Hemophagocytic Lymphohistiocytosis accompanying Still's Disease: a case report

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May 30, 2023

Introduction

Hemophagocytic lymphohistiocytosis (HLH) is a hyperinflammatory syndrome that is associated with a high mortality rate. HLH is characterized by hemophagocytosis and histiocytic proliferation (1). Primary HLH has a familial pattern and secondary HLH is reactive and also called macrophage activation syndrome (MAS). This type of HLH is usually acquired following autoimmune diseases, infection, and malignancy (2).

The prevalence of HLH is not completely measurable because the diagnosis of this disease is hard and there are other comorbid diseases at the time of diagnosis. In a study that was done in Sweden from 1987 to 2006, the prevalence of HLH was 1.5 per million (3).

The manifestations of HLH are fever and cytopenia. The diagnosis of HLH is made by clinical suspicion of physicians. The criteria for diagnosis of HLH include fever; splenomegaly; cytopenia (affecting at least two of three lineages in the peripheral blood); fasting triglyceride levels [?]3 mmol/L and/or fibrinogen level [?]1.5 g/L; serum ferritin level [?]500 ng/ml; CD25 level [?]2400 U/ml; decreased or absent natural killer (NK) cell activity; or hemophagocytosis in bone marrow, spleen, or lymph nodes (4).

Adult-onset Still's disease (AOSD) is an autoimmune disorder that can predispose patients to HLH. The co-incidence of AOSD and HLH is rare (5).

In this report, we present a woman with a co-incidence of AOSD and HLH.

Case presentation

A 36-year-old woman was referred to our hospital with chief complaints of fever and night sweeting. The patient mentioned that she had pain in the Interphalangeal joints from about 1.5 years ago, after receiving COVID-19 vaccine. She was referred to different physicians and oral corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs) were prescribed for her. She didn't have fever, night sweeting, pharyngitis symptoms, or skin rash at that time. She denied photosensitivity, malar rash, or Raynaud phenomenon. The patient had unwilling weight loss about 10 kilograms in less than 6 months.

On the first day of admission, the patient had pharyngitis, fever, red macular rashes in the trunk without face involvement (figure1), pain in knees and little small joints of the hands since two weeks before referring to us and the fever responded to NSAIDs first, but after a few days, the fever didn't respond to NSAIDs. There was no pain in back, pelvic, or chest. And also she didn't have dyspnea.

She was referred to another hospital and physicians prescribed antibiotic for her and infectious work-up was performed for her. She had anemia in evaluations and packed cell was prescribed for her. In that center, 2ME, wright, coombs wright, anti-nuclear antibodies (ANA), anti-double-stranded DNA (anti-ds-DNA),

anti-citrulinated peptide antibody (anti-CCP), human leukocyte antigen (HLA) B-27 were checked and all were negative. Also, blood culture was negative. All laboratory data are seen in table 1. The patient was referred to our hospital for more evaluations.

In our center, due to persistent fever, pharyngitis symptoms, cutaneous rashes, digital arthralgia, and negative serology tests, Still's disease was diagnosed for the patient. Also, rheumatologists were suspicious to Hemophagocytic Lymphohistiocytosis (HLH) and malignancy due to decreasing trends of blood cells. So, hematology consult was request for her. Hematologist requested bone marrow aspiration (BMA). The report of BMA confirmed HLH disease because hemophagocytosis was observed in her BMA specimen.

With this diagnosis, 4 milligrams of intravenous dexamethasone every 8 hours was prescribed for him and all blood parameters and blood ferritin had improving trends.

We were suspicious to malignancies and we requested CT scan with contrast. In CT scan we observed mediastinum, supraclavicular, and axillary lymphadenopathy. There were no significant findings in the CT scan. CT scans of other organs were normal.

The patient was discharged with a good condition, without any complaints, and with oral drugs (tab Dexamethasone 0.5 mg/daily, tab Cyclosporine 50mg/daily, tab Hydroxychloroquine 200 mg/daily).

Discussion

We presented a young female patient who had HLH secondary to AOSD. His clinical and laboratory findings included fever, arthralgia, salmon-colored rash, lymphadenopathy, negative ANA, negative rheumatoid factor. She had hemophagocytosis. So she had five out of the eight diagnostic criteria of HLH. Then, the patient was diagnosed with HLH followed by AOSD (6, 7).

