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Treated Non Seminomatous Germ Cell Tumor of Testes Post Resection of Teratomatous Lung Nodule

Deepthi Silymon[1], Aref Chehal[1], Ashraf ALakkad[2*], Aisha Alsalami[1], Hassan Shahryar Sheikh[1], Ashish Vittalrao Chintakuntlawar[1]

[1]Department of Oncology and Hematology, Sheikh Shakhbout Medical City, Abu Dhabi, UAE
[2]Department of Internal Medicine, Madinat Zayed Hospital, AL Dhafra Region, UAE

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***Corresponding author:** Ashraf ALakkad
Department of Internal Medicine, Madinat Zayed Hospital, AL Dhafra Region, UAE

Abstract

***Background*:** Testicular tumors are relatively rare, accounting for only 1% of all malignancies in men. Among the different types of testicular tumors, germ cell tumors are the most common. They are very sensitive to chemotherapy and are curable even when metastatic. Cure rates approximates 90%-95% in good risk and early stage tumors. Earlier on, metastatic testicular cancer was usually incurable and fatal, but newer treatments including high-dose chemotherapy and stem cell rescue have changed the scenario. ***Case Presentation*:** This case report presents a case of a 30-year-old male with a large testicular tumor, diagnosed as a mixed germ cell tumor consisting of a yolk sac tumor, teratoma with immature elements, and seminoma with germ cell neoplasia in situ. After undergoing radical orchiectomy, the patient experienced a postoperative decline in alpha-fetoprotein levels and was placed on surveillance. Subsequent imaging revealed the development of a lung nodule, accompanied by an increase in alpha-fetoprotein levels. The patient received chemotherapy with three cycles of BEP (bleomycin, etoposide, platinum), resulting in a partial response. Due to the patient's COVID-19 infection, the final cycle of chemotherapy was modified. Further imaging showed a marginal decrease in the size of the lung nodule, prompting surgical resection. The lung nodule was found to be a post-pubertal teratoma without significant immature elements. Following surgery, the patient's alpha-fetoprotein levels decreased to a baseline nadir. Close follow-up continues, demonstrating no evidence of disease recurrence. ***Conclusion*:** This case emphasizes the importance of a multidisciplinary approach, including surgery and chemotherapy, in managing testicular germ cell tumors with metastasis, leading to favorable outcomes and long-term disease control.

Keyword: Testicular tumors, chemotherapy, radical orchiectomy, COVID-19 infection.

INTRODUCTION

Testicular tumors are the most prevalent cancerous condition detected among young men between the ages of 20 and 35 years [1]. The incidence of these tumors has been steadily increasing over the past century, making them a significant health concern. While the exact causes of testicular tumors are not fully understood, several factors have been suggested to contribute to their development. These factors include cryptorchidism (undescended testicles), genetic susceptibility, family history of testicular cancer, and a prior history of testicular cancer in the affected individual [2].

Testicular tumors make up 1% of all cancers in males and 5% of urological tumors. In Western countries, the annual occurrence of new cases ranges from 3 to 10 per 100,000 males [3]. Among the various types of testicular tumors, yolk sac tumors (YST) belong to the category of non-seminomatous germ cell tumors. The "World Health Organization" (WHO) 2016 classification of germ cell tumors of the testis distinguishes between two types of YST: prepubertal and postpubertal. Prepubertal YSTs primarily affect infants and young children, and they are not associated with "germ cell neoplasia in situ" (GCNIS). These tumors typically occur in a pure form [4]. On the other hand,

postpubertal YSTs are associated with GCNIS and occur in adults. The presence of YSTs in their pure form raises greater concern, particularly in postpubertal cases.

Regarding symptoms, the most common symptom of testicular tumors is a painless swelling or the presence of a nodule in the testis [5]. However, it is important to note that in rare cases, symptoms related to metastasis may be the initial presenting feature [6]. Metastasis occurs when cancer cells from the primary tumor spread to distant sites in the body, such as the lungs [7]. Lung metastasis in testicular tumors can significantly impact the prognosis and management of the disease [7].

The primary treatment for testicular cancer typically involves performing an orchiectomy (surgical removal of the affected testicle), retroperitoneal lymph node dissection (RPLND) to remove any affected lymph nodes in the abdomen, and chemoradiation to target any remaining cancer cells [8]. The specific treatment plan depends on various factors, such as the stage and type of tumor, as well as individual patient characteristics.

