View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by Elsevier - Publisher Connector

Available online at www.sciencedirect.com
www.jdds.org

ScienceDirect

Journal of Dermatology & Dermatologic Surgery 18 (2014) 35–37

Case report

Hemophagocytic syndrome and acute pancreatitis in acute systemic lupus erythematosus

Bushra Alblewi [a], Iqbal A. Bukhari [a,*], Manal Hasan [b], Abdulaziz Alzahani [a], Raed Bukhari [b], Layla Bashawri [c], Muhammad Al Shawarby [c]

[a] *Dermatology Department, College of Medicine, University of Dammam and King Fahd Hospital of the University, Dammam, Saudi Arabia*
[b] *Internal Medicine Department, College of Medicine, University of Dammam and King Fahd Hospital of the University, Dammam, Saudi Arabia*
[c] *Pathology Department, College of Medicine, University of Dammam and King Fahd Hospital of the University, Dammam, Saudi Arabia*

Received 4 June 2013; accepted 6 November 2013

Abstract

Hemophagocytic syndrome (HPS) is characterized by the activation of histiocytes with prominent hemophagocytosis in bone marrow and other reticuloendothelial systems. It has two forms: primary and secondary. The precise pathogenesis of HPS is unclear but a dysregulation of macrophage–lymphocyte interactions with subsequent increases in the levels of both T-cell-derived and macrophage-derived cytokines has been suggested. Cardinal symptoms of HPS are prolonged high fever, hepatosplenomegaly, cytopenias, lymphadenopathy and neurological symptoms. In this report, we present a case Systemic Lupus Erythematosus associated with HPS and acute pancreatitis.
© 2014 Production and hosting by Elsevier B.V. on behalf of King Saud University. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/3.0/).

Keywords: Hemophagocytic syndrome; Acute systemic lupus erythematosus; Acute pancreatitis

1. Introduction

Hemophagocytic syndrome (HPS) is a clinicopathological entity characterized by activation and proliferation of benign macrophages with hemophagocytosis throughout the reticuloendothelial system. Reactive HPS can be associated with numerous diseases including acute leukemia, malignant lymphoma, infections (viral, bacterial, fungal, and parasitic), and systemic autoimmune diseases (Wong et al., 1991; Papo et al., 1999; Dhote et al., 2003).

* Corresponding author.
E-mail address: ibukhari@ud.edu.sa (I.A. Bukhari).
Peer review under responsibility of King Saud University.

2. The case

A 31-year-old indonesian female presented to our dermatology outpatient clinic at the king Fahd Hospital of the University with a complaint of erythematous rash affecting both cheeks of one month duration. There was a positive history of fever, fatigue, weight loss, abdominal pain and diarrhea. The patient was admitted to the hospital. Upon admission she had low grade fever and hypotension. Systemic examination revealed two enlarged cervical lymph nodes of 2 by 2 cm in diameter, splenomegally was detected with no other organomegaly. Neurological examinations were unremarkable and there were no signs of joint involvement. Dermatological examination revealed bilateral erythematous scaly slightly raised lesions affecting both cheeks with the nasal bridge (Fig. 1). Her white blood cell count was 2200, hemoglobin 11.4 g/dl and platelet count 89,000/ml. Reticulocyte index was low. Direct

http://dx.doi.org/10.1016/j.jdds.2014.03.004
2352-2410/© 2014 Production and hosting by Elsevier B.V. on behalf of King Saud University.
This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/3.0/).

Coombs test was positive and the indirect was negative. Fibrinogen was 358 mg/dl. Erythrocyte sedimentation rate was increased to 92 and C-reactive protein was 17.2 mg/l (NR < 5.0). Her levels of serum Alanine Aminotransferase (ALT), Aspartate aminotransferase (AST), and lactate dehydrogenase were 11, 24, and 159 which increased to 950, 258, and 3484. High levels of serum ferritin (4864 ng/ml, NR: 2.20–178) and fasting triglycerides (702 mg/dl, NR: 35–135) were detected. Antinuclear antibody titer was 1:320 of speckled pattern, antismith antibodies were strongly positive while Anti-double stranded DNA and rheumatoid factor were negative. Serum amylase and lipase were129 U/l and 774 U/dl respectively which increased to 905 and 12501. A skin biopsy for the facial lesion was suggested but unfortunately the patient refused. Based on these findings we managed the patient as a case of systemic lupus erythematosus. During her hospitalization, she developed generalized tonic clonic seizures for which a metabolic and septic cause was ruled out. Bone marrow aspirate revealed moderately hypercellular bone marrow with increased megakaryocytes and mildly increased hemophagocytic histiocytes (5% of bone marrow mononuclear cells) which were engulfing both myeloid and erythroid cells (Fig. 2). So the patient was finally diagnosed as a case of systemic lupus erythematosus and acute pancreatitis with HPS. She was started on high dose steroids in addition to hydroxychloroquine and mycophenolate mofetil.

