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CASE REPORT

A RARE CAUSE OF HEMOLYTIC ANEMIA: PARANEOPLASTIC SYNDROME

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ABSTRACT

In this article, we investigate the association between testicular cancer and hematological paraneoplastic syndrome, which is seen infrequently among all types of tumors in the literature. This case report provides a comprehensive evaluation of a 28-year-old patient admitted to the emergency department with symptoms of vomiting, nausea, and a medical history of epilepsy. Although the initial presentation did not exhibit specific symptoms or signs associated with anemia, subsequent blood tests were interpreted in favor of hemolytic anemia. Our study provides detailed radiological findings and laboratory tests that provide comprehensive information about the progression of the lesions and the patient's response to our treatment.

Keywords: Hemolytic anemia, neoplasms, testicles

INTRODUCTION

Testicular tumors are the most common solid neoplasms in the male population under 45 years of age, and they comprise 1-2% of all malignant tumors in male patients (1). Depending on the type and stage of testicular cancer, the patient may receive one of several treatments or a combination of them. Testicular malignancy usually presents as a unilateral lump or painless swelling that is found incidentally. Less commonly, testicular cancer presents with pain, with about one-third of the patients having dull pain, whereas acute pain is noted in about 10% of patients (2). Testicular tumors may present themselves asymptomatically, but they can also manifest paraneoplastic symptoms, which occur in oncological cases and cannot be attributed to the primary location of the tumor or its metastasis (3). These conditions result from the release of hormones, peptides, cytokines, or immune reactions between cancerous and healthy tissues (3). Paraneoplastic syndrome may affect various systems, mostly the endocrine, neurological, dermatological, rheumatological, and hematological systems (3). In this article, we present the association between testicular cancer and hematological paraneoplastic syndrome, which is rare in the literature.

CASE REPORT

A 28-year-old male patient was admitted to the Trakya University Hospital with vomiting and nausea symptoms. He also had a history of epilepsy, and his physical examination showed cervical and para-aortic lymphadenopathy, in addition to splenomegaly. The results of his blood tests indicated hemolytic anemia (Table 1). His coombs and paroxysmal nocturnal hemoglobinuria tests were negative, but his antinuclear antibody test was positive (++). Although folate and vitamin B12 levels were in normal range, the patient's anemia treatment started with 5 mg folate, because active hemolysis can consume folate and cause megaloblastosis. 1000 mcg/mL intramuscular B12 was also administered. The bone marrow biopsy of the patient revealed 90% cellularity, myeloid hypoplasia, erythroid hyperplasia, and grades 1-2 reticular fiber proliferation. His

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computed tomography scanning for the chest, abdomen, and cervix showed a 16-centimeter conglomerated mass-like lymphadenopathy in the para-aortic area and a 15-millimeter nodular lesion in the lower left area of the left lung (Figure 1). Also, his spleen was measured at 23 cm on the long axis, and his liver at 17 cm. Moreover, his scrotal ultrasonography showed 22 millimeters of heterogeneous nodular structure, including vascularization in the left testicle.

After examining the test results, it was concluded that the general condition of the patient might worsen due to severe tumor status and hemolytic anemia. We diagnosed a mixed germ cell testicular tumor clinically and radiologically, without any orchiectomy for tissue fixation, and started bleomycin, etoposide, and cisplatin (BEP) combination treatment. After the first cycle of the treatment, follow-up controls showed improvement in anemia as well as regression of bilirubin and tumor markers. Following four cycles of the BEP treatment, tomography controls showed partial recovery (Figure 2),

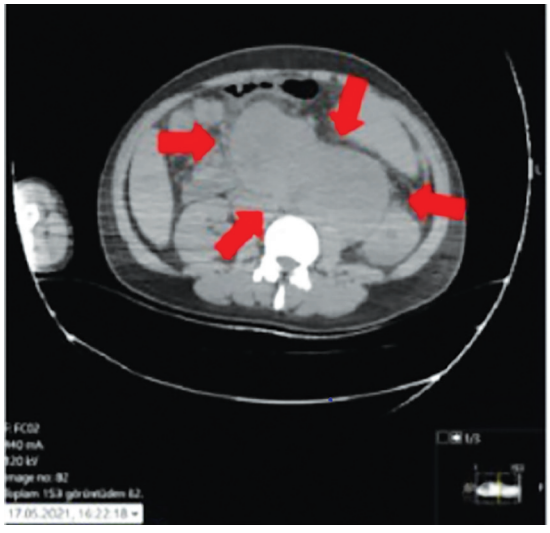

Figure 1: Computerized tomographic image of the patient's retroperitoneal mass at the time of admission.

Table 1: The result of the patient's blood test.

