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Case Report

Case report: Challenges, treatment, prognosis and outcome of a patient with partially treated seminomatous testicular carcinoma

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ABSTRACT

Background: Testicular carcinoma is a rare malignancy in men. It is ranked the 18th most common male cancer in Malaysia with seminoma representing 40% of the primary testicular neoplasms. Early detection of the tumour and the immediate initiation of treatment and disease management provide high possibilities of positive outcomes for patients.

Case presentation: A 36-year-old male was initially diagnosed with a left cryptorchidism and metastatic testicular seminoma. However, due to socioeconomic circumstances and the Coronavirus-19 (COVID-19) pandemic, he defaulted on his chemoradiotherapy follow-up treatments. He returned to us four years later with a progressively enlarging testicular mass with normal tumour marker values and subsequently underwent a successful radical left orchidectomy. Histopathological examination revealed features of regressed germ cell tumour (GCT). He successfully underwent chemoradiotherapy treatment and surveillance follow-ups did not show tumor recurrences.

Discussion: Seminoma is the commonest type of testicular carcinoma with good prognosis among young patients. In huge masses, as seen in our patient, early chemoradiotherapy with the intention to reduce tumor bulk and invasiveness after which will be followed by radical orchidectomy. Residual mass post chemotherapy for patients with seminomas should be properly assessed for viability of tumor cells within it.

Conclusion: Undescended testis and cryptorchidism present key risk factors for developing testicular carcinomas which are uncommon among men. Early detection, surgery and chemoradiotherapy on seminomas would usually lead to positive outcomes. The remarkable chemosensitivity of a seminomatous type tumour towards a platinum-based regiment in combination with radical resection entails good prognosis and effective local disease control.

1. Introduction

Testicular carcinoma is a rare malignancy which affects mostly males of Caucasian origin [1]. The incidence of testicular carcinoma among the Asian population is reported to be 2.3 per 100,000 population [2] and frequently detected among young men with a median age of 33 years old upon diagnosis [3]. In this report, we present the perioperative challenges in the case of a patient with massive neglected metastatic testicular seminoma who subsequently underwent successful radical orchidectomy. This work is reported in line with the SCARE criteria [4].

2. Case presentation

A 36-year-old male with a history of left undescended testis presented to our institution with a progressively swelling left inguinoscrotal and occasional abdominal discomfort which he had endured for three years. The patient had been diagnosed four years earlier with a left testicular tumour with left para-aortic lymph node. Due to the distribution and bulk of the disease, he was referred to the oncology team for bleomycin, etoposide and cisplatin (BEP) chemotherapy for testicular seminoma. The patient at that point of time was a heavy smoker and had been consuming methamphetamine for one year. Six months prior

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to his current presentation, he had also been diagnosed with hepatitis C, a condition possibly related to his high-risk lifestyle. His drug abuse habit and the recent Coronavirus-19 (COVID-19) pandemic had unfortunately led to the patient defaulting on his subsequent prescribed chemotherapy treatment regimen after receiving only one cycle of BEP. He was referred to us for methamphetamine abuse with incidental findings of a huge testicular swelling upon routine physical examination.

Our clinical examination found the patient alert and comfortable with stable hemodynamics. The left inguinal swelling measured 20cm × 11cm x 10cm and extended into the scrotum; superiorly it extended along the inguinal ligament towards the anterior superior iliac spine (ASIS). The mass was firm in consistency and non-tender to touch. There was absence of the inguinal lymphadenopathy of normal contralateral testis. No other significant abnormalities were found on systemic examination.

His initial tumour markers four years previously had revealed an increased serum beta human chorionic gonadotrophin (β-hCG) at 16mlU/m (normal value:<5mIU/mL), grossly elevated lactate dehydrogenase (LDH) at 1176U/L (normal 125–220U/L), and a normal level alpha feto-protein (AFP) at 3.8ng/mL (normal 0.6–8.5ng/mL). These tumour markers however remained within normal values during his current admission. A contrast-enhanced computed tomography (CECT) of the abdomen and pelvis revealed a huge inguino-scrotal mass measuring 10cm × 15cm x 30cm and left paraaortic mass measuring 4.0cm × 4.3cm x 10.9cm (Fig. 1). The para-aortic mass superiorly abutted the stomach and laterally with the inferior pole of the left kidney compressing the left proximal ureter resulting in gross hydronephrosis. No other significant distant lesion was observed in the CT. An endoscopic ultrasound guided biopsy of the left suprarenal mass, an extension of the left para-aortic mass, yielded necrotic tissue.

