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Transient Localized Hemophagocytosis in Pleural Effusion

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ABSTRACT

Epstein-Barr virus (EBV) is one of the most important causes of hemophagocytic syndrome. We report a 76-year-old man who presented with pneumonia like symptoms and pleural effusion following upper respiratory tract infection. He underwent thoracentesis and pleural fluid cytology revealed large number of histiocytic macrophages that had phagocytosed RBCs and other inflammatory cells like lymphocytes and neutrophils.

Pleural fluid analysis showed Epstein-Barr virus Antigen (EBNA) as the causing agent and corticosteroid therapy was initiated. A few days later, pleural effusion subsided and further cytologic examinations revealed no trace of hemophagocytosis. ***(Tanaffos2010; 9(4): 61-63)***

Key words: *Hemophagocytosis, Pleura, Pleural effusion*

CASE SUMMARY

The patient was a 76-year-old male driver who used to smoke 1 pack /year till 2 months ago. He had no history of illness expect for a short hospital stay due to unstable angina 4 years ago. He had undergone surgery for pseudoaneurysm of aorta in another center 2 weeks ago. Three days later, he developed fever, malaise and rhinorrhea and was treated symptomatically. He presented to the same medical center later to have his surgical site examined. He was hospitalized because of a leakage from the surgical site. He developed dyspnea, severe cough and chest discomfort 2 days after hospitalization. Initial evaluations were performed to rule out a cardiac disease which were all normal. The patient was referred to our center for further investigations. On physical examination, respiratory sounds were clearly diminished in the right side. Chest x-ray also showed pleural effusion.

Abdominal examination and sonography showed no evidence of organomegaly. Spleen and kidneys were also normal. Echocardiography was performed and EF=50-55% with mild enlargement of the right ventricle was reported. The patient was also evaluated for tuberculosis because of cough and history of intermittent streaky bloody sputum especially in the morning. He tested negative for tuberculosis.

Laboratory examination showed normochrome normocytic anemia, mild leukocytosis and ESR=40.

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Pleural fluid analysis showed semi-bloody fluid with WBC=4,400(PMN=52%, lymph=42% and eosinophil=6%), RBC=16,000, glucose=77mg/dl, pr =3.8mg/dl , LDH=117u/l, and ADA=17.

A great number of histiocytes that had phagocytosed RBCs, lymphocytes and neutrophils were detected in pleural fluid cytology. In analysis of pleural fluid for detection of EBV, pleural effusion supernatant and isolated deposit were evaluated with PCR, which was positive for EBNA.

Corticosteroid therapy was started for the patient due to the diagnosis of hemophagocytosis. Several days later, the amount of pleural fluid significantly decreased and the symptoms resolved. Meanwhile, he underwent thoracentesis again, which showed no evidence of hemophagocytosis.

There was no hemophagocytosis in peripheral blood smear and no evidence of involvement of other organs like spleen, liver or bone marrow was detected. Therefore, based on the patient's improvement after corticosteroid therapy and negative pleural fluid cytology for hemophagocytosis, we concluded that hemophagocytosis was caused by EBV and presented as transient localized hemophagocytosis in pleura.

DISCUSSION

Hemophagocytic syndrome (HPS) is a group of disorders characterized by histiocytic proliferation, which can manifest in all hematopoietic tissues and is defined by activated macrophages that have phagocytosed erythrocytes, leukocytes, platelets and their precursors (1). Hemophagocytic syndrome comprises familial and acquired forms. Familial form is an autosomal recessive disorder that affects children more commonly. It is also known as familial hemophagocytic lymphohistiocytosis (2).

Acquired form is accompanied by viral, bacterial, fungal and parasitic infections, collagen vascular diseases and also malignancies especially T cell lymphomas and that is the reason why it is called "reactive hemophagocytosis". Clinically, it is characterized by fever, pancytopenia, splenomegaly and hemophagocytosis in bone marrow, liver and lymph nodes (2).

Hemophagocytic syndrome (HPS) is usually presented as systemic and is accompanied by a fulminant clinical course along with high mortality rate. It has multi-organ involvement (3). However, there was no multi-organ involvement in our patient. Sometimes an organ is involved locally in the acquired form, which can be transient or fulminant. In several studies performed on children, the transient form was accompanied by infections like brucellosis and infectious mononucleosis (4).

The mechanism of hemophagocytosis in these disorders is uncontrollable activity of cellular immunity resulting in activation of phagocytic macrophages engulfing blood cells (especially erythrocytes), WBCs (i.e. lymphocytes) and platelets in some degrees.

Meanwhile, the patient develops fever and other symptoms and then anemia. Organomegaly like splenomegaly or hepatosplenomegaly will occur afterwards. If liver or spleen is involved, liver enzyme levels will be elevated and coagulation disorders will develop. In case of bone marrow involvement, anemia and pancytopenia occur which can lead to multi-organ damage and death in 50% of patients in case of no control of the disease with prednisolone and anti-inflammatory pulse steroid therapy (5).

Although viruses can rarely cause disease in healthy individuals, latent genes that remain in memory B cells after primary infection can be a potential oncogen and present within any organ. It is consistent with EBV status that can be accompanied by various types of benign or malignant epithelial lymphoid diseases.

EBV can be established as a latent infection with

a range from intermittent activation periods to fatal multiplication during lifetime. Primary infection occurs in infancy and childhood subclinically (5). EBV infection may be detected in pleural space, which can be related to B cell lymphoma presenting primary effusion lymphoma as primary infection. However, the role of EBV in non-lymphoma pleural effusion has not been evaluated precisely.

EBV infection can cause interstitial pneumonitis either as chronic active or primary form and pleural effusion is a rare complication in EBV infection (6).

In our patient, the presence of hemophagocytosis in post EBV infection pleural effusion was confirmed. Pleural fluid analysis showed hemophagocytosis accompanied by EBNA.

A study conducted by Thijsen et al.,(7) showed that EBV had a role in development of pleural effusion with unknown cause at high percentage. The authors demonstrated that in nearly 40% of pleural effusions, real-time quantitative EBV-PCR was positive. Although it was expected that patients have positive EBV in their serum, 12 out of 18 patients showed negative serum EBV, which indicated that absence of EBV in serum could not be indicator of its absence in pleural effusion. It seems that EBV is presented within activated B cells in pleural fluid due to insufficient T-cell control. Additionally; the author explained that reactivation of EBV in pleural fluid could be the indicator of reduced cellular immunity or activation of B cells by another infection or microorganism.

In our patient, the presence of significant hemophagocytosis by intrapleural macrophages and negative cytology for malignancy led us to evaluate viral causes of this syndrome especially EBV in pleural fluid.

Spiral CT scan was also performed to detect pulmonary embolism whish was negative. The result of pleural fluid analysis was positive for EBV DNA; whereas, PCR was negative in serum indicating local reactivation of virus in pleural fluid.

In our patient, hemophagocytosis was the reason for further evaluation of pleural fluid for presence of viruses.

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