CASE PRESENTATION

On June 27, 2021, a 30-year-old male presented to the Urology clinic with a one-month history of testicular pain and heaviness. Upon examination, imaging studies were conducted to investigate the source of the symptoms. An ultrasound of the scrotum with Doppler assessment on June 26, 2021, revealed a large heterogenous mixed echo left testicular mass lesion measuring 10.3 x 6.4 cm. These findings were indicative of a left testicular neoplastic lesion, most likely a seminoma. Subsequently, a CT scan of the pelvis and abdomen on June 27, 2021, showed a large 10.7 cm left testicular mass favoring a neoplastic lesion, most likely a seminoma. There was no evidence of abdominal or pelvic lymphadenopathy, and no distant metastasis was observed. A CT scan of the chest on the same day revealed no metastasis in the chest.

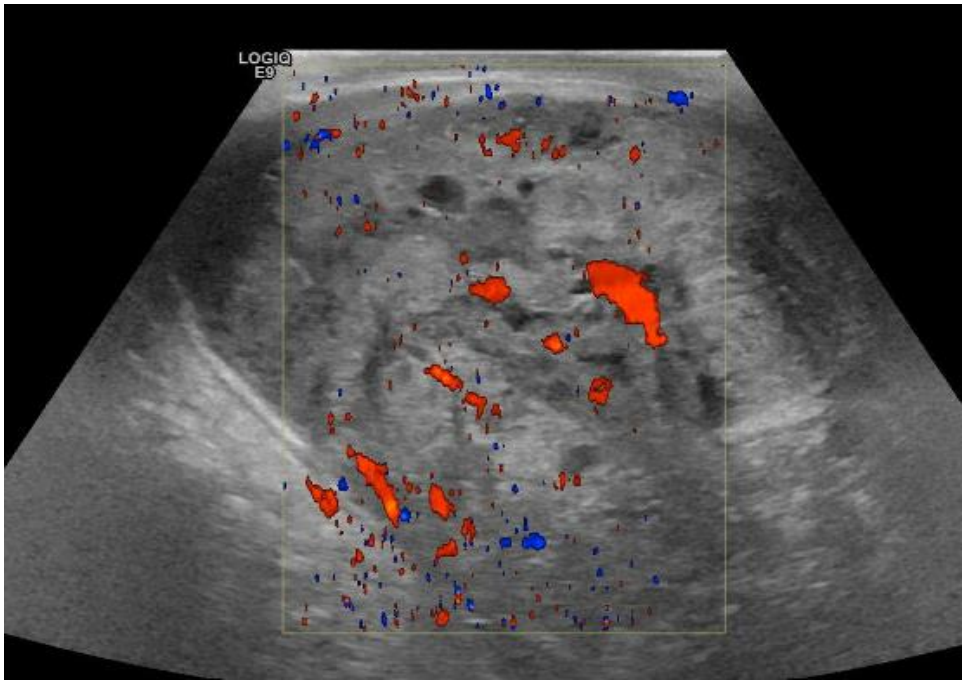

Figure 1: US scrotum 26/6/2021 revealed a large heterogenous mixed echo left testicular mass

Later, the patient underwent laboratory investigations: The patient's pre-operative alpha-fetoprotein (AFP) levels were elevated at 1710 ng/mL, while “beta-human chorionic gonadotropin” (β-hCG) levels were within the normal range. The lactate dehydrogenase (LDH) levels were mildly elevated at 265 U/L. Given the clinical suspicion of testicular malignancy, the patient underwent a radical high inguinal radical orchiectomy on June 27, 2021.

The pathology report indicated a diagnosis of a mixed germ cell tumor of the left testicle, consisting of a Yolk sac, teratoma with immature elements, and seminoma with germ cell neoplasia in situ (GCNIS). The tumor exhibited negative margins, and no vascular invasion was observed. The tumor was staged as P1T1B N0 M0 non-seminomatous germ cell tumor (NSGCT), with the tumor limited to the testes. Notably, there were no additional risk factors such as lymphovascular invasion, involvement of the spermatic cord, scrotal involvement, or embryonal elements. Following the surgery, the patient's AFP levels decreased to 122 ng/mL. Based on the National Comprehensive Cancer Network (NCCN) guidelines, the patient was placed on close surveillance for postoperative follow-up.

