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Case report

Compound Nevus with Severe Dysplastic Feature in Mixed Germ Cell Tumor: A Case Report

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HIGHLIGHTS

- Testicular cancer patients are at risk for secondary malignancies.
- These patients are better to avoid ultraviolet ray, as much as possible.
- Recent studies reported melanoma and malignant skin changes as secondary malignancies in this patient.

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ABSTRACT

Introduction

Testicular cancer is the most common tumor of the genital tract of 18-39 years-old men; its incidence is increasing in recent decades. However, the 10-year survival rate of testicular cancer is above 90%, which can result from radiation and chemotherapy used to treat patients. Testicular cancer patients are at risk for secondary malignancies; in this regard, the effects of radiation are brighter than chemotherapy. Recent studies reported melanoma and malignant skin changes as secondary malignancies in these people.

Case presentation

This study tends to introduce a 31-year-old patient with mixed germ cell tumor and severe dysplastic changes in a compound nevus. Our patient had long-term exposure to sunlight and numerous skin nevi before the diagnosis of testicular cancer.

Conclusions

The findings do not certainly support the relationship between the emergence of nevus with severe dysplastic changes and testicular tumor.

Keywords: Testicular Tumor; Compound Nevus; Germ Cell; Second Malignancy

Introduction

Testicular cancer is the most common tumor of the genital tract of 18-39 years-old men; its incidence is increasing in recent decades (1, 2). The ten-year survival rate of testicular cancer, despite other malignancies in adults, is above 90% (3, 4), which can result from chemotherapy (5), and radiotherapy in its treatment. Radiotherapy and chemotherapy used in these patients are associated with the risk of side effects. Some studies reported heart and lung complications, nephrotoxicity, neurotoxicity, and gonadal toxicity at 5-10 years after chemotherapy or radiotherapy in patients with testicular cancer (6, 7). On the other hand, these patients are at risk for secondary cancers. In this regard, the effects of radiation are brighter than chemotherapy; some studies reported that the risk of solid tumors in patients who have radiotherapy is 1.7-3.5 times greater than others (6, 8). Recent studies on the incidence of secondary malignancies after chemotherapy in these patients show the increased risk of solid tumors (tumors of kidney, thyroid, bladder, prostate, melanoma,

etc.) in patients with non-seminoma germ cell tumors (NSGST) after chemotherapy based on cisplatin (9). Since recent studies report melanoma as a secondary malignancy of testicular tumors, skin examination is seriously recommended in these patients (10).

Case presentations

The patient was a 31-year-old, married man who had a daughter; about a year ago. The informed consent was completed by the patient to report the case, and the case was reported based on CARE guidelines. The patient experienced vague pain and increased size of left testis before admission (May 2014).

The patient had no history of previous similar pain, trauma, fever, chills, unsafe sex, discharge from meatus, weight loss, and constitutional symptoms. The patient also complained of occasional non-productive cough during this period and did not tend to prevent or treat. The patient had no history of the underlying disease and previous surgery. The patient did not smoke or take certain medications. His younger brother had died at the age of 14 years because of leukemia. Physical examination only revealed numerous small and pale spots in the face, neck, and Thunder mass of the left testis (Figure 1).

In the ultrasound, the patient's left testis was 28×35 mm and his right testis was 18×35 mm. A heterogeneous area with irregular and relatively hypervascular borders (28×35 mm) and three hypoechoic areas around it (Satellite lesion) was observed in the left testicle. The epididymis was normal in both testicles and there was no evidence of hernia and hydrocele and varicocele in scrotal and inguinal areas.

In the patient's requested experiments, alpha-fetoprotein (AFP): 69.5 ng / ml (Up to 8.5) and Beta human chorionic gonadotropin (HCG): 5.6mIU/ml (<5) and lactate dehydrogenase (LDH): 502U/L (<480). No pathologic cases were observed in other experiments. computed tomography (CT) scan of the abdomen and pelvis with and without intravenous injection reported Para aorta Fullness in the lower-left renal artery in favor of adenopathy. In chest X-ray done for patients, suspicious lesions existed in the preferably right lobes of the lung. CT scan of the lungs reported multiple nodules caused by metastasis in both lungs, the largest of which was 2 mm in the lower lobe of the right lung.

Within two weeks after diagnosis, the patient underwent a left radical orchiectomy. Pathology showed mixed germ cell tumor (2.5×6×4 cm) with extensive necrosis and invasion to tunica albuginea A and without encroaching on tunica vaginalis and lymphovascular invasion in the form of embryonal carcinoma: 85%, seminoma: 10 %, Yolk sac tumor5%.

About a month after surgery, 4 times of chemotherapy with cisplatin, bleomycin, and etoposide-containing regimen began for the patient after saving sperm. CT scan of the lungs, abdomen, and pelvis did not report any pathological lesions. The requested tumor markers decreased after surgery and were within the normal range after chemotherapy. During visits at determined times, the patient complained of back pain and right shoulder due to trauma for which conservative treatments were considered. Liver enzymes were requested for the patients, which were within normal ranges. Since the pain was not relieved, a bone scan was done for the patient; the scan reported no pathologic case other than a lesion caused by trauma in the right shoulder.

About a year after the first visit (May 2015), the patient noticed that one of the nevi on his neck started to change color and got bigger; however, he has not followed up. In one of the regular visits for follow-up,the patient was referred to an otolaryngologist due to an obvious change in color and size of that nevus compared to other nevi and its irregular margins. The nevus prone to malignant melanoma was examined by excisional biopsy with sufficient margins. Pathologic results were reported as compound nevus with the severe dysplastic feature. Because the margin of the excisional biopsy was not involved, the dermatologist only recommended regular and closed follow-up. Currently, no pathologic case has been reported in the last and periodic examinations.