	17.05.2021	21.06.2021
Hb (13.7-17.5)	10.7 g/dL	11.5 g/dL
Leukocyte (4.23-9.07)	7.5x10^3/uL	4.09x10^3/uL
Hematocrit	31.4%	34.6%
AFP (0-7)	3000 ng/mL	4.78 ng/mL
Total bilirubin (0.3-1.2)	9.0 mg/dL	3.7 mg/dL
Direct bilirubin (0-0.2)	1.1 mg/dL	0.3 mg/dL
LDH (0-247)	633 U/L	228 U/L
Creatinine (0.72-1.25)	0.67 mg/dL	0.59 mg/dL
B-hCG (<2.6)	24759 IU/L	<0.2 mIU/mL
Reticulocyte (0.5-2.5)	11.30	8.5 (08.08.2022)
Haptoglobin (30-200)	<29.5 mg/dL	-

Hb: Hemoglobin, AFP: Alpha-fetoprotein, LDH: Lactate dehydrogenase, B-hCG: Beta-human chorionic gonadotropin

however retroperitoneal lymph nodes larger than one centimeter were also spotted. Therefore, we applied consolidation treatment by providing two cycles of the paclitaxel, ifosfamide, and cisplatin (TIP) combination. In the control scanning, a 55-millimeter para-aortic lymph node was detected, and as a result, orchiectomy and retroperitoneal lymph node dissection procedures were performed (Figures 3, 4). The pathology results showed multiple retroperitoneal lymph nodes consisting of necrotic tissue. Furthermore, in the testicular tissue pathology, a mixed germ cell testicular tumor with a diameter of 5 cm, containing 60% yolk sac, 30% choriocarcinoma, and 10% teratoma components was observed. We presented a case report in which the patient's paraneoplastic hemolytic anemia improved after the first cycle of chemotherapy, the patient had tumor shrinkage after continued chemotherapy, and treatment was completed with a successful operation.

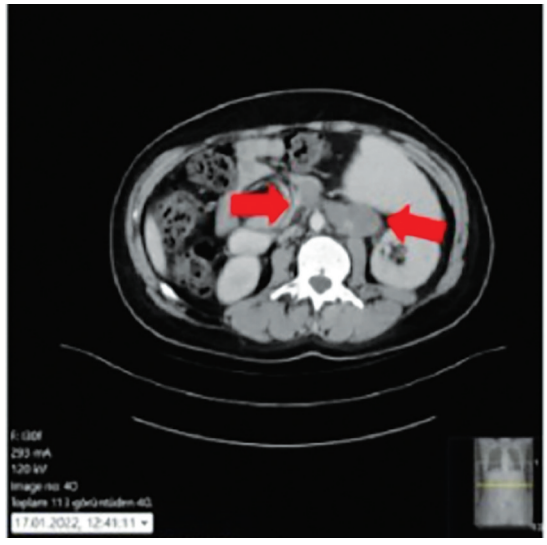

Figure 2: Computerized tomographic imaging of the patient's retroperitoneal mass after chemotherapy.

Figure 3: Uniformly bordered tumor on the testicular cross-sectional face.

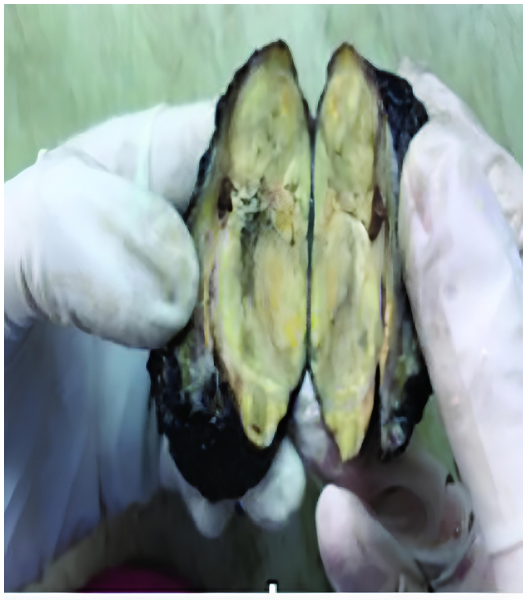

Figure 4: Sectional surface of retroperitoneal mass.

DISCUSSION

Anemia is typically defined as a condition characterized by a reduced number of circulating erythrocytes or a hemoglobin level below the thresholds established by the World Health Organization, which is below 13 g/dL in adult men and below 12 g/dL in non-pregnant adult women (4). Hemolysis is characterized by the destruction of red blood cells, leading to a diverse range of physiological and pathological findings observed in both laboratory and clinical tests. It is also used to address situations where an erythrocyte's lifespan is reduced due to mechanical, chemical, autoimmune, or infectious causes (5).

Between 1945 and 2009, case reports or series involving 52 patients associated with autoimmune hemolytic anemia (AIHA) with solid cancers were examined. The revealed number of cases linked to testicular cancer with AIHA was only 3 (6). However, anemia has been observed in cancer patients, usually secondary to chronic lymphocytic leukemia, some lymphomas, and in some cases, non-lymphoid tumors such as ovarian tumors (7). Hemolytic anemia secondary to germ cell testicular tumors, which has been described in our case report, is rare in literature (7, 8). Since paraneoplastic syndromes often cause increased morbidity, effective treatment can improve the patient's quality of life and prolong life expectancy (3). Treatment of paraneoplastic syndromes includes the process of assessment and treatment of the underlying malignancy, immunosuppression, and electrolyte and hormone disorders (3).

Paraneoplastic syndrome should always be included in the differential diagnosis since malignancies may present with various symptoms, such as nausea and vomiting, in the surrounding or distant tissues other than the involved organ. However, the primary etiology should be revealed and followed up while handling the secondary symptoms during the treatment phase. In our case, the causes of anemia were tried to be treated in the first place. However, following the supplementary examinations such as bone marrow biopsy and computed tomography scanning, the patient received a successful diagnosis which indicated that anemia resulted from the malignancy rather than being the primary ailment. The patient's clinical progress was observed to improve as a result of the main target-oriented treatment.

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