The patient was subsequently scheduled for elective left radical orchidectomy under general anaesthesia (GA). He fasted for 8 h prior to the surgery and was successfully intubated using modified rapid sequence intubation (RSI). In view of his hepatitis C, the teams involved in the surgery had to put on adequate personal protective equipment (PPE). Intraoperatively, the intra-abdominal portion of the tumour had calcifications while the inguino-scrotal mass was mainly cystic in nature. The 'foot-shaped' tumour weighed approximately 2kg (Fig. 2). No obvious abdominal lymph nodes were detected. During closure, a 30cm × 30cm sublay mesh was positioned below the transversalis abdominis muscle layer to strengthen the abdominal wall defect. Bleeding was minimal, and the patient was later successfully extubated. He was discharged two days after the procedure.

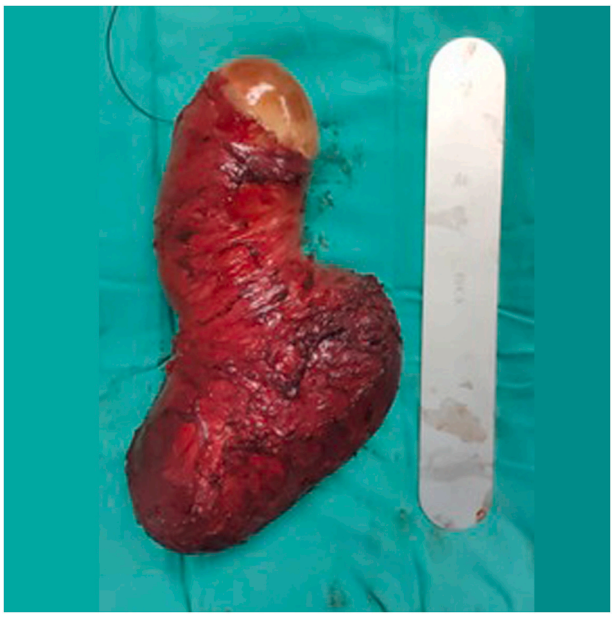

Fig. 2. "Foot shaped tumour" measuring 29cm × 9cm x 13cm and weighing 2kg with the left spermatic cord tagged.

Histopathological examination (HPE) showed the mass to be a regressed germ cell tumour with the fibrocartilaginous cyst wall devoid of epithelial linings and covered mainly with fibrin, aggregates of hemosiderin laden macrophages, necrotic tissue, coarse calcifications and cholesterol clefts with multinucleated giant cells. There was no germ cell neoplasia in situ (GCNIS), granuloma, atypical cells or overt malignancy in all the sampled sections. Immunohistochemical staining was negative for Placental Alkaline Phosphatase (PLAP) and SALL4 (Sal-like protein 4) (Fig. 3). The patient was referred to the oncology unit for completion of chemotherapy and surveillance.

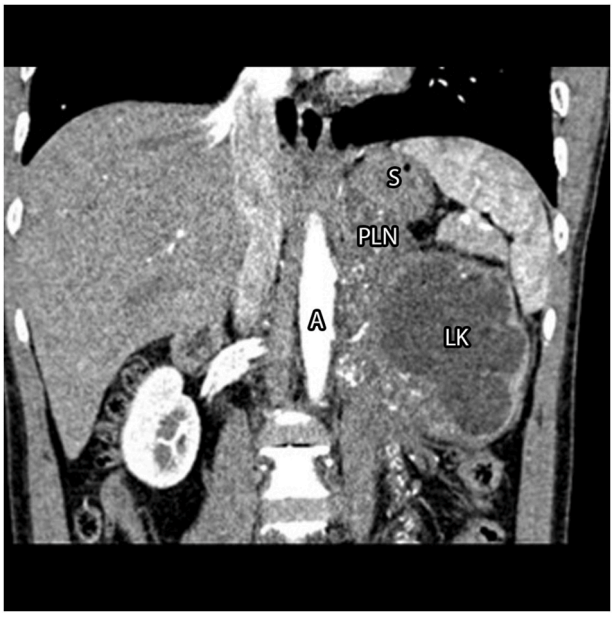

Fig. 1. Pre-operative CECT showing relationship of the huge left para-aortic lymph nodes with other abdominal structures. A – Abdominal Aorta, S – Stomach, PLN – Left Para-aortic Lymph Node, LK- Hydronephrotic Left Kidney.