During the follow-up period, a CT scan of the chest, abdomen, and pelvis on October 19, 2021, revealed the presence of a 1.5 x 1.3 cm lung nodule in the left upper lobe.

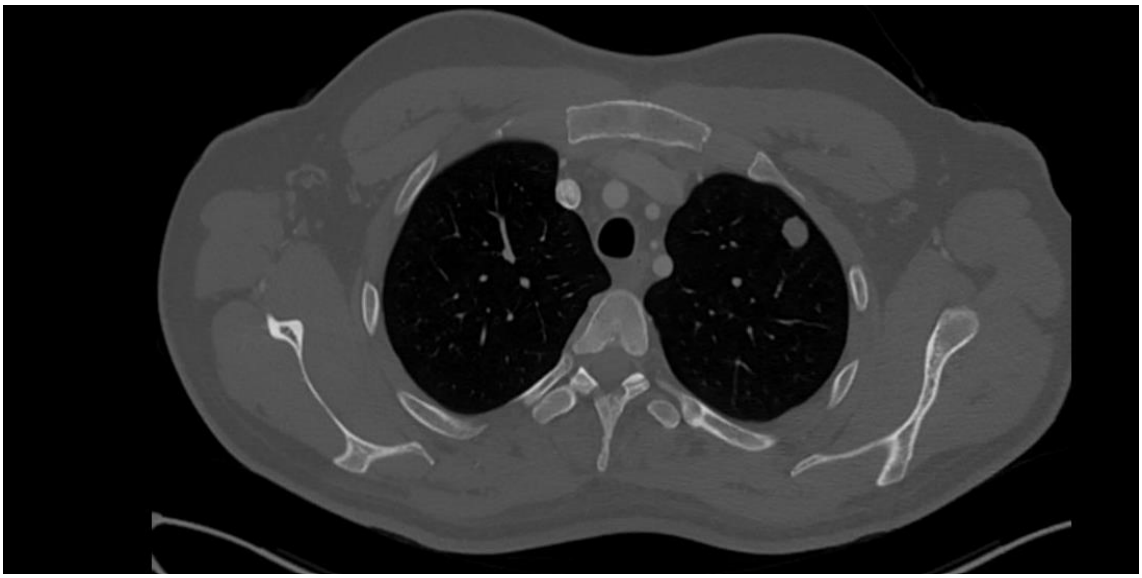

Figure 2: CT scan of the chest on October 19, 2021, revealed the presence of a lung nodule in the left upper lobe

Additionally, the AFP levels increased from a nadir of 3.8 ng/mL to 8.3 ng/mL, indicating disease progression. In light of the rising AFP levels and increasing size of the lung lesion, the decision was made to initiate chemotherapy.

The patient received three cycles of chemotherapy using the BEP regimen (bleomycin, etoposide, cisplatin). After three cycles, the AFP levels plateaued, indicating a partial response. It was determined that the patient should undergo a total of four cycles of chemotherapy. However, due to the patient's concurrent COVID-19 infection and respiratory symptoms, bleomycin was avoided in the last cycle to minimize pulmonary toxicity. A follow-up CT scan of the pelvis, abdomen, and chest on February 25, 2022, showed a marginal decrease in the size of the lung nodule from 1.4 cm to 1.

On the basis of the marginal reduction in the size of the lung nodule and the absence of metastasis in other parts of the body, it was determined that the lung nodule may be chemo-insensitive. Therefore, the decision was made to proceed with surgical resection of the lung nodule. The patient underwent a radical resection of the lung nodule on April 8, 2022. The biopsy results revealed the presence of a post-pubertal teratoma with no significant immature elements. This indicated that the tumor consisted of mature tissue derived from more than one germ cell layer.

Following the surgical intervention, the patient's AFP levels started to decline, eventually reaching a baseline nadir of 5.8 ng/mL in August 2022. The patient has been under close follow-up and surveillance, and he continues to show positive progress with no evidence of disease recurrence.

