International Journal of Research in Medical Sciences
Shaik AB et al. Int J Res Med Sci. 2021 Jan;9(1):273-277
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20205459

Case Report

Mixed germ cell tumour of the testicle: a case report of a patient presenting with acute abdomen

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Received: 07 December 2020
Accepted: 11 December 2020

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ABSTRACT

Testicular tumours are a group of heterogenous neoplasms seen commonly in men between the ages of 15 and 35 years. The two main types are seminoma and non-seminomatous germ cell tumour (NSGCT). Testicular cancers are highly treatable and usually curable, even if they present at an advanced stage of the disease with a five-year survival rate of over 95 percent. The symptoms at initial presentation can vary depending on the metastasis, but a nodule or painless swelling of testicle is usually noted. In this case report we will study how a patient with metastatic testicular tumour presents with symptoms indicative of gastrointestinal infection of acute nature with no associated features. We will review current literature on testicular cancers, reasons for delay in treatment and its impact on patient care.

Keywords: Testicular germ cell tumour, Metastatic cancer, NSGCT, Primary health care corporation Qatar

INTRODUCTION

Testicular cancers account for just 1 percent of all cancers in men, despite their recent increase in incidence there is a decline in the mortality rates.[1] Among the two different types the germ cell tumours are the most common accounting for over 95 percent of total neoplasms. They may consist of one histological pattern or can be a combination of different histological types. No definite cause is known but several predisposing factors have been identified such as cryptorchidism, carcinoma *in situ*, previous testicular cancer, hypospadias, inguinal hernia, Caucasian origin, and family history.[2] Physical examination, ultrasound and tumour markers can aid in diagnosis, but confirmation of the type is done by biopsy. Early identification and treatment are ideal, but both doctor and patient factors can contribute to a delay in diagnosis. The basic treatment modalities include surgery, chemotherapy and radiotherapy depending on the staging of the cancer. This case highlights some of the factors which led to delayed presentation and its effect on overall outcome.

CASE REPORT

This case report is of a 30-year-old man who presented to our primary health care clinic with a history of progressively worsening abdominal pain especially after meals associated with loss of appetite which he thought started following a restaurant meal a week ago. He also reported weight loss of about 2 kilos during this short span. Based on his symptoms he was referred to secondary care for further evaluation. Initial ultrasound abdomen showed an irregular hypoechoic mass lesion 7.5×5.4 cm in left hypochondrial area followed by CT abdomen and pelvis that revealed a heterogenous enhancing infiltrating mass lesion measuring 9.8×7.7×5.9 cm in retroperitoneum at the level of left kidney till L3-L4 disc with infiltration of left renal vessels, aorta and psoas muscle and tumour thrombus of the left renal vein with a discrete necrotic deposit. Origin of lesion was indeterminate, and a possible retroperitoneal sarcoma was suspected. A further MRI revealed small multiple lesions on the liver and multiple bilateral pulmonary nodules suggestive of metastasis.

A thorough physical examination revealed a slightly enlarged left testicle which he apparently noticed the same week but failed to report due to embarrassment. There were two previous encounters in primary care on at least 2 occasions for intermittent low back pain in recent past which he attributed to being overweight (weight 115 kg) and inactivity. Based on these new findings a testicular ultrasound was arranged, which showed splayed left testis (5.3×4.1×2.5 cm), a well-defined heterogenous mass lesion with increased vascularity and few tiny hyperechoic areas (largest being 4.5 mm) without posterior shadow. Mild to moderate left hydrocele with internal debris and varicocele on left side. A 5.3 cm left intratesticular neoplasm suspicious of germ cell tumour was reported.

A CT guided retroperitoneal biopsy of tumour mass confirmed metastatic germ cell tumour. Tumour markers were raised-LDH 671, CA 19-9, BhCG 686, AFP 25. The CAP synoptic report of testicular lesion indicated a unifocal 6×4.2×3.5 cm tumour with the histology of mixed germ cell tumour (embryonal carcinoma 75%, teratoma-post-pubertal type 20% and yolk sac tumour 5%) invading rete testis with lymph vascular invasion. Other findings identified were germ cell neoplasia *in situ* (GCNIS), tubular sclerosis, tumour perineural invasion and rare syncytiotrophoblast. A diagnosis of non-seminoma left testicular mixed germ cell tumour was made with metastasis to lungs, liver, retroperitoneal para-aortic lump nodes with pulmonary embolism and splenic vein thrombosis. The staging was pT2Nx, cT3N3Mb with CSIII poor risk.