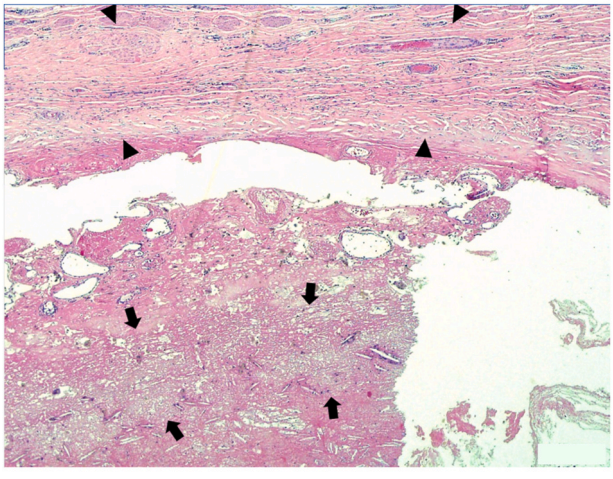

Fig. 3. Fibro collagenous cyst wall (arrowhead) devoid of epithelial lining and mostly covered by fibrin, hemosiderin laden macrophages and necrotic debris (arrow). These areas are negative for SALL4 and PLAP.

3. Discussion

Testicular carcinoma, an extremely rare urological malignancy, usually occurs among men in the 20–34 years old age group [2,3]. Most patients with testicular carcinoma will present with testicular discomfort or swelling which would initially be attributed to infection or inflammation such as epididymitis or orchitis (in the case of younger patients). Enlarged lymph nodes at the inguinal and supraclavicular region with a retroperitoneal mass are commonly associated with this condition.

Risk factors for the development of testicular carcinoma include cryptorchidism, germ cell neoplasia in situ, previous history of testicular malignancy, testicular dysgenesis syndrome, and hypospadias. As many as 10% of mal-descent testis have been reported to be associated with testicular cancer and are 5–10 times more common than those not affected [5–8].

Although the patient's left undescended testis condition had existed since his childhood, he (or his family) had not sought any particular treatment. He first became aware the progressive swelling in the left testicular and the intermittent testicular discomfort four years earlier. Corrective surgery on the ectopic testis should ideally be performed soon after diagnosis or preferably before puberty to hinder germ cell insult and risk of malignant transformation [9]. His initial screening tests revealed a raised β-hCG level and LDH which were consistent with malignant germ cell tumour (GCT). Although β-hCG is commonly elevated in testicular carcinomas, it could also be raised in both seminomatous and non-seminomatous tumours (Table 1). Normal serum markers levels do not exclude presence of testicular carcinoma.

In patients with seminoma with elevated β-hCG >1,000IU/L, the possibility of non-seminomatous tumours should be considered. Since levels of >5,000IU/L are frequently associated with brain metastases, these become useful for assessing pre and post treatment as significantly elevated β-hCG could signal a rare clinical entity choriocarcinoma syndrome – spontaneous or chemotherapy induced haemorrhage at site of metastatic disease [10].

Serum LDH, although less significant as a tumour marker as compared to AFP and β-hCG, plays a role in staging and prognostication [10,11]. LDH, a metabolic enzyme that is expressed in almost all tissues, catalyses the conversion of pyruvate and lactate during glycolysis and gluconeogenesis, a key component of anaerobic glycolysis. LDH is elevated in many types of cancer tissue and linked to tumour growth, maintenance and invasion. Its concentration is proportional to tumour volume and elevated in 80% of patients with advanced testicular cancer. Beyer J et al. included LDH as an additional adverse prognosticator in their modern series of patients comparing initial International Germ-Cell Cancer Collaborative Group (IGCCCG) classification [12]. Progression-free survival (PFS) and overall survival (OS) at three years were significantly better in the group with lower LDH at 3-year PFS of 92% versus 80% for those with higher LDH.