DISCUSSION

This case presents a unique combination of Yolk sac, teratoma with immature elements, and seminoma components in a mixed germ cell tumor of the testes. YST, also known as endodermal sinus tumor, exhibits various patterns that resemble the embryonic yolk sac, allantois, and extraembryonic mesenchyme [9]. In the context of the testis, YST manifests in two distinct age groups: infants, young children, and postpubertal males [10]. Among children, it represents the most prevalent form of testicular neoplasm, accounting for 80% of cases [11]. However, the occurrence of pure YST in adults is exceptionally rare, with a prevalence of only 2.4% among adult patients [12]. In adults, YST typically appears as a component of a “mixed germ cell tumor” [13]. Our patient also presented with a "yolk sac tumor” as a part of a “mixed germ cell tumor”.

Scrotal ultrasound is the primary diagnostic imaging method used for testicular cancers. If the ultrasound results suggest the presence of malignancy, further “whole-body imaging” is conducted, including CT scans of the chest, abdomen, pelvis, and brain MRI, to identify any potential metastatic disease [14]. Moreover, the patient's “blood tumor markers”, including LDH, AFP, and β-hCG are routinely examined to evaluate the outlook and track the progress of treatment [15].

Elevated levels of serum AFP indicate the presence of certain types of germ cell tumors (GCTs) that contain “embryonic yolk sac cells”, including teratomas, “yolk sac tumors” or embryonal carcinomas [16].

However, choriocarcinomas and seminomas lack these yolk sac cells and do not exhibit a rise in AFP levels in the bloodstream. β-hCG, a glycoprotein secreted by the neoplastic components of choriocarcinomas and seminomas, known as syncytiotrophoblasts, is another tumor marker used for diagnosis [17]. While both choriocarcinomas and seminomas produce β-hCG, seminomas typically result in β-hCG levels below 1,000 mIU/mL, whereas choriocarcinomas are associated with levels exceeding "5,000 mIU/mL" [18].

In our case, the patient initially underwent an ultrasound examination, followed by a CT scan of the abdomen and pelvis. These imaging studies revealed the presence of seminoma in the left testicle. Prior to the surgical procedure, the patient's alpha-fetoprotein (AFP) levels were found to be elevated at 1710 ng/mL, while "beta-human chorionic gonadotropin" (β-hCG) levels were within the normal range. The pathology report confirmed a diagnosis of a mixed germ cell tumor in the left testicle, comprising components of a yolk sac tumor, teratoma with immature elements, and seminoma with germ cell neoplasia in situ (GCNIS).

Treatment approaches for testicular tumors vary depending on the nature of the tumor. Benign teratomas are typically managed through surgical resection, while malignant tumors require a combination of chemotherapy and surgical resection [19]. Among the chemotherapy options, BEP (bleomycin, etoposide, platinum) is commonly utilized for germ cell tumors [20]. In cases of metastatic non-seminomatous germ cell tumors, a standard treatment protocol involves administering four cycles of BEP chemotherapy for patients in the moderate-to-high-risk group. In instances of recurrence after achieving complete remission, the second-line treatment options include the VIP combination (cisplatin, iphosphamide, and etoposide) or TIP (cisplatin, iphosphamide, and paclitaxel) [21]. High-dose treatment may be considered for cases that do not respond to conventional therapies or experience recurrence after initial treatment, as it has the potential to induce long-term remission [22].

In the specific case of our patient, the histopathological diagnosis showed a "mixed germ cell tumor" consisting of teratoma with immature elements and seminoma. After "three cycles of BEP chemotherapy", a partial radiological response was observed. Subsequently, It was determined that the patient should undergo a total of four cycles of chemotherapy. However, due to the patient's concurrent COVID-19 infection and respiratory symptoms, bleomycin was avoided in the last cycle to minimize pulmonary toxicity.

It is important to mention here, lymphatic dissemination is a common route through which testicular tumors spread to the retroperitoneal lymph nodes, and hematological spread can lead to the involvement of organs and tissues such as the lungs, liver, brain, and bones. Pulmonary metastasis is observed in approximately 15% of testicular seminomas [23]. In our case during follow-up, the patient's lung nodule was also found to be involved.

CONCLUSION

In our case, the patient presented with testicular pain and heaviness, which led to the discovery of a large mixed germ cell tumor in the left testicle. The tumor was surgically removed, and subsequent surveillance revealed the development of a chemo-insensitive lung nodule. The patient underwent chemotherapy followed by surgical resection of the lung nodule, resulting in a decline in AFP levels and no evidence of disease recurrence. This case highlights the importance of multimodal management in the treatment of testicular germ cell tumors with metastasis, including surgical intervention and chemotherapy, to achieve optimal outcomes for patients.

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