Nodular Panniculitis with Hemophagocytic Lymphohistiocytosis

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To the Editor: A 27-year-old Chinese man presented to the hospital complaining of red nodules on the chest and back that gradually enlarged with spiking fever up to 39°C. He had nodular panniculitis when he was 21 years old. The family history was silent. Physical examination on admission revealed skin pigmentation, skin nodules (four, 2 cm × 2 cm, without movement and tenderness), and red rash without pain and pruritus over the body. Laboratory tests showed pancytopenia, especially for white blood cell (WBC) and platelet (PLT), raised triglycerides (TGs) and ferritin levels, liver enzyme abnormalities, decreased albumin value, and deranged coagulation profile. Other autoantibody profile including antinuclear antibody and anti-cyclic citrullinated peptides and thyroid function tests showed no abnormity. Ultrasound suggested splenomegaly and hepatic calcification. Chest high-resolution computed tomography indicated ground-glass opacities on the right upper lobe of the lung, in line with pericardial and pleural effusion, and increased number of bilateral enlarged axillary lymph nodes. Biopsy of skin nodules and subcutaneous tissue showed septal and lobular fibroplasia and lymphocytic infiltration within the lobular septa and around the skin appendages [Figure 1]. The result was manifested as nodular panniculitis. Bone marrow aspiration suggested proliferation of hematopoietic cells. The patient met the classification criteria and was diagnosed as nodular panniculitis.[1] In addition, he was diagnosed as hemophagocytic lymphohistiocytosis (HLH) according to the 2004 HLH Trial Guideline (raised TG and ferritin levels, decreased WBC and PLT counts, and low fibrinogen, fever, and splenomegaly).[2]

According to the guideline of HLH and suggestion reported in literature, the patient was treated with dexamethasone (25 mg/d and regular decrement of dosage) and cyclosporine A (200 mg/d). He became better and his laboratory abnormality improved gradually. Drug therapy was continued for 6 months. Till now, he is in good health without recurrence.

Nodular panniculitis is a rare autoimmune disease with unknown etiology. Its clinical presentation shows recurrent attacks of painful subcutaneous nodules which get mainly distributed over the lower limbs and thoracic and dorsal parts of the body, often accompanied by fever, myalgia, arthralgia, and other systemic symptoms.[3] The typical pathological lesion is the gold standard for the diagnosis of nodular panniculitis, which is necrotic lobular adipose tissue accompanied by vasculitis. Necrotic adipose tissue is characterized by foam cell after the phagocytosis by a large number of macrophages. Inflammation subsides subsequently and foam cells are replaced by fibroblast form into fibrous tissue. The location of panniculitis determines the clinical presentation and prognosis. The subcutaneous adipose tissue is the most frequent one, followed by liver, spleen, bone marrow, and mesenteric adipose tissue. Corticosteroids are the first-line treatment, but if patient is in the case of refractory clinical situation, other options such as some immunosuppressants (methotrexate, leflunomide, cyclosporine A, and cyclophosphamide) and biologics (infliximab) should be considered.[4]

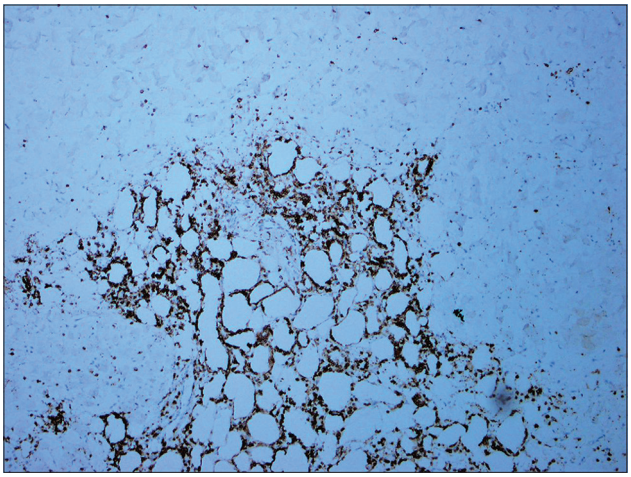

Figure 1: Biopsy specimens of cutaneous tubercle of the left chest. Photograph showing septal and lobular fibroplasia and lymphocytic infiltration involving the lobular septa and around the skin appendages by anti-CD43 (immunohistochemical staining, ×100).

HLH is a rare life-threatening condition characterized by systemic inflammatory response, hyperlipidemia, and multiple

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Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.246077

Received: 03-09-2018 **Edited by:** Xin Chen

How to cite this article: Liu H, Chen YD, Wu Y, Yin G, Xie QB. Nodular Panniculitis with Hemophagocytic Lymphohistiocytosis. Chin Med J 2018;131:2860-1.

system injury caused by the excessive activation of innate and adaptive immune systems.[2] HLH commonly presents with fever, hepatosplenomegaly, hepatic injury, hypertriglyceridemia, decreased fibrinogen, elevated serum ferritin, etc., HLH has primary and secondary types according to its etiology. Most of the primary HLH cases appear in infants and children with gene mutation: *PRFl* gene was the first one found to be related to familial HLH, followed by the discovery of other genes such as *UNCl3D* (encoding MUNCl3-4), *STXll* (encoding synaptic fusion protein 11), and *STXBP2*. Moreover, all of them can cause lymphocyte degranulation. The etiology of secondary HLH includes infection (especially Epstein-Barr virus infection), autoimmune diseases, and malignancies.[5] The pathological features of HLH are mononuclear macrophages and tissue cells from the bone marrow, spleen, liver, or lymph nodes phagocytose hemocytes which form a phenomenon of hemophagocytosis. A trail guideline in 2004 suggested that treatment can be divided into initial and maintenance periods for the first 8 weeks based on dexamethasone, etoposide, and cyclosporine, and then intrathecal injection can also be given. The use of gamma globulin during acute phase can help alleviate the disease.[2,5] Till now, the case of nodular panniculitis accompanied by HLH is rarely reported. Despite its rarity, nodular panniculitis associated with HLH may increase the severity of its own.

Accurate diagnosis of this severe illness associated with HLH and immediate drug treatment is the key to improving prognosis. Dexamethasone combined with cyclosporine A could be the first-line therapy, while other immunosuppressants such as cyclophosphamide and mycophenolate are also alternative therapies.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

This research was supported by grants from National Natural Science Foundation of China (No. 30901339 and No. 81172869), and the Application Foundation Project in Sichuan Province (No. 2016JY0021 and No. 2017JY0025).

Conflicts of interest

There are no conflicts of interest.

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