Initial management of a solid testicular mass includes thorough physical examination and imaging. Serum tumour markers AFP, β-hCG and LDH should be obtained as baselines prior to any intervention, as was in the case of our patient. *Trans*-scrotal ultrasound with Doppler should be performed if testicular cancer is suspected as this would help differentiate between intra-testicular or extra-testicular in origin [13]. Any testicular solid lesion with elevated tumour markers should be considered as malignant until proven otherwise. Testicular GCT is typically heterogenous, hypoechoic and vascular on ultrasonography. Appropriate radiological imaging to assess for distant metastases to the brain, chest, abdomen and pelvis should be performed.

When our patient was initially presented to us four years before, he had metastatic left testicular seminoma as evidenced by raised β-hCG, LDH, and normal AFP coupled with a huge left para-aortic lymph node. Due to the distribution and bulk of the disease, he was referred to oncology for BEP chemotherapy since delaying systemic therapy would have outweighed the benefit of tissue diagnosis, which was in accordance with our current guidelines [15,16]. Treatment options in patients with metastatic seminomatous GCT include radiotherapy (RT) consisting of 36Gy target doses to para-aortic and extended to ipsilateral iliac lymph nodes against three cycles of BEP chemotherapy regime [14,17]. Although both RT and chemotherapy have been reported as effective in both stages, long-term toxicity is more frequent and of concern following RT.

For patients who present with testicular mass which biochemically or radiologically indicates malignancy, radical inguinal orchidectomy with the division of spermatic cord at internal inguinal ring would form the primary treatment option [14,17]. Our patient four years earlier had been scheduled for consolidative orchidectomy after completion of systemic therapy with three cycles of BEP regime. Unfortunately, he defaulted after only one chemotherapy cycle and did not complete his treatment cycle.

However, despite receiving only one cycle of BEP, he returned three years after that initial treatment with normal tumour markers but with a huge left testicular mass and substantial left para-aortic lymph node. Due to the limited resources available at our centre, fluorodeoxyglucose-Positron emission tomography (FDG-PET) scan could not be conducted to ascertain tissue viability of the left para-aortic lymph node. Small to no safety window was available for computed-tomography (CT) guided biopsy of the left para-aortic lymph node. We then proceeded with radical orchidectomy without retroperitoneal lymph node dissection (RPLND) since our patient did not consent to the significant surgical morbidities due to the bulky residual tumour, post chemotherapy fibrosis and possible post operative complications such as ejaculatory failure and subsequent fertility, lymphocele and renovascular injury.

Compared to non-seminoma, residual mass post chemotherapy in seminoma needs to be further investigated with regards to the viability of cancer cells within the residual tumour. It should not be resected but rather guided by adequate radio-imaging and tumour markers. Patients with residual mass of less than 3cm after chemotherapy could be observed without further intervention as these lymph nodes may represent benign fibrotic lesions [18–23]. For patients with residuals of more than 3cm, FDG-PET scan should be performed six weeks post chemotherapy to ascertain any persistent viable or metabolically active disease. Tissue biopsy may be offered as an alternative whereas for those with actively progressive disease, salvage therapy would be indicated such as chemotherapy or RT.

Post operative abdominal wall complications including incisional hernia in male and female patients are established complications after

Table 1
Tumour markers, age group and prognosis of germ cell tumours (GCTs).

Type	Tumour Marker		Age Group	Prognosis
	β-hCG (Normal value: <5mIU/mL) (% rise on presentation)	AFP (Normal value: <10ng/mL) (% rise on presentation)		
Seminoma	10–20%	Pure seminoma does not secrete	35–45yr	5-year PFS: 79–89% 5-year survival: 88–95%
Nonseminoma (nonseminomatous germ cell tumour)	40–60%	50–70%	20–35yr	5-year PFS: 54–96% 5-year survival: 67–96%

*PFS: Progression-free survival.

urological operation [24,25]. A major challenge faced by our patient was abdominal wall closure consequent from the huge defect post orchidectomy. To reduce the risk of incisional hernia, we placed a 30cm × 30cm sublay mesh prophylactically to strengthen the posterior abdominal wall. The Rives-Stoppa technique in sublay placement offers even tension distribution, no cutaneous or visceral exposure, and intra-abdominal pressure resistance. Sublay mesh placement has been shown to have a low recurrent hernia incidence rate of 5% [26–29].