Patient was commenced on enoxaparin initially for DVT and pulmonary embolism and later changed to rivaroxaban 20 mg. A left inguinal radical orchiectomy was performed soon after the diagnosis followed by 4 cycles of chemotherapy of VIP protocol (etoposide, ifosfamide, cisplatin). This regime was chosen instead of BEP in view of lung metastasis and to avoid bleomycin toxicity in case patient develops COVID-19 infection. Subsequently a laparotomy was performed for hepatic and retroperitoneal metastasis resection.

During the course of treatment, he developed several complications including severe anaemia with haemoglobin dropping to 4.1 gm/dl. This was attributed to ineffective erythropoiesis from folate and vitamin B12 deficiency and possible haemolysis due to tumour infiltration and was corrected by multiple PRBC transfusions and replacement of folate and vitamin B12. He was also neutropenic with chemotherapy sessions requiring monitoring and treatment. He then had perioperative and post-operative complications with abdominal aortic artery and duodenal injuries and small bowel adhesions which were managed appropriately.

Following successful treatment, a repeat MRI and CT scan showed marked regression of his left paraaortic lymph nodes with no evidence of liver metastasis or lung lesions and no new findings. His overall health improved significantly with normalisation of laboratory parameters including the tumour markers. He is currently being followed up by oncology and surgical specialties.

DISCUSSION

Testicular neoplasms are rapid growing, painless solid tumours most commonly occurring from adolescence through to age 40. Due to its sensitivity to both radiotherapy and chemotherapy it has a very good prognosis even if it presents late in the disease.[3] The cure rates can be 99 percent in early stage without metastases and a 5-year survival rate of over 90 percent with retroperitoneal lymph node involve. In advanced metastatic stages the 10-year survival can be 66 to 94 percent depending on site and extent of the disease.[4] There has been an increase in trend over the last 3-4 decades affecting mainly the Caucasian population.[5] The increased incidence was thought to be due to birth cohort effects, suggestive that the risk is largely attributed to the era in which a person is born and it appears that the individual retains their risk of their original region even if they migrate to a different area.[6,7] However, there is no clear reason why some people are more at risk and why geographic variation exists.