Discussion

In the United States, testicular cancer is the most common cancer among men aged 20 to 40 years and the second malignancy after leukemia at the age of 15 to 19 years. Bilateral germ cell tumor incidence is estimated at 2%. The incidence of germ cell tumor is growing worldwide. Four proven risk factors of testicular cancer include cryptorchidism, family history, personal history, and intratubular germ cell neoplasia (ITGN). Testicular

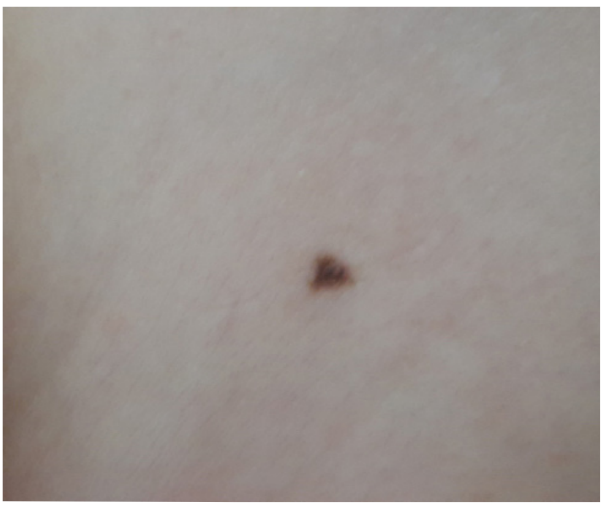

Figure 1. Compound melanocytic nevus

tumors are divided into two general categories: NSGST and seminoma germ cell tumor (SGST). Testicular cancer occurs in the form of a painless testicular enlargement. Ultrasound and measurement of tumor markers such as LDH, BHCG, and AFP help diagnosis of testicular tumors. Several therapies are currently used for testicular tumors. Radical orchiectomy is the main treatment of this malignancy and it is used based on the final diagnosis, radiotherapy, and chemotherapy in the treatment (11).

Antigens of melanoma detected by autologous T cells or antibodies include mutant tumor antigens such as mutant pl6 [CDKN2A] and antigens of cancer/testis family shared tumor-specific such as MACE-I, MAGE, and NY-ESO-I as well as cell type-specific differentiation antigens. High incidence of melanoma and dysplastic nevi in patients with immunodeficiency support the hypothesis that melanoma is an immunogenic tumor. Dysplastic nevi are also likely to become malignant types of nevi (12).

The ten-year survival rate of testicular cancer is over 90% (3-5). Due to the high survival rate of these patients compared with other malignancies of adults and the young age of most patients as well as the higher risk of other malignancies in these people, it is important to consider periodic examinations for these people. Several studies have been conducted on the effect of chemotherapy and radiotherapy in long run on secondary malignancies in these patients. Most studies consider esophageal cancer, gastric cancer, malignant melanoma, leukemia, Hodgkin's lymphoma, thyroid cancer, kidney cancer, and soft tissue sarcoma as secondary malignancy of testicular cancer (13). The relationship between dysplastic nevi and germ cell tumors was first reported in four patients in 1988. Epidemiologic studies suggest an increased incidence of germ cell tumors and malignant melanoma at high social levels. On the other hand, risk factors of malignant melanoma include exposure to ultraviolet ray, white phenotype, the number of nevi, and genetic factors (14, 15). According to Lorenzo Richiardi, although genetic factors are involved in the development of testicular cancer, little is known about effective genes (16, 17). S.D. Fossa showed that patients who underwent radiation were at increased risk of solid tumors, particularly lung tumor, malignant melanoma, and gastric tumor compared with others (6). The origin of malignant melanoma is not clear in patients with testicular cancer; however, it may be due to changes in skin factors (13). Despite the increase in solid malignancies in people who underwent radiotherapy for testicular tumors, a clear relationship was reported between chemotherapy and the incidence of solid malignancies. However, the increased risk of skin malignancies following chemotherapy should be considered in the future (18, 19). The incidence of multiple atypical nevi was significantly higher than the control group in Raghavan (20). The patient examined in this report had multiple nevi of different sizes in all regions of the skin; before the development of testicular tumors, no change occurred in size. Due to job specifications, long-term exposure to sunlight, which can be a risk factor for melanoma and other skin malignancies, is seen in history of this patient. Although most studies consider radiotherapy as a factor of secondary malignancies following testicular tumor, the patient did not undergo radiotherapy. The risk of skin malignancies was higher in patients receiving cisplatin-based chemotherapy than others (9). According to studies, physicians should consider secondary malignancies in reviews and examinations and periodic follow-ups of patients with testicular tumor. In particular, skin examination should be taken seriously due to importance of early detection of changes in previous nevi or creation of new nevi. These patients are better to avoid ultraviolet ray, as much as possible. However, there is no specific guideline for follow-up of melanoma in patients with testicular cancer.

Conclusions

Since the patient examined in this study had long-term exposure to sunlight and numerous skin nevi before the diagnosis of testicular cancer, findings do not certainly support the relationship between the emergence of a nevus with severe dysplastic changes and testicular tumor.

Authors' Contribution

All authors contributed equally.

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Conflict of interest

All authors claim that there is not any conflict of interest.

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Ethical Statement

All authors ensured our manuscript reporting adheres to CARE guidelines for reporting of case reports. Patient agreed to report the case by signing the informed consent.

Abbreviations

AFP	Alpha-fetoprotein
CT	Computed tomography
HCG	Human chorionic gonadotropin
ITGN	Intratubular germ cell neoplasia
LDH	Lactate dehydrogenase
NSGST	Non-seminoma germ cell tumor
SGST	Seminoma germ cell tumor

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