During her admission the patient developed status epilepticus which was believed to be secondary to neurolupus and was admitted to the intensive care unit. Her illness course was further complicated by the development of sepsis and acute renal failure on top of existing lupus nephritis. She was managed effectively by methylprednisolone, hydroxychloroquine, mycophenolate mofetil and plasmapheresis with proper antibiotics and antifungal. After 12 weeks, the patient improved and her skin lesions cleared with postinflammatory hyperpigmentation with no scarring.

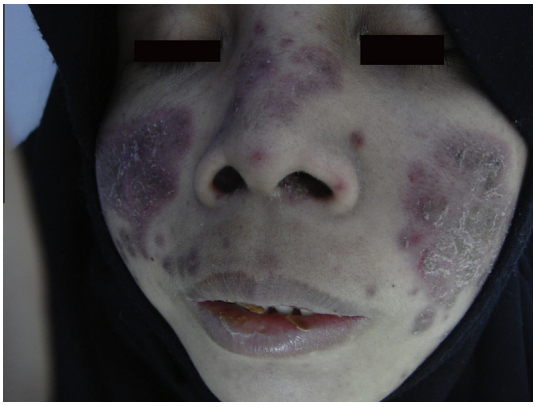

Fig. 1. Erythematous scaly raised lesions affecting both cheeks and the nasal bridge.

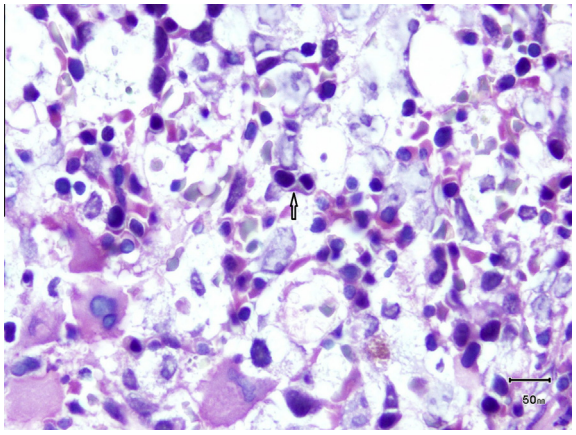

Fig. 2. Bone marrow trephine biopsy. Note two lymphocytes within cytoplasm of phagocyte (arrow). H&E ×1000.

3. Discussion

Hemophagocytic syndrome (HPS) was first described in 1939 by Scott and Robb-Smith. It is characterized by the activation of histiocytes with prominent hemophagocytosis in bone marrow and other reticuloendothelial systems. It has two forms primary and secondary. Primary HPS comprises a group of distinct genetic diseases resulting in impaired immune cell function, and are typically fatal without immunosuppressive therapy and bone marrow transplantation. Secondary HPS may occur at any age, in the setting of malignancy, autoimmune disease, drug hypersensitivity reaction, or infection (Janka and Stadt, 2005; Rouphael et al., 2007; Brastianos et al., 2006).

In 1995 and 1997, Kumakura et al., proposed a new disease entity called autoimmune-associated hemophagocytic syndrome (AAHS) Kumakura et al., 2004. The precise pathogenesis of HPS is unclear but a dysregulation of macrophage–lymphocyte interactions with subsequent increases in the levels of both T-cell-derived and macrophage-derived cytokines, particularly TNF-a, M-CSF receptors, interleukin (IL)-1, IL-6, interferon gamma (IFN)-g, sIL-2R, and soluble TNF receptors (sTNFRs), leads to an intense systemic inflammatory reaction (Osugi et al., 1997; Pringe et al., 2007).

Cardinal symptoms of HPS are prolonged high fever, hepatosplenomegaly, cytopenias, lymphadenopathy and neurological symptoms such as cranial nerve palsies or seizures. Characteristic laboratory findings include high triglycerides, ferritin, transaminases, bilirubin, and decreased fibrinogen. The hemophagocytosis can be seen in the bone marrow, lymph nodes, liver and spleen (Janka and Stadt, 2005; Rouphael et al., 2007). Active macrophages with engulfed leucocytes, erythrocytes, platelets and their precursor cells are the typical findings. In 2004, Kumakura et al. suggested important points for the diagnosis of AAHS (Kumakura et al., 2004).

Which include the following:

1. Cytopenia (affecting >2 of 3 lineages in the peripheral blood and not caused by an aplastic or dysplastic bone marrow).
2. Histiocytic hemophagocytosis in bone marrow or other reticuloendothelial systems including spleen, liver or lymph nodes. Active phase of underlying autoimmune disease at the occurrence of hemophagocytosis.
3. Other reactive hemophagocytic syndrome such as virus or malignancy-associated hemophagocytosis syndrome is excludable trigger of AAHS, exclusion of an infectious complication is very important for the establishment of the appropriate therapeutic strategy (Pringe et al., 2007).

