CASE REPORT

A Rare Combination of Mixed Germ Cell Tumour of Testis- A Case Report

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ABSTRACT

A 20 years old man presented with 4 year history of painless swelling of the left testis. He ignored this swelling until he started having pain in the abdomen. Ultrasonography revealed testicular malignancy with multiple para-aortic lymph nodes enlargements in the abdomen. His X-ray chest showed pulmonary metastasis. One tumor marker was raised. Histology revealed mixed germ cell tumour with a rare combination of seminoma and embryonal carcinoma. Because of this rare combination of 2 varieties of testicular germ cell tumor and extensive systemic metastasis we presented this case. We discussed the epidemiology, incidence, classification, staging, treatment and prognosis of testicular cancer.

Key Words: Testicular cancer, Seminoma, Embryonal carcinoma, Orchiectomy

Introduction

Primary testicular tumors are the most common solid malignant tumor in men between the ages of 20 and 35 years. For unknown reasons, the incidence of this cancer has increased during the last century[1]. Most testicular tumours are derived from the germ cells of the testis, although about 5% of testicular tumours are derived from other cells, including Leydig cells and lymphocytes (lymphoma)[2].

The cause of testicular tumours is unknown, but several predisposing factors are recognized. Any solid, firm mass within the testis should be considered testicular cancer until proven otherwise. Prompt diagnosis and early treatment are required for cure. Testicular cancer may be painless, in which case they are sometimes ignored by the patient. In painful testicular swelling should be differentiated from epididymo-orchitis. The clinician should consider the full differential diagnosis of a testicular mass, which includes epididymo-orchitis, testicular torsion, hydrocele, hernia, hematoma, spermatocele, varicocele, and syphilitic gumma.

In the past, metastatic testicular cancer was usually fatal, but recent advances in treatment, including high-dose chemotherapy and stem cell rescue, have considerably improved the prognosis. Indeed, testicular cancer is a bright spot in the oncological landscape and are now considered to be the model for treatment of solid tumors3. Testicular cancers are highly curable, even in patients with metastatic disease at diagnosis. The prognosis depends upon the histologic type of cancer (seminoma versus non-seminoma), stage, and other features such as tumor marker and type of metastatic disease. Cure rates for good-risk disease is nearly 90-95%.

Case Presentation

A 20 years old male presented with four years history of painless swelling of the left testis. He ignored this swelling all this years probably due to lack of pain and he was ashamed of revealing to others. He came to the hospital as he experienced pain in his abdomen also. On examination his left testis was swollen, firm to hard in consistency and having smooth surface. It was oval in shape but size was about 10cm/6 cm. (Fig-A1)The testis was not fixed with the scrotal wall. He had vague lump and moderate tenderness in the lower abdomen on palpation. Ultrasonography showed a complex mass, partly solid and partly cystic in his left testis (Fig-B3). There was no fluid collection in the scrotum. This was typical combined solid and cystic component of mixed germ cell tumour. There were multiple enlarged para aortic lymph nodes in the abdomen.(Fig-B1) His chest x-ray showed a huge cannon ball opacity occupying upper and mid zone of the Right lung.(Fig-B2) Blood sample for serum marker was sent. β-HCG and LDH were found to be within normal limit. ?-feto protein was 287 nmol/ml (normal < 10nmol/ml). Left

radical orchiectomy was done through inguinal approach. His abdominal lump and tenderness were reduced within a week of orchiectomy. Histology of the tumor showed combined variety of testicular carcinoma. On gross view the tumour had solid and cystic component.(Fig-A2) Microscopy revealed a combination of seminoma(Fig-A3) and embryonal carcinoma(Fig-A4) After healing of the wound patient was sent to oncologist in national Cancer Institute for further chemotherapy and radiotherapy.

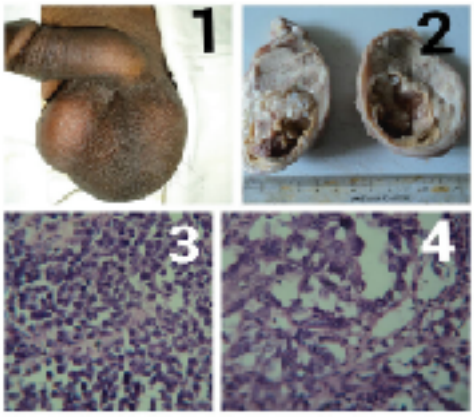

Figure-A

(1. Clinical picture,

2.Gross picture of the bisected tumour,

3. Photo micrograph of the Seminoma component, 4.Embryonal carcinoma component)

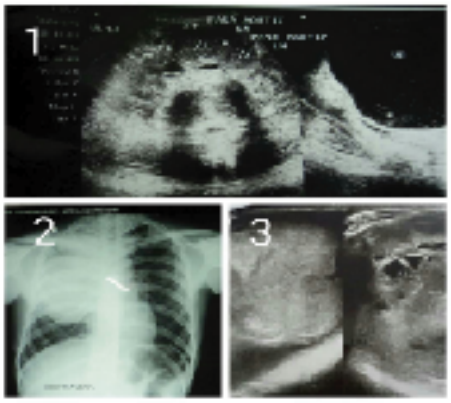

Figure B

(1.Enlarged multiple paraaortic lymph nodes on USG,

2.A large cannon ball of pulmonary metastasis

3.Solid and cystic component of the mixed tumour on USG of scrotum)

