confirm the diagnosis when parvovirus IgM came to be negative. As the interpretation of the serological tests for parvovirus are often complicated by false negative results.[4]

Thirdly, the authors have stated to use the "HLH-2004"[5] criteria for diagnosis of HLH in the index patient but the aforementioned criteria requires a hemoglobin (Hb) of < 9 gm/dl and an absolute neutrophil count (ANC) of <1000/mm^3 to diagnose anemia and leucopenia respectively. But the patient had an Hb of 9.1 gm/dl and a total leucocyte count of 1600/mm^3 (ANC not mentioned).

Fourthly, the patients abnormal CSF findings were attributed to "a diagnosis of SAH / ? Partially treated bacterial meningitis" but HLH with CNS involvement can also give rise to a similar picture.[6] An MRI of the brain with gadolinium could have helped in this case.

Though it is not mentioned we presume that such a patient of assault with subarachnoid hemorrhage may have received blood component therapy. This is of special interest in this case as the patient had fever, skin erosion and cytopenias along with hemophagocytes in the bone marrow. All of these could be seen in transfusion-associated graft-versus-host-disease (TA-GVHD) which is very difficult to differentiate from HLH without a skin biopsy.[7]

References

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Reply from Author

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Sir,

I would also want to thank Anirban Mandal and Puneet Kaur Sahi for reading the case report and raising questions.

Firstly, we have not mentioned EBV as a probable cause, its Parvovirus as a probable cause.[1] Enterococcus is a rare cause for HLH and in the case cited, occurred in a patient with AML post allogeneic transplant and was associated with bacteremia.[2] Here, in our patient, a patient had Enterococcus growth in urine culture, but blood culture was sterile.

Secondly, parvovirus has been associated with multiple inclusion bodies. There are many case reports wherein Patients with Parvovirus infections whose inclusion bodies are basophilic.[3] I would completely agree with them that PCR should have been done for this Patient, we also wanted to do a PCR for Parvovirus but could not be done due to logistic issues.

Thirdly, we have not stated that we have used "HLH -2004" criteria for diagnosis. We have used 2009 Diagnostic criteria for diagnosis.[1]

Fourthly, HLH with CNS involvement was not considered because we had done an MRI with gadolinium enhancement for this patient, which showed only a resolving SAH and it did not fit in with classical findings associated with CNS involvement in HLH.[4]

Finally, Patient did not receive any blood components, PRC was not required because Hemoglobin was never below 9 mg/dl. So the question of GVHD does not arise here.

References

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