Case Report

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Pathology Section

Pure Embryonal Cell Carcinoma: A Rare Entity

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ABSTRACT

Malignancy of the testes constitutes only one percent of all male cancers. Most testicular malignancies are Germ Cell Tumours (GCTs), which are broadly categorised into seminomatous and non-seminomatous types. Non-seminomatous GCTs are further classified into several subtypes based on their histopathological features. This case report presents a case of Pure Embryonal Cell Carcinoma (PECC) of the testes in a 32-year-old male. The diagnostic work-up involved a detailed medical history, physical examination, and imaging tests, including a scrotal ultrasound and Positron Emission Tomography-Computed Tomography (PET/CT) scan. These tests helped identify a testicular mass without metastasis. Additionally, serum tumour markers such as Alpha Fetoprotein (AFP), human chorionic gonadotropin, and lactate dehydrogenase were elevated, further confirming the presence of testicular malignancy. The management of the patient included surgery and chemotherapy. Histopathology and immunohistochemistry were performed, resulting in a diagnosis of pure embryonal carcinoma. This case highlights the significance of timely diagnosis and prompt management in improving the prognosis of patients with PECC.

Keywords: Germ cell tumour, Metastasis, Testicular tumour

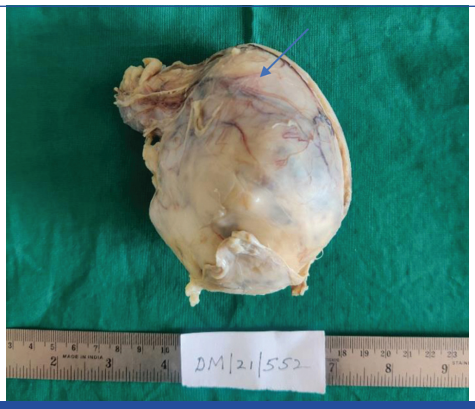
CASE REPORT

A 32-year-old male patient visited the clinic with a complaint of a painless mass in his right testicle for six months. The patient reported no other symptoms and had no noteworthy personal or family history. On physical examination, a firm, tender, non-transilluminating mass was felt in the right testis. The left testis appeared normal. The serum tumour markers were elevated as shown in [Table/Fig-1].

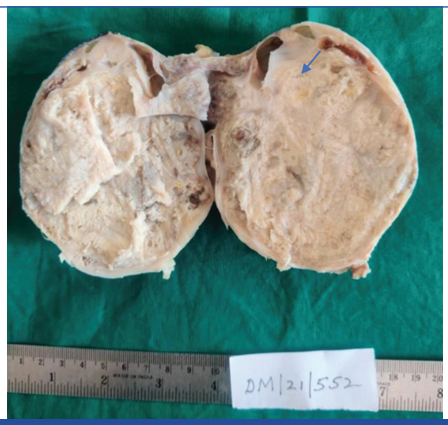
S. No.	Tumour markers	Test value	Normal value
1	Lactate dehydrogenase	1934 IU/L	105-333 IU/L
2	Alpha Fetoprotein (AFP)	363 ng/mL	0-40 ng/mL

[Table/Fig-1]: Values of serum tumour markers.

A scrotal ultrasound was performed, revealing a solid right testicular mass measuring 10 cm in diameter with areas of necrosis and calcification. The mass appeared highly suspicious for malignancy. Several enlarged lymph nodes were observed, but they were reactive in nature. A PET-CT scan was conducted, which indicated carcinoma of the testis without metastasis. The patient underwent a right inguinal high orchidectomy, and the specimen was sent for histopathology. Gross examination revealed a testicular tumour measuring 7.3×6.4×6 cm in the right testis. The external surface appeared enlarged and congested, as shown in [Table/Fig-2]. The cut section displayed a soft grey, white to tan mass with haemorrhage and necrosis, as shown in [Table/Fig-3]. Histopathological analysis confirmed a diagnosis of primitive embryonal carcinoma of the right testis. The tumour consisted of undifferentiated cells with large nuclei, prominent nucleoli, and scanty cytoplasm. The tumour cells were arranged in solid sheets, pseudo-glandular, alveolar, and tubular-papillary patterns. Numerous mitotic figures were present. These cells exhibited pleomorphism, hyperchromatic nuclei, large nucleoli, and ambiguous cell boundaries with nuclear overlapping. Areas of necrosis were also observed, as shown in [Table/Fig-4,5]. No areas of yolk sac tumour, teratoma, or seminoma were identified. Immunohistochemical staining showed positivity for OCT-4 and CD30, supporting the diagnosis of primitive embryonal carcinoma. Staging was performed according to the American Joint Committee on Cancer (AJCC) staging system, classifying it as pT1N0M0 [1].