Discussion

Testicular cancer can occur at any age but is most common between the ages of 15 and 35 years. There is also secondary peak in incidence after age 60. Seminoma is rare in boys younger than 10 years of age but is the most common histologic type in men older than 60. Various risk factors have been associated with testicular tumors, but the specific etiology is not known. Cryptorchidism, genetic predisposition, family history and prior testicular cancers are important etiological factor.

Painless swelling or nodule of one testicle is the most common presenting symptom. On physical exam this mass/nodule can not be separated from the testis. Quick loss of testicular sensation could be presenting symptom also. Our patient presented with long 4 years history of slow growing painless swelling of the testis. Disseminated disease have symptom of lymphatic or hematogenous spread. Presenting symptoms could be neck mass in supraclavicular lymph node, anorexia, nausea and other gastrointestinal symptom. Bulky retroperitoneal disease could present as back pain. Cough, chest pain, hemoptysis and shortness of breath could be presenting symptom of mediastinal lymadenopathy or lung metastatic disease. Our patient did not have symptoms of chest symptom despite of pulmonary metastasis.[4]

Classification[4]

Approximately 95% of testicular tumors are germ cell tumors. These are divided into two types: pure seminoma (no nonseminomatous element present) and nonseminomatous germ cell tumors (NSGCT)

A. Germ cell Tumour

1. Seminoma
2. Non-seminoma (Teratoma)

B. Mixed germ cell tumour

C. Yolk sac tumour

D. Sex cord stromal tumor(Sertoli cell, Leydig cell tumor)

E. Lymphoma

Seminoma

Seminoma constitutes roughly 50% of pure germ cell tumors. A seminomatous component is present in 20% of mixed germ cell tumors. Serum tumor markers are usually at normal levels, but if syncytio-trophoblastic giant cells are present, β-hCG may be elevated.

Nonseminoma

- Embryonal carcinomas constitute about 2% of all testicular germ cell tumors but are the histological type in 85% of mixed germ cell tumors. They have large pleomorphic cells with different architectural patterns.
- Teratocarcinomas are part of the mixed germ cell tumor and are generally benign but have the potential for metastasis. They have elements from all three germ layers: ectoderm, endoderm, and mesoderm.
- Choriocarcinomas are the least common type of nonseminoma but are very aggressive. Widespread hematological metastasis can occur very early in the disease course; the retroperitoneum may be spared. Choriocarcinomas are associated with increased levels of β-hCG.
- Yolk cell tumors, also called endodermal sinus tumor, are the most common testicular tumor in infants and young children. In adults, pure yolk cell tumors are rare, but yolk cell elements are found in approximately 40% of mixed germ cell tumors. Yolk cell tumors are associated with elevated alpha fetoprotein levels but they do not produce β-hCG.

Mixed germ cell tumors have two or more germ cell types. These constitute approximately one third of testicular cancer. Mixed germ cell tumors behave like nonseminomas. The average age at diagnosis is older than 30 years. Our case falls in this category as it has two components seminoma and embryonal carcinoma.

Diagnostic Workup

Ultrasongram of the scrotum- USG has 100% accuracy for diagnosis of testicular malignancy. Seminoma appears as hypoechoic homogenous appearance. Non-seminoma appears as complex cystic and solid masses. Our patient showed typical combined solid and cystic component of mixed germ cell tumour. USG of the abdomen and Chest x-ray are minimum requirement for staging of the tumour. USG or CT Scan of the abdomen is necessary to see the enlargement of the para-aortic lymph nodes in the abdomen. This was very much positive in our case. Chest x-ray shows pulmonary metastasis in the form of multiple cannon ball especially in non-seminoma. This cannon ball in our case is due to the non-seminomatous component of the tumour.

Tumour Markers

Blood must be taken for marker evaluation before surgical removal of the testis. This is important for staging and also for postoperative follow up and to know the response of the treatment and surveillance. α-fetoprotein (AFP) is produced by the yolk sac elements and is elevated in 50-70% of NSGCT. It is not usually elevated in pure seminoma. Its half-life is about 5 days. β-human chorionic gonadotrophin (β-HCG) is produced by trophoblastic elements in the tumour. It is raised in 40 to 60% of NSGCTs and in up to 30% of pure seminomas. It has a half-life of 1 day. Lactate dehydrogenase (LDH) is less specific, but is more common in seminoma. Overall, 90% of NSGCTs elaborate at least one tumour marker, while markers are elevated in <40% of seminomas. Rise of α-fetoprotien in our patent was again due to presence of non-seminoma component.