Still's disease is an autoimmune disorder. Still's disease with adult onset (AOSD) has two ranges of presentation including 15-25 and 36-46 years of age (8). The etiology of this disease is not clear. Some factors including infections genetic factors, (viral or bacterial), and immune disorders are suggested (8).

AOSD is characterized by fever, non-suppurative pharyngitis, transient rash (salmon-colored, maculopapular, nonpruritic, and often observed during febrile episodes) involving the trunk and proximal extremities, arthralgia that commonly involving the wrists, ankles, knees, and elbows (8). Our case had fever, pharyngitis, rashes with trunk involvement, and arthralgia especially in phalanxes.

Laboratory findings in AOSD are similar to other autoimmune disorders. Common laboratory findings are elevated white blood cell (WBC) count, abnormal LFTs, and elevated levels of CRP, and ferritin. In this disease, RF and ANA are usually negative. For diagnosis of AOSD, physicians should exclude infections disorders, vasculitis, malignancies, and other connective tissue disorders (8). We were suspicious to AOSD but we also excluded malignancies and infections disorders by different evaluations of the patient.

Of the most serious complications of AOSD is HLH. AOSD and HLH have similar clinical findings and laboratory results. These similar features make a diagnostic challenge for physicians (9). HLH unlike to AOSD may have thrombocytopenia or leukopenia, and very high levels of triglyceride in serum (10). We observed significant elevation in LFT, LDH, Ferritin, CRP, WBC levels. Thrombocytopenia and anemia (low level of hemoglobin) were observed in the laboratory tests of our case. Laboratory and clinical findings accompanying with decreasing trends of lineage blood cells suspected us to diagnose AOSD + HLH in the patient.

We found high levels of serum ferritin in our case. It seems that a key to diagnosis AOSD is very high serum ferritin. Such a finding occurs in AOSD with HLH (11).

The treatment of HLH are corticosteroids and cyclosporine. Non- steroid anti inflammation drugs and corticosteroids were recommended for treatment of AOSD. We used a combination of these treatments for our patient and she responded to these treatments and was discharged with a good condition.

Conclusion

Diagnosis of HLH accompanying still's disease is important because it is rare and it may be misdiagnosed and can prone patients to mortality. The presence of fever, pharyngitis, arthralgia as clinical manifestations with high levels of blood inflammatory parameters including CRP, ferritin, and also increasing trends of lineage blood cell counts should suspect physicians to diagnose HLH + AOSD.

Ethics approval and consent to participate

Approval was not needed by the local Clinical Research Ethics Committee for case reports.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Conflict of interests

The authors declare that they have no competing interests.

Data availability statement

Data is available if requested

Funding

We received no funding.

Authors' contributions

AA conceived the idea to report the case. SB was responsible for data collection. FF and NB drafted the manuscript. SA and AA commented on the manuscript. All authors read and approved the final manuscript.

Acknowledgments

Not applicable.

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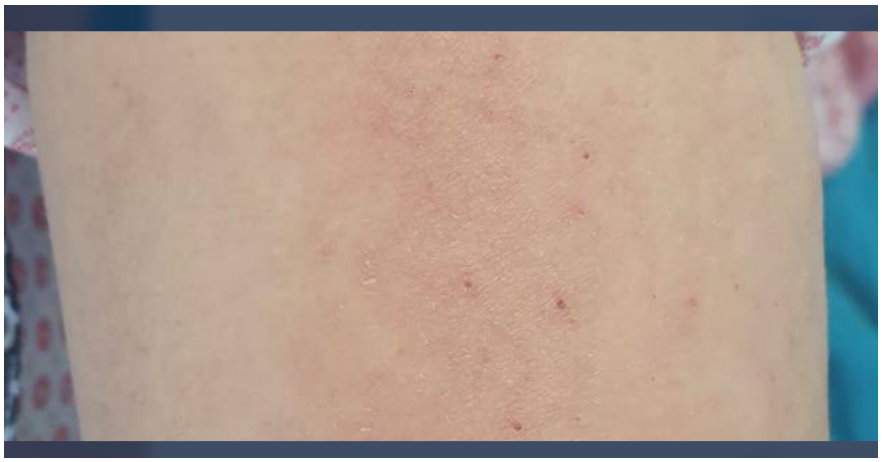

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