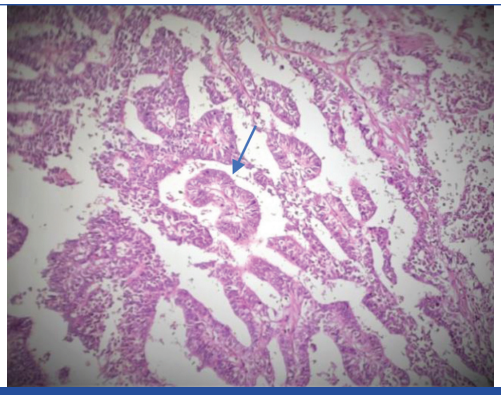


[Table/Fig-2]: Gross specimen consisting of right testicular mass measuring 7.3×6.4×6 cm. The external surface was congested.

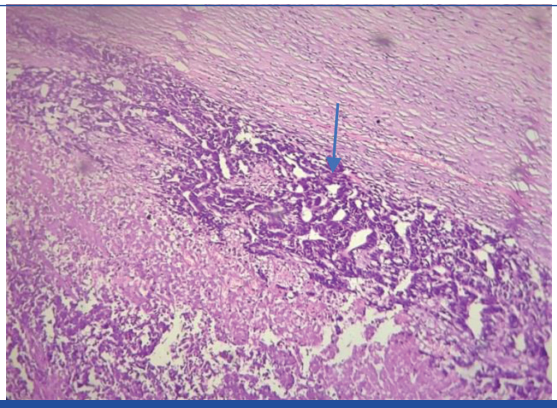


[Table/Fig-3]: Cut section showed grey, white to tan areas with haemorrhage and necrosis.

The patient underwent four cycles of chemotherapy with the Bleomycin, Etoposide, and Cisplatin (BEP) regimen. Follow-up scrotal ultrasound and CT scans of the pelvis, abdomen, and chest were conducted, revealing no residual disease or metastasis. The patient was regularly followed-up every three months with physical examination, tumour markers, and imaging studies. The treatment was well-tolerated, and there was no evidence of disease recurrence during the 12-month follow-up period.



[Table/Fig-4]: Arrangement of tumour cells in solid sheets of pseudo glandular, alveolar, and tubular-papillary patterns (10x H&E).



[Table/Fig-5]: The tumour comprised of undifferentiated cells with large nuclei, prominent nucleoli, and scanty cytoplasm (10x H&E).

DISCUSSION

Malignancy of the testes is a relatively infrequent cancer that affects males, with only 1% of all male cancers being testicular in nature. However, testicular cancer is commonly seen in males in their second and third decades [1,2]. Germ Cell Tumours (GCTs) are the most prevalent type of testicular cancer and can be classified into several subtypes based on their histopathological features. Testicular GCTs can be broadly categorised as seminomatous or non-seminomatous. Non-seminomatous tumours can be further classified into choriocarcinoma, yolk sac tumour, teratoma, and mixed GCTs. Combined GCTs are more common than pure GCTs. Mixed GCTs comprise two or more subtypes of GCT, while pure GCTs are exclusively composed of only one type of germ cell [3].

One such subtype is PECC, which accounts for only 1-3% of all GCTs. PECC is an aggressive tumour that arises from the undifferentiated embryonic cells of the testes. In this case report, we present a case of PECC of the testes in a 32-year-old male. This case highlights the significance of timely diagnosis and treatment in improving the outcome of patients with this rare and aggressive form of testicular cancer. Embryonal carcinoma is found as a part of 80% of mixed GCTs and is the second-most prevalent type of testicular cancer. Embryonal carcinoma is most frequently seen in men between the ages of 20 and 40. The factors that increase the risk of developing testicular malignancy are cryptorchidism and a previous history of similar illness or a family history of testicular tumours [3-5].