Staging

American Joint Committee on Cancer (AJCC) stage groupings uses both TNM and Serum tumor marker for staging of the disease.[5,6]

Risk Classification

Good- Risk Non-Seminoma

- Testicular or retroperitoneal primary tumor, and
- No non-pulmonary visceral metastases, and
- Good markers-S1

Intermediate- Risk Non-seminoma

- Testicular or retroperitoneal primary tumor, and
- No non-pulmonary visceral metastases,
- Intermediate marker-S2

Poor risk non-seminoma

- Mediastinal primary, or
- Non-pulmonary visceral metastases, or
- Poor markers-S3:

Good-risk Seminoma

- Any primary site, and
- No non-pulmonary visceral metastases, and
- Marker-S1

Intermediate-Risk Seminoma

- Any primary site, and
- Nonpulmonary visceral metastases, and
- Marker-S1

Poor-risk Seminoma

No Patients are Classified as Poor Prognosis

According to this risk classification our case falls under good risk non-seminomas. So final diagnosis becomes Stage IIIA mixed germ cell tumor and prognosis will be like good risk non seminomas.

Treatment

Initial therapy is selected according to AJCC stage group; risk stratification (good, intermediate, or poor risk), as per the guidelines of the International Germ Cell Cancer Collaborative Group[7] and histology (seminoma versus non-seminoma). Modalities of treatment for testicular cancer are surgery, adjuvent therapy. Adjuvent therapy includes radiotherapy, chemotherapy and surgery for residual disease. Initial therapy consists of radical orchiectomy. Radical orchiectomy means removal of testis and spermatic cord through inguinal approach. Our patient is in advanced stage of mixed germ cell tumour and needs multimodalities treatment. Mixed germ cell tumour behaves like non-seminoma. Current guidelines recommend treatment approach according to AJCC staging.

Our patient should be managed as stage IIIA nonseminoma -good risk. Before we go to the management of this particular case we look into the various modalities of testicular cancer and their efficacy and indication.

Radical Orciectomy- Cure Clinical stage I seminoma can sometimes be achieved by radical inguinal orchiectomy alone. Options after orchiectomy include active surveillance, adjuvant chemotherapy, and adjuvant radiation therapy.

Active surveillance- consists of a history and physical exam and measurement of AFP and hCG every 3 to 4 months for the first 3 years, every 6 months for years 4 to 7, then annually up to year 10. A CT scan of the abdomen and pelvis is recommended at each visit and a chest x-ray at alternate visits. It is essential that patients maintain strict adherence to the surveillance program for at least 10 years.

Adjuvant radiation therapy- consists of delivery of 20-30 Gy to the infradiaphragmatic area, including th para-aortic lymph nodes and in some cases the ipsilateral ileoinguinal nodes. According to surveillance data, the overall incidence of disease failure without radiation therapy is 15% to 25%. With radiation therapy, failure rates were 2% to 5%.

Adjuvant chemotherapy- with a single dose of carboplatin is currently recommended as an alternative to radiation therapy in stage I seminoma.

Nonseminoma stage IIIA good risk: Standard treatment is with three cycles of bleomycin, cisplatin and etoposide (BEP) given over 5 days at intervals of 22 days. The overall cure rate using this regimen is 90%. Bleomycine has pulmonary toxicity and side effects must be monitored closely.

Surgery for residual disease

Surgical resection is recommended for patients with residual disease after chemotherapy[10]. Laparoscopic LN dissection is recommended for stage I and II disease[11]. Retroperitoneal lymph node dissection (RPLND) should clear the region of residual disease. Open nerve-sparing RPLND is preferred over laparoscopic RPLND. Patients in whom RPLND reveals viable cancer, post-chemotherapy residual masses are treated with subsequent chemotherapy[12]. We feel that our patient should receive chemotherapy as mentioned. He should be on active surveillance. Open RPLND may be needed if chemotherapy fails to control the residual disease in the abdomen. Pneumonectomy is also sometimes done for selected cases of pulmonary metastasis[13].

Prognosis[14]

Good-prognosis nonseminoma: 5 year survival is 90%.

Good-prognosis seminoma: 5-year survival is 85%

Intermediate-prognosis nonseminoma: 5-year survival is 80%

Intermediate-prognosis seminoma: 5-year survival is 70%

Poor-prognosis nonseminoma: 5-year survival is 70%

Poor-prognosis s eminoma: No seminoma patients are classified as poor prognosis.[14]

Our patient as good risk non seminoma has chance of survival of about 90% 5 year survival if he can receive all modalities of treatment discussed above.

Anatomical Diagnosis

Mixed germ cell tumour with combination of seminoma and embryonal carcinoma.

Conflict of interest: No conflict of interest.

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