Malignancy-associated hemophagocytosis in children

Çocuklarda malignite ile ilişkili hemofagositoz

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To the Editor,

Hemophagocytic syndrome (HPS) is a clinical entity characterized by prolonged fever, splenomegaly and cytopenias. Secondary HPS can be related to underlying conditions including malignancies. HPS in association with malignant diseases, especially lymphoma, is a well-known entity in adults but is rare in children [1-5]. We report three cases of malignancies associated with HPS according to the criteria of hemophagocytic lymphohistiocytosis (HLH)-2004 [6]. All the clinical and laboratory findings of the patients are summarized in Table 1.

Case 1

An 11-year-old patient was admitted with cervical lymphadenopathy. Bone marrow aspiration was normal, and the patient was diagnosed as anaplastic large cell lymphoma by lymph node biopsy. One week after initial low-dose chemotherapy, fever, hepatosplenomegaly, bicytopenia, and clinical findings of disseminated intravascular coagulopathy (DIC) developed. In spite of supportive treatment, clinical findings worsened. Because of myelosuppression, which was unexpected from chemotherapy, hyperbilirubinemia, hypertriglyceridemia, and hypofibrinogenemia, the patient was thought to have HPS. Bone marrow aspirations showed hemophagocytosis and chemotherapy was restarted. Clinical and laboratory findings had improved in 10 days.

Case 2

A 15-year-old patient was hospitalized with swellings over her face and neck, fever, hepatosplenomegaly, pancytopenia, and hypertriglyceridemia. She was diagnosed as subcutaneous panniculitis-like T-cell lymphoma by skin biopsy. Hemophagocytosis was found in bone marrow aspiration and inside tumor lesions. During the first week of treatment, the fever resolved, and regression of lesions and improvement in hematological findings were noted.

Case 3

A 10-year-old patient admitted with fever, purpuric lesions, hepatomegaly, lymphadenopathies, and pancytopenia. Skin biopsy was compatible with Kaposi sarcoma, and inguinal lymph node biopsy was reported as Castleman disease. Bone marrow aspiration was hypocellular. In the second week of chemotherapy, there was an improvement in clinical and laboratory findings. Treatment was ceased for two weeks because the drug could not be provided. Fever, hepatomegaly and pancytopenia were observed again with addition of hyperferritinemia. Chemotherapy was restarted. Repeated bone marrow aspirations revealed dysplastic changes and hemophagocytosis. Hemophagocytosis disappeared in bone marrow in the first month of treatment. Unfortunately, her condition failed to improve and she died due to respiratory failure.

In conclusion, although rare, HPS may manifest secondary to malignancies. In hemophagocytosis, at

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Table 1. Clinical and laboratory manifestations of three patients with concomitant malignancies

Clinical/Laboratory Findings	Patient 1	Patient 2	Patient 3
Fever	+	+	+
Splenomegaly	+	+	-
Hepatomegaly	+	+	+
Lymphadenopathy	+	-	+
Rash	-	-	-
Neurological signs	-	-	-
Anemia	+	+	+
Thrombocytopenia	+	+	+
Neutropenia	+	+	+
Hypertriglyceridemia	+	+	-
Hypofibrinogemia	+	-	-
Hyperbilirubinemia	+	-	-
Hyperferritinemia	Not done	-	+
Hemophagocytosis in bone marrow	+	+	+
Hemophagocytosis in other parts	-	+	-

the time of diagnosis or during the treatment of malignancies, it is not easy to establish whether clinical findings are due to malignancy, chemotherapy or hemophagocytosis. Thus, if there is an unexpected or prolonged myelosuppression in oncology patients presenting with fever and DIC findings, HPS should be included in the differential diagnosis.

Conflict of interest

No author of this paper has a conflict of interest, includingspecific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included in this manuscript.

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