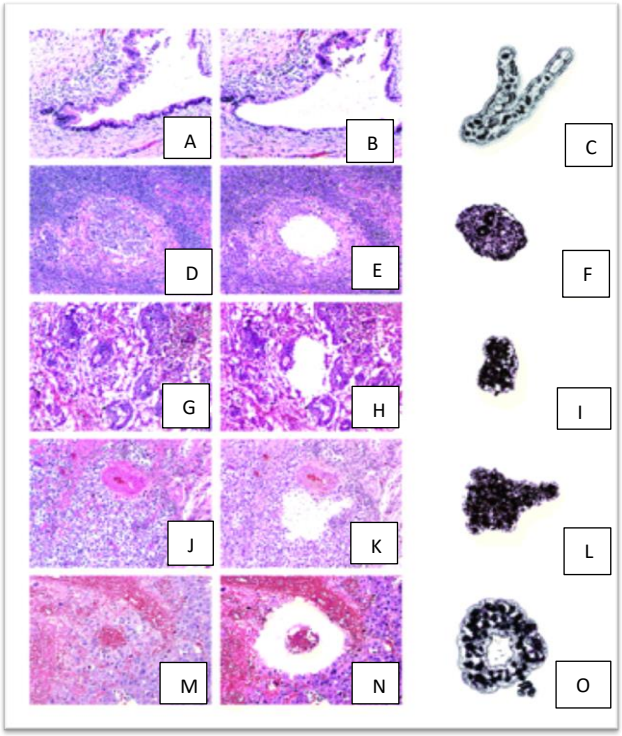
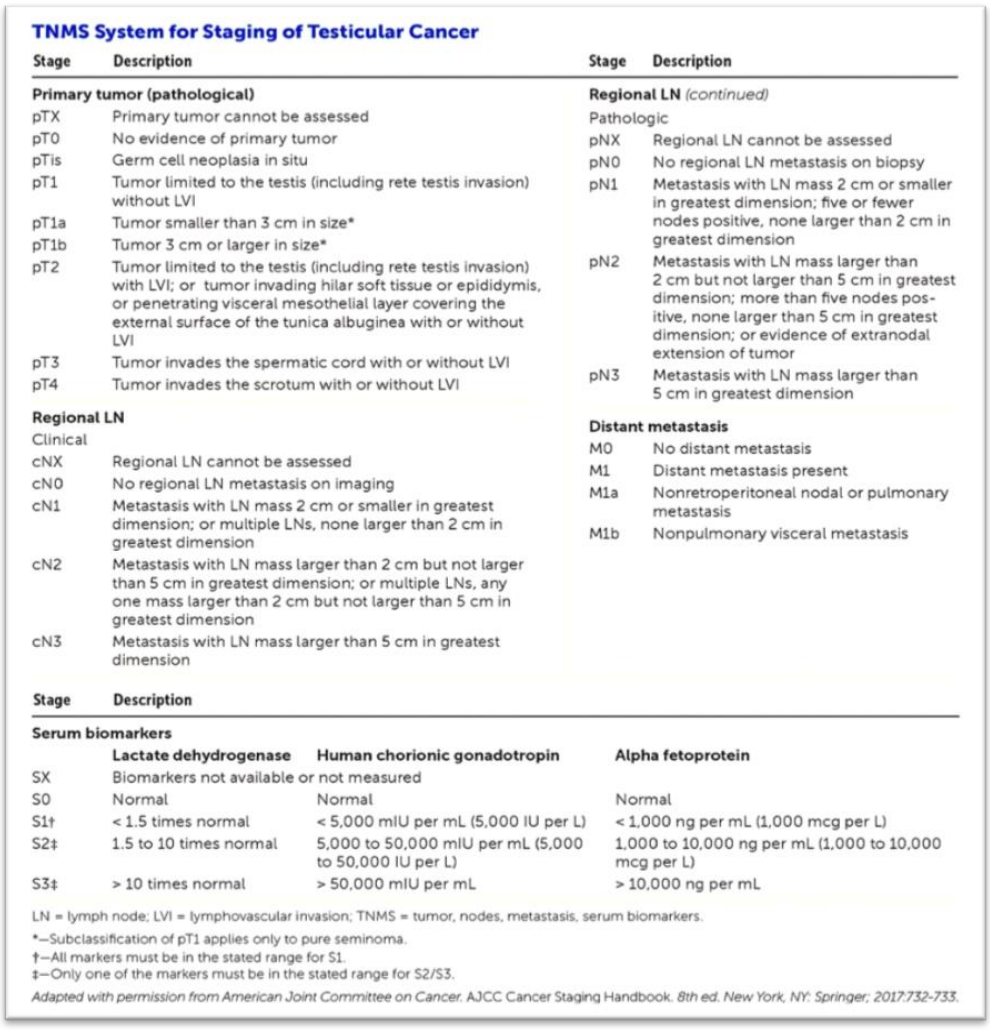


Figure 1: Histological images of metastatic germ cell tumour in retroperitoneal lymph nodes.[13](A) Pre-microdissection, (D) embryonal, (G) yolk sac tumour, (J) seminoma, (M) and choriocarcinoma. (B, E, H, K, and N, respectively) post laser microdissection images and (C, F, I, L, and O) micro dissected tissue for DNA analysis.



TNMS System for Staging of Testicular Cancer

Stage	Description
Primary tumor (pathological)	
pTX	Primary tumor cannot be assessed
pT0	No evidence of primary tumor
pTis	Germ cell neoplasia in situ
pT1	Tumor limited to the testis (including rete testis invasion) without LVI
pT1a	Tumor smaller than 3 cm in size*
pT1b	Tumor 3 cm or larger in size*
pT2	Tumor limited to the testis (including rete testis invasion) with LVI; or tumor invading hilar soft tissue or epididymis, or penetrating visceral mesothelial layer covering the external surface of the tunica albuginea with or without LVI
pT3	Tumor invades the spermatic cord with or without LVI
pT4	Tumor invades the scrotum with or without LVI
Regional LN	
Clinical	
cNX	Regional LN cannot be assessed
cN0	No regional LN metastasis on imaging
cN1	Metastasis with LN mass 2 cm or smaller in greatest dimension; or multiple LNs, none larger than 2 cm in greatest dimension
cN2	Metastasis with LN mass larger than 2 cm but not larger than 5 cm in greatest dimension; or multiple LNs, any one mass larger than 2 cm but not larger than 5 cm in greatest dimension
cN3	Metastasis with LN mass larger than 5 cm in greatest dimension

