A Case Report of Hemophagocytic Lymphohistiocytosis (HLH)

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ABSTRACT

Hemophagocytic lymphohistiocytosis or HLH is a very rare underdiagnosed potentially fatal entity which frequently leads to multiorgan failure and death due to immune dysregulation. It can be either primary which is supposed to be an inherited disorder seen in infancy and childhood or secondary to infections, connective tissue disorders or malignancies. The disease manifestation is due to massive release of inflammatory cytokines (cytokine storm) into the circulation. The cytokines activate the macrophages which lead to phagocytosis of the hemopoietic cells including precursors leading to cytopenias. We report a case of Hemophagocytic Lymphohistiocytosis in a 36 year female presenting with fever, lymphadenopathy and pancytopenia due to Connective tissue disorder.

Background :

Haemophagocytic lymphohistiocytosis (HLH) was first reported by Scott and Robb-Smith in 1939. The disease is characterised by inappropriate and uncontrolled activation of the immune system, which results in excessive inflammation and tissue damage.[1] Common manifestations include prolonged fever, rash, hepatosplenomegaly, various cytopenias, hyperferritinaemia, hypertriglyceridaemia and hypofibrinogenaemia.[2] It is a great mimicker of common clinical diseases and remains a diagnostic challenge.

We report a 36 years / F, housewife, resident of Gondia, Maharashtra, who presented for low grade fever, easy fatigability, itching, along with weight loss since last 1 year. She had generalized lymphadenopathy, mild splenomegaly, a pruritic maculopapular skin rash. She was a known case of Hypothyroidism for the past one year on thyroxine supplementation. Her BMI was 14.33 kg/m2.

Her haemoglobin was 5.1 gm%, reticulocyte count of 1%, TLC 3800, platelet count 80,000/mm3, ESR 140 mm at the end of 1 hour, serum LDH 1662 IU/L, serum ferritin 3000 ng/ml, serum triglyceride levels 450 mgm%, ANA positive, ANCA negative. Abdominal ultrasonography showed mild

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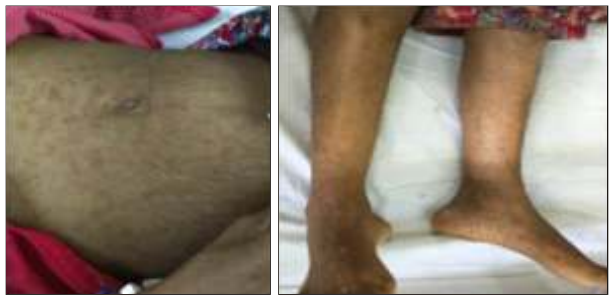
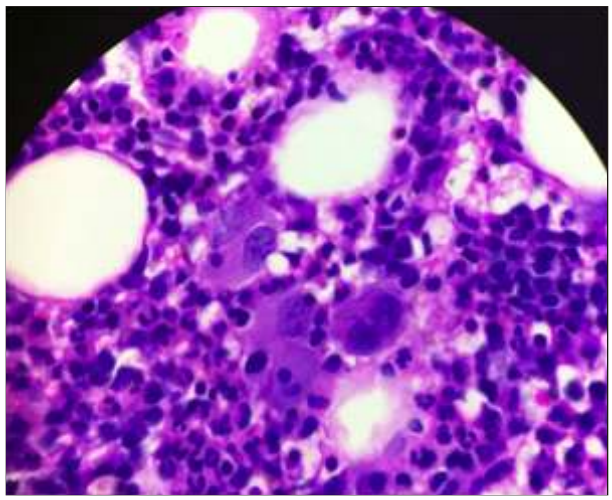


splenomegaly. Her bone marrow was Hypercellular with M:E ratio 4.5:1, normoblastic with moderate degree of dyserythropoeiesis. Myeloid hyperplasia with maturation upto neutrophils. Increase in Macrophages in marrow & some of them showed hemophagocytosis.



The patient was treated with Steroids, Hydroxychloroquin, Thyroxine, Blood Transfusion along-with supportive treatment. Patient showed

improvement and was discharged with advice for follow up.

Discussion :

Hemophagocytic lymphohistiocytosis is a syndrome characterized by fever, pancytopenia, splenomegaly, and hemophagocytosis in bone marrow, liver, or lymph nodes. HLH in adults is characterized by cytokine dysfunction and results in the systemic accumulation of activated T-lymphocytes and activated histiocytes (macrophages). Natural killer (NK)-cell and cytotoxic T cell activity in HLH patients is commonly depressed. It can be classified as familial (primary) or acquired (secondary) HLH.

Primary HLH is due to mutations in genes of the cytolytic secretory pathway, and secondary due to infections, malignancy, autoimmune, or metabolic conditions. Primary or familial HLH is diagnosed when the patient has one of the described mutations (STX11, PRF1, UNC13D, etc.) in the correct clinical setting. Prompt and early recognition is needed, but often challenging and prognosis is poor.