Although relatively rare, testicular tumour is a typical example of a curable tumour and good prognosis with seminomatous type. If he had not defaulted on his consolidative orchidectomy post completion chemotherapy treatment, with the disease confined to Stage II (infra-diaphragmatic lymphadenopathy), his 5-year survival rate and progression-free survival (PFS) post orchidectomy would have been relatively higher at 95% and 89% respectively [17,30]. The initial chemotherapy had played a significant role in disease control in our patient as evidenced by his regressing cyst and para-aortic nodule, normal β-hCG level, and yielding of necrotic tissue from the left supra-renal mass on endoscopic guided ultrasound biopsy.

In accordance to current guidelines, our decision to excise the primary tumour post induction chemotherapy was due to local tumour growth despite a substantial decline in his tumour markers. There is a high probability that the initial induction with only one cycle of BEP chemotherapy had been significant in confining the disease for three years even though the patient had defaulted on his complete treatment cycle.

Although any case of partial response seminomatous testicular carcinoma has yet to be reported, incidences of 'burned-out' testicular GCT or spontaneous tumour regression [31–33] have been documented. Rita and Budak et al. reported the case of primary testicular GCT and normal tumour markers of their patient who underwent radical orchidectomy. Histopathological examination however revealed no evidence of GCT or total regression. 'Burned-out' GCT or spontaneous tumour regression is not usually related to the progression of cancer; it is instead partial or complete regression without any treatment. This phenomenon is extremely unusual and often challenging since they lack molecular sequencing.

Subsequent follow up treatment for our patient involves frequent interval monitoring of serum tumour markers and abdominopelvic CECT, focusing on the residual left para-aortic lymph node (Table 2). PET scanning is useful in persistently enlarging mass to identify evidence of active tumour. When PET is unavailable, residuals of >3cm can be biopsied, resected or monitored until resolution or progression [31]. Presence of active viable tumour would necessitate further treatment such as retroperitoneal lymph node dissection (RPLND) or salvage chemotherapy (or radiotherapy for those who were not administered this initially) [16,27].

4. Conclusion

Testicular carcinoma is a rare malignancy among men and afflicts mostly males in the younger age groups. Early identification of malignancy and immediate initiation of chemoradiotherapy would usually yield positive patient outcomes. The chemosensitivity of seminomatous type tumour to a platinum-based regiment in combination with radical resection leads to good prognosis and effective local disease control.

4.1. Patient's perspective

I am very grateful to the team of urologists, radiologists, oncologists and anaesthetists for their excellent teamwork in the management of my critical situation. I am fortunate that the testicular cancer did not metastasise to any other parts of my body apart from being localised below the diaphragm. The best news for me is the tumour has regressed after one cycle of chemotherapy treatment. I feel this is a second chance given by God for me to continue the follow-up treatment sessions diligently and to heed my doctors' advice.

Table 2
Minimal follow-up post adjuvant treatment or complete remission for advanced testicular carcinoma.

Investigation	Year 1	Year 2	Year 3	Year 4 & Year 5
Tumour markers - β-hCG, AFP, LDH	4 times	4 times	2 times	2 times
Chest x-ray	1-2 times	Once	Once	Once
CT Thorax, Abdomen, Pelvis (CT-TAP)	1-2 times	Once	Once	Once at 60 months

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Provenance and peer review

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Please state any conflicts of interest

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Ethical approval

This case report does not need any ethical approvals.

Consent

Informed and written consents were obtained from the patient and parents involved.

Author contribution

Dr Tien Chuen Chew, Dr Suriaraj Karppaya, Dr Shankaran Theverajah and Dr Huan Lee Tan were the clinicians involved in the management of the patient.

They are the co-authors for this manuscript as well with Dr Boon Tat Yeap and Dr Raja Mohd Syahmi bin Raja Othman.

Registration of research studies

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Guarantor

BOON TAT YEAP.

Declaration of competing interest

The authors declare that no relevant or material financial interests exist.

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Appendix A. Supplementary data

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