The concept of "cytokine storm," is characterized by the secretion of huge amounts of cytokines, including interferon-g, interleukin (IL)-2, IL-12, IL-18, and tumor necrosis factor-a, by activated Th1 cells and macrophages (Larroche and Mouthon, 2004; Osugi et al., 1997). In autoimmune-related HPS, IL-18, a strong inducer of Th1 cytokines, has been suggested (Larroche and Mouthon, 2004).

Immunosuppressive therapy is indicated when HPS occurs during the course of active SLE. Administration of IVIG and G-CSF (in cases of severe neutropenia) may be indicated for supportive care (Kumakura et al., 2004; Verbsky and Grossman, 2006). In a review of English-language literature through MEDLINE, we have identified two cases of HPS and acute pancreatitis with SLE and ours is the third (Wong et al., 1991; Dhote et al., 2003; Qian and Yang, 2007; Yoshida et al., 2009; Hagiwara et al., 2006; Silva Dda et al., 2008; Elqatni et al., 2012; Abdallah et al., 2005).

4. Conclusion

In this report we are emphasizing the possible occurrence of SLE, secondary HPS and acute pancreatitis in patients who might have skin lesion as their main complaint. Association of HPS and acute pancreatitis in acute SLE is very rare. Besides, when unexplained cytopenia progresses during the course of autoimmune disease, the physician should be aware of the possibility of HPS.

References

Abdallah, M., B'Chir Hamzaoui, S., Bouslama, K., et al., 2005. Gastroenterol. Clin. Biol. 29 (10), 1054–1056.
Brastianos, P.K., Swanson, J.W., Torbenson, M., et al., 2006. Tuberculosis-associated haemophagocytic syndrome. Lancet Infect. Dis. 6, 447–454.
Dhote, R., Simon, J., Papo, T., et al., 2003. Reactive hemophagocytic syndrome in adult systemic disease: report of twenty-six cases and literature review. Arthritis Rheum. 49, 633–639.
Elqatni, M., Mekouar, F., Sekkach, Y., et al., 2012. Haemophagocytic syndrome as a complication of acute pancreatitis during systemic lupus erythematosus. Ann. Dermatol. Venereol. 139 (1), 46–49.
Hagiwara, K., Sawanobori, M., Nakagawa, Y., et al., 2006. Reactive hemophagocytic syndrome in a case of systemic lupus erythematosus that was diagnosed by detection of hemophagocytosing macrophages in peripheral blood smears. Mod. Rheumatol. 16, 169–171.
Janka, G., Stadt, U.Z., 2005. Familial and acquired hemophagocytic lymphohistiocytosis. Hematology Am. Soc. Hematol. Educ. Program, 82–88.
Kumakura, S., Ishikura, H., Kondo, M., et al., 2004. Autoimmune-associated hemophagocytic syndrome. Mod. Rheumatol. 14, 205–215.
Larroche, C., Mouthon, L., 2004. Pathogenesis of hemophagocytic syndrome (HPS). Autoimmun. Rev. 3, 159–165.
Osugi, Y., Hara, J., Tagawa, S., et al., 1997. Cytokine production regulating Th1 and Th2 cytokines in hemophagocytic lymphohistiocytosis. Blood 89, 4100–4103.
Papo, T., Andre, M.H., Amoura, Z., et al., 1999. The spectrum of reactive hemophagocytic syndrome in systemic lupus erythematosus. J. Rheumatol. 26, 927–930.
Pringe, A., Trail, L., Ruperto, N., et al., 2007. Macrophage activation syndrome in juvenile systemic lupus erythematosus: an under-recognized complication? Lupus 16, 587–592.
Qian, J., Yang, C.D., 2007. Hemophagocytic syndrome as one of main manifestations in untreated systemic lupus erythematosus: two case reports and literature review. Clin. Rheumatol. 26, 807–810.
Rouphael, N.G., Talati, N.J., Vaughan, C., et al., 2007. Infections associated with haemophagocytic syndrome. Lancet Infect. Dis. 7, 814–822.
Silva Dda, F., Anunciação, F.A., Arcoverde Jda, C., et al., 2008. Hemophagocytic syndrome: a clinical presentation of systemic lupus erythematosus. Acta Reumatol. Port 33, 91–97.
Verbsky, J.W., Grossman, W.J., 2006. Hemophagocytic lymphohistiocytosis: diagnosis, pathophysiology, treatment, and future perspectives. Ann. Med. 38, 20–31.
Wong, K.F., Hui, P.K., Chan, J.K.C., et al., 1991. The acute lupus hemophagocytic syndrome. Ann. Intern. Med. 114, 387–390.
Yoshida, S., Takeuchi, T., Itami, Y., et al., 2009. Hemophagocytic syndrome as primary manifestation in a patient with systemic lupus erythematosus after parturition. Nihon Rinsho Meneki Gakkai Kaishi 32, 66–70.