Acquired HLH is associated with several viral, bacterial, fungal and parasitic infections, autoimmune diseases and malignancies. In adults it is often associated with infections (i.e. Epstein-Barr virus, herpes simplex, cytomegalovirus), rheumatologic diseases (i.e. rheumatoid arthritis, systemic lupus erythematosus, adult onset systemic Still's disease), malignancy (i.e. natural killer cell leukemia, peripheral T-cell lymphoma, EBV in T-cell lymphoma, B-cell lymphoma, and a variety of other lymphomas).

For secondary HLH diagnosis, 8 criteria are proposed (fever, hemophagocytosis in biopsy, splenomegaly, high ferritin, elevated soluble CD25, cytopenia, low natural killer cell activity, and hypertryglyceridemia or hypofibrinogenemia). The presence of 5 of these criteria 8 criteria confirms the diagnosis in the correct scenario[9].

The standard chemo-immunotherapy protocol as recommended by the Histiocyte Society (HLH-2004) includes therapy with dexamethasone, etoposide (VP-16), cyclosporine A upfront and, in selected patients intrathecal methotrexate.

Very often the clinician is alerted to the possibility of HLH only after receiving the bone marrow report showing hemophagocytosis. In order to save the patient, it has to be suspected clinically on receiving the hemogram report showing pancytopenia and we need to look for the supporting evidence of HLH and a search for all possible secondary causes is to be done. Timely initiation of treatment for the possible secondary causes and the suppression of cytokine storm with steroid and immunosuppressant are essential to save the patient. Therefore good clinical approach and a high index of suspicion are absolutely essential to save the patient. Spontaneous partial regression has also been reported in the literature[4].

The prognosis for people with acquired HLH varies. The mortality rate reportedly is lower when HLH is associated with autoimmune diseases, and greater when it is associated with tumors (especially T-cell lymphoma)[10].

Conclusion :

HLH is a rare fatal disease as it remain undiagnosed. Prompt start of therapy is critical and lifesaving however, therapy is often delayed due to delays in establishing the diagnosis. A high degree of suspicion and awareness is essential to save the lives of these patients.

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Case Report

Doege Potter Syndrome

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ABSTRACT

Doege Potter Syndrome is a benign solitary fibrous tumor of pleura having a paraneoplastic presentation in the form of recurrent hypoglycemic episodes. An elderly male presented to us with recurrent attacks of hypoglycemic seizures. On imaging studies, the patient was found to have a large mass extending into right middle and lower lobes of lung. A CT- guided biopsy was performed, which on microscopy and immunohistochemistry, was suggestive of a benign solitary fibrous tumour of pleura. Surgical resection of the tumor is the treatment of choice and is curative. Unfortunately, our patient succumbed to an episode of hypoglycemia before operative intervention could be undertaken.

Key-words : Doege Potter Syndrome, solitary fibrous tumour, hypoglycemia, paraneoplastic manifestation.

Introduction :

Solitary fibrous tumors are uncommon soft tissue tumors of mesenchymal origin initially reported as a pleura based lesion but now found to occur at any site. They account for about 5% of all pleural tumors.[1,2] About 80% are benign and 50% present as an asymptomatic mass.[3] 10-20% cases present with hypertrophic osteoarthropathy, also known as Pierre-Marie-Bamberg syndrome. In 2-4% cases, it presents as recurrent attacks of hypoglycemia as was in our case. It is then called Doege Potter Syndrome. Hyopoglycemia occurs due to increased production of insulin-like growth factors, chiefly IGF-2. Symptoms are directly related to size of tumour. Immunohistochemical markers used for confirmation include vimentin, CD34 and BCL-2. Surgical resection is curative.

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Case Report :

A 62 year old male patient came with chief complaints of generalized seizures since two months with a frequency of 4-5 episodes per day. The patient always had a documented low blood sugar (40-50 mg/dl) at the time of seizures. The seizures were aborted on administration of intravenous dextrose. There was a history of removal of a mass from right thorax twenty years back, details of which were not available. The patient was non-diabetic. On physical examination, he had a pulse of 80/min, respiratory rate of 14/min, blood pressure of 140/90 mmHg. There were no signs of superior vena caval obstruction, pallor or clubbing. He had a postoperative scar in right subcostal region extending upto right infrascapular area. Trachea was central. There was dull note on percussion and decreased intensity of breath sounds in right mammary, axillary and infrascapular areas.

The hemogram, liver function test and renal function test were normal. Glycosylated haemoglobin was 5.5%, fasting insulin, serum cortisol and C-peptide were normal. Chest roentgeogram revealed a mass in right middle and lower zone ***(Figure 1).***