Like any other oncological disease, testicular tumours are formed due to complex interactions among genetic, environmental, and hormonal risk factors. The multiple-hit hypothesis plays a crucial role in the malignant transformation and development of testicular cancer. The hallmark of most invasive GCTs is the alteration in the short arm of chromosome 12 [6,7]. Embryonal carcinoma is relatively rare (10.8%) among pure Testicular Germ Cell Tumours (TGCTs). However, in mixed TGCTs, embryonal carcinoma is the most common histological element (80.4%). Pure embryonal carcinoma more frequently affects younger males in their twenties and thirties, with a median age at diagnosis of 15 years. Embryonal carcinoma is quite uncommon in the ovary [7-9].

Embryonal carcinoma is an aggressive tumour and is associated with early metastatic spread [10]. Besides metastasis, the prognosis of a patient with embryonal carcinoma also depends on factors such as location, post-orchiectomy levels of tumour markers (AFP >10,000 ng/mL, beta-hCG >50,000 IU/L, LDH >10 times the upper limit of normal). While apoptotic particles, extensive necrosis, and single-cell necrosis draw attention, the prognosis is not dependent on the histological pattern [11].

The management of PECC (Pure Embryonal Carcinoma of the Testes) poses a challenge for healthcare providers due to its rarity. The widespread use of testicular ultrasonography has led to an increased detection of tiny, non-palpable tumours compared to earlier times [12]. Histopathological analysis reveals tumour cells exhibiting various patterns, often involving multiple patterns simultaneously. The most frequently observed patterns are solid, syncytial, tubular, and tubular-papillary [13]. Tumour cells have an epithelial appearance and may exhibit significant anaplasia. They appear polygonal with thickened nuclear membranes, vesicular nucleus, dense granular cytoplasm, and clear boundaries [13,14].

The range of possible differential diagnosis for testicular tumours is extensive and includes large cell lymphoma, yolk sac tumour, and seminoma. The therapy varies greatly depending on the subtype of testicular tumour, underscoring the importance of accurately diagnosing a particular type [14]. Therefore, extensive sampling of specimens is crucial to provide a diagnosis of "pure embryonal carcinoma" and exclude the possibility of mixed germ cell neoplasia [15].

The patient complained of progressive scrotal swelling with pain. A CT scan was performed, which revealed a testicular tumour with metastasis. The patient underwent surgery, and the tumour was sent for histopathology. On histopathological examination, the tumour cells were arranged in solid, pseudo-glandular, alveolar, and tubular-papillary patterns. These cells displayed pleomorphism, hyperchromatic nuclei, large nucleoli, ambiguous cell borders with nuclear overlapping, and mitotic figures. The stromal component showed squamous metaplasia. Areas of necrosis and haemorrhage were observed, while the surrounding areas exhibited fibrosis and adipose tissue. Multiple tissue samplings were performed to rule out the presence of other GCT components since mixed GCT is more frequent than pure GCT. However, no other GCT component was identified.

The diagnosis of PECC is based on the morphological features observed during histopathological examination of the testicular tissue obtained from orchiectomy. PECC is characterised by undifferentiated malignant cells that resemble the embryonic cells of the testis. The tumour cells showed positive staining for Placental Alkaline Phosphatase (PLAP) and CD117, which are specific markers for GCTs. The presence of these markers, along with characteristic histopathological features, helps differentiate PECC from other subtypes of GCTs [16,17].

The treatment for PECC involves a multimodal approach, including surgery, chemotherapy, and radiation therapy. Radical orchiectomy is the primary treatment for localised PECC. The purpose of the surgery is to remove the entire tumour and any potential metastatic lesions. Adjuvant chemotherapy is administered after surgery to minimise the risk of recurrence and metastasis. The most commonly used chemotherapy regimen for PECC is the BEP regimen. Radiation therapy is reserved for cases with residual disease after surgical intervention and chemotherapy or in cases with metastatic lymph nodes [18,19].

Patients with pure embryonal carcinoma have a better prognosis than those with mixed GCTs. The prognosis for PECC depends on the stage of the disease at diagnosis, with patients diagnosed at an early stage having a better prognosis than those with advanced-stage disease. PECC is associated with a high-risk of recurrence, and patients require close follow-up after treatment to monitor for any signs of recurrence [19,20].

CONCLUSION(S)

PECC is a rare and highly malignant subtype of GCT that affects young males. The diagnosis of PECC is based on histopathological examination, which shows undifferentiated malignant cells that stain positive for PLAP and CD117. Treatment for PECC typically involves radical orchiectomy followed by adjuvant chemotherapy. Since a localised malignant tumour has a higher probability of being cured than a metastatic malignancy, detecting it at an earlier stage is the most significant factor that determines the survival and outcome of cancer patients.

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