Stage	Description
Regional LN *(continued)*	
Pathologic	
pNX	Regional LN cannot be assessed
pN0	No regional LN metastasis on biopsy
pN1	Metastasis with LN mass 2 cm or smaller in greatest dimension; five or fewer nodes positive, none larger than 2 cm in greatest dimension
pN2	Metastasis with LN mass larger than 2 cm but not larger than 5 cm in greatest dimension; more than five nodes positive, none larger than 5 cm in greatest dimension; or evidence of extranodal extension of tumor
pN3	Metastasis with LN mass larger than 5 cm in greatest dimension
Distant metastasis	
M0	No distant metastasis
M1	Distant metastasis present
M1a	Nonretroperitoneal nodal or pulmonary metastasis
M1b	Nonpulmonary visceral metastasis

Stage	Lactate dehydrogenase	Human chorionic gonadotropin	Alpha fetoprotein
Serum biomarkers			
SX	Biomarkers not available or not measured		
S0	Normal	Normal	Normal
S1†	< 1.5 times normal	< 5,000 mIU per mL (5,000 IU per L)	< 1,000 ng per mL (1,000 mcg per L)
S2‡	1.5 to 10 times normal	5,000 to 50,000 mIU per mL (5,000 to 50,000 IU per L)	1,000 to 10,000 ng per mL (1,000 to 10,000 mcg per L)
S3‡	> 10 times normal	> 50,000 mIU per mL	> 10,000 ng per mL

LN = lymph node; LVI = lymphovascular invasion; TNMS = tumor, nodes, metastasis, serum biomarkers.

*—Subclassification of pT1 applies only to pure seminoma.
†—All markers must be in the stated range for S1.
‡—Only one of the markers must be in the stated range for S2/S3.

Adapted with permission from American Joint Committee on Cancer. AJCC Cancer Staging Handbook. *8th ed. New York, NY: Springer; 2017:732-733.*

Figure 2: Tumor, node, metastasis system (TNMS) for staging of testicular cancer.[18]

It has been speculated that testicular germ cell tumours develop as part of testicular dysgenesis syndrome, their sequalae include cryptorchidism, testicular atrophy and other features.[8] The exposure to endogenous factors including in utero oestrogen and environment was thought to have played a role in negatively changing the normal embryonic gonadal development and cryptorchidism.[9] All testicular germ cell tumours arise from a common precursor called intratubular germ-cell neoplasia unclassified (ITGCNU).[10] Their incidence in Caucasian men is comparable with the life term risk of developing germ cell tumour, suggesting that ITGCNU eventually leads to development of testicular germ cell tumour without regression.[11]

There are two main types, germ cell tumour and non-germ cell tumour. Seminoma is the most common germ cell tumour accounting for 40% of total cases. It is slow growing, responds well to radiotherapy and has good prognosis. The non-seminoma germ cell tumour can include embryonal carcinoma which can be seen in 25% cases, it is highly malignant, can be painful and has poor prognosis. Teratoma is common in children and usually benign in nature. Choriocarcinoma is rare but can be highly malignant and very aggressive. Yolk sac tumour is often seen in prepubertal age group with malignant potential, AFP levels are usually high.[12] Mixed germ cell tumour accounts for 30% of all tumours where both AFP and hCG levels can be elevated.

The clinical features of testicular cancer include painless testicular swelling or nodule, scrotal discomfort and other symptoms which correspond to the site of metastasis like cough, chest pain, lower back pain, abdominal pain and gynaecomastia.[14] There are other testicular disorders which are more common than testicular cancer, painless conditions such as varicocele, hydrocele, spermatocele, hernia and painful conditions like epididymitis, torsion, trauma, orchitis and epididymal cysts. Using a light source to transilluminate the scrotum often aids the physical examination in differentiating between these pathologies. Scrotal ultrasound should be arranged urgently to rule out extra or intratesticular mass, the latter being highly suggestive of cancer.[15] Serum tumour markers such as lactate dehydrogenase (LD), human chorionic gonadotropin (hCG), and α-fetoprotein (AFP)

should be measured. Imaging by CT and MRI with the histology report can help in diagnosing and staging of the tumour. Tumour markers also have a role in assessing prognosis, monitoring progress to treatment and check for relapse. Those who present with a rise in all three markers often tend to have poor prognosis. All patients are advised to use sperm bank before the treatment begins due to risk of infertility.[16]

