Paraneoplastic Polycythemia Secondary to Testicular Mixed Germ Cell Tumor

Mikst Germ Hücreli Testis Tümörüne İkincil Gelişen Paraneoplastik Polisitemi

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ABSTRACT

Paraneoplastic syndrome (PNS) is characterised by a clinical manifestation due to humoral factors such as hormones or cytokines secreted by tumor cells or by an immune response against the tumor. This clinical condition usually disappears by treatment of primary disease or recurs with disease progression. Development of polycythemia as a PNS is rare in the literature and is particularly reported to occur in renal cell carcinoma, hepatocellular carcinoma and gynecological cancers. However, there is only a small number of paraneoplastic polycythemia cases associated with germ cell tumors (GCT). Herein, we report an uncommon case of paraneoplastic polycythemia due to testicular cancer.

Key Words: Secondary, Erythrocytosis, Testicular cancer, Paraneoplastic, Mixed germ cell

ÖZ

Paraneoplastik sendrom (PNS) tümör tarafından salınan hormonal ya da tümöre yanıt olarak immün sistem tarafından salınan sitokinlerce oluşan klinik bir durumdur. Bu klinik durum çoğunlukla altta yatan primer tümörün tedavisi ile ortadan kalkmakta ya da tümörün ilerlemesi ile tekrar ortaya çıkmaktadır. Literatürde paraneoplastik polisitemi olguları çok nadirdir ve genellikle altta yatan renal hücreli kanser, hepatoselüler kanser ve jinekolojik kanserlere bağlı olgular olarak bildirilmiştir. Literatürde çok az sayıda germ hücreli tümör ve paraneoplastik polisitemi birlikteliği bildirilmiştir. Bu nedenle biz bu nadir birlikteliğe dikkat çekmek için testis kanserli hastada saptanan paranoplastik polisitemi olgusunu sunduk.

Anahtar Sözcükler: İkincil, Eritrositoz, Testis kanseri, Paraneoplastik, Mikst germ hücreli

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INTRODUCTION

PNSs result in clinical conditions due to the indirect effects of tumor cells (1). Symptoms in PNS are generally mediated by factors such as hormones or cytokines secreted from tumoral tissue. The most common symptoms associated with PNS appear in the haematological system, nervous system, skin, muscle and joints, in decreasing order of frequency.

Erythrocytosis is defined as increased hemoglobin levels and is divided into two subgroups as absolute and relative erythrocytosis (2). Of these, absolute erythrocytosis is generally associated with polycythemia vera, hypoxia or primary tumor effect. It is believed that increased levels of erythropoietin (EPO) secreted by tumor cells and failure of its feedback mechanism resulting in overstimulation of the bone marrow may play role in the development of erythrocytosis as a paraneoplastic polycythemia.

Herein we aimed to emphasise that polycythemia may develop as a paraneoplastic erythrocytosis due to mixed germ cell tumor in light of the literature.

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CASE

A 30-year-old male presented to hospital complaining of a left testicular mass for the last week. Pre-operative levels of testosterone, tumor markers and biochemical parameters were unremarkable. White blood cell count and platelet count were within normal ranges as 5.8 x 10^9 / L, and 167 x 10^9 / L, respectively. However, marked erythrocytosis was detected on blood tests. Red blood cell count was 6.72 X 10^9/L, hemoglobin was 17.1 g/dL and hematocrit was 51%. Thoraco-abdominal computed tomography identified multiple lymph nodes of various sizes ranging between 10-20 mm in the paraaortic, paracaval, aortocaval, left parailiac and both inguinal regions. Further investigations including JAK-2 mutation and arterial blood gas sampling, which were performed for the differential diagnosis of primary polycythemia, were unremarkable. However, serum EPO levels were found to be above the normal range. On the basis of these findings, it was thought that erythrocytosis might be due to PNS associated with testicular cancer. The patient underwent surgery for high inguinal orchiectomy following the diagnosis of primary testicular cancer. Post-operative histopathological findings revealed a mixed GCT with composition of 95% embryonal carcinoma and 5% yolk sac tumor. After the operation, the red blood cell count, hematocrit and hemoglobin concentration decreased to 5.11x10^9/L, 44.3% and 15.1 g/dL, respectively.

DISCUSSION

There are various theories regarding the occurrence of PNS. The direct effects of hormones, cytokines and fetal proteins produced by tumor cells or indirect effects of steroid metabolism induced by the tumor mass or immunological reactions caused by tumor-associated antigens are widely accepted opinions. However, there are still unknown reasons in the etiology of PNSs (3).

Erythrocytosis may develop as a result of hypoxia or EPO hormone secretion which is increased secondary to tumor cells (secondary polycythemia) or may develop irrespective of EPO secretion in myeloproliferative disease such as polycythemia vera (primary polycythemia). In general, development of polycythemia as a PNS is infrequent and reported to occur mostly in renal cell carcinoma, hepatocellular cancer and gynecological malignancies (4-6). In our case, the absence of laboratory findings indicating myeloproliferative disease and absence of hypoxic erythrocytosis were likely to be associated with a paraneoplastic process. Another important finding in our case that strongly supports our opinion is the self-recovery of blood counts following the testicular operation.

It is known that human testicular germ cells may secrete EPO. However, there is a limited number of cases concerning the paraneoplastic polycythemia associated with GCT in the literature (7). It was suggested in a study that the development of polycythemia was linked to increased steroidal end-point products such as testosterone and estradiol, which were secreted from Leydig cells due to excessive human chorionic gonadotropin hormone secretion by the paracrine mechanisms of primary tumors (8). Increased levels of testosterone are known to lead to polycythemia (9). However, the testosterone level in our case was within the normal range. This was another interesting finding that makes our case different from the literature.

The most important criterion in the diagnosis of paraneoplastic erythrocytosis associated with testicular cancer is the presence of high EPO levels in both the serum and the pathological specimen. Although we could show an increased level of EPO in serum samples, tissue EPO levels could unfortunately not be measured in our case. Nevertheless, post operative EPO levels decreased to the normal range.

In the literature, the relationship between EPO levels and testicular cancer has been shown in cases of seminoma and mixed GCT with a seminoma component (2, 10). Our case exhibits an important property with the absence of a seminoma component, unlike the literature information.

Blood EPO levels in GCT may increase by cytokines or hormones secreted from malignant cells or may increase by direct tumoral production. Moreover, an increased expression of growth hormone and transforming growth factor was shown in seminoma tissue (11, 12). These substances are the known mechanisms that lead to an increase in EPO levels. However, in the present case, it is not possible to suggest which mechanisms cause EPO production and erythrocytosis. More investigations on this issue should be performed to illustrate the possible pathways.

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