The staging of testicular tumours combines TNM stages and tumour marker levels. However, a simplified AJCC classification includes: stage 1-cancer limited to testicles with no lymph node involvement. Stage 2-retroperitoneal lymph node spread (IIA: if lymph nodes <2 cm, IIB: if lymph nodes 2-5 cm, IIC: if lymph nodes >5 cm). Stage 3 for distant metastasis or involvement of nonregional lymph nodes or retroperitoneal nodal involvement with high tumour markers.[17] Following completion of treatment patient should be counselled about future fertility issues, risk of recurrence, and treatment complications which may include azoospermia, neuropathy, pulmonary disease, kidney impairment, ear disorders, cardiovascular disease, and risk of secondary metastasis due to the treatment. There should be a clear follow-up plan from multidisciplinary team as per local guidelines and protocols.

Testicular cancer stages using the eighth TNM staging system developed jointly by the American joint committee on cancer (AJCC) and the Union for international cancer control (UICC).[18]

Delay in seeking help can affect the stage of disease at presentation, the prognosis and increase the morbidity and mortality rates as people present when the cancer is more advanced requiring aggressive treatment options.[19] Both doctor and patient factors can lead to delays and are significantly associated with more advanced disease. Delay in presentation has been seen as a major cause for the delay in diagnosis than just delay in referral pathways.[20] Primary care physicians play a significant role in early recognition and timely referral to specialist care, but as testicular cancer is rare, they don't see many cases often which can contribute to delay due to possible misdiagnosis and failure to take prompt action.[21] Other factors such as low prevalence, vague and ambiguous presentations, unfamiliarity of the disease can lead to misdiagnosis and delays in secondary care referrals. From patient's perspective embarrassment in discussing testicular disorders with a doctor acts as a barrier to take actions leading to delays. The people in this age group are conscious about attractiveness, masculinity, sexual functioning and perceive themselves as healthy with no risk of developing serious disease, therefore they are less likely to seek help.[22] It has been reported that men often fail to act quickly after being aware of the testicular abnormality.[23] There is conflicting evidence that patients' level of education may have a role in delayed presentation.

Studies suggest that developing education programs to increase testicular cancer awareness and being well informed about the disease enables men to seek help earlier and avoid delays.[24] There has been a push to promote health education in young men with testicular disorders, as it may encourage them to act fast when they notice any change. Over the last few decades progress has been made in encouraging young men to seek medical help. However, there is a lot that needs to be done to improve early diagnosis and referral process. Doing monthly self-examination of testicles in young men is recommended, although studies have not shown it to improve outcomes. To promote the diagnostic skills and competency among primary care physicians, organising regular educational programs on testicular cancers, peer reviews and other educational activities may help to decrease delays. These measures can lower the percentage of advanced cancers, improve disease free intervals, decrease cost and overall survival. Testicular and breast cancer are the two most common cancers that can be detected by performing regular self-examination. However, routine screening is not advised by various international guidelines for testicular cancer because it's a rare cancer, having highly effective treatment leading to good outcomes despite the staging of the disease, and it was not certain that screening would help reduce the morbidity and mortality.[25] Nonetheless, there should be more focus on public health campaigns in promoting testicular self-examination and opportunistic health education of patients by health care providers using leaflets and other social media.

CONCLUSION

This case presents an opportunity to review mixed germ cell tumour of testicle which is a common malignancy of the young men as detailed in this report. It highlights the importance of self-examination and significance of seeking early medical advice to avoid unnecessary delays. A multidisciplinary team involvement was pivotal with his unusual and advanced disease presentation and complex management with multiple sequelae. It stresses the merits of aggressive approach with treatment in such young individuals and significance of vigilant follow up to prevent recurrence. The emphasis should also be on early detection and treatment by improving awareness of testicular tumours and its presentations in both young men and healthcare professionals.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Shaik AB, Shaik NF. Mixed germ cell tumour of the testicle: a case report of a patient presenting with acute abdomen. Int J Res Med Sci 2021;9:273-7.