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CASE REPORT

A RARE CASE REPORT OF MIXED GERM CELL TUMOR (SEMINOMA, EMBRYONAL CARCINOMA, YOLK SAC TUMOUR AND IMMATURE TERATOMA) OF TESTIS

Ashok M. Patil[1], Sayeed M. Yendigeri[2], Mohammad Arifulla K[3], Nadia Shafi[4], Sarita Nair[5]

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ABSTRACT: Germ cell tumors occur at all ages. The tumors are identified as pure form (those of one histologic type) and mixed form (more than one histologic type). Over half of germ cell tumors consist of more than one cell type, requiring appropriate sampling for the correct diagnosis and correlation with the serum tumor markers & immunohistochemistry. We report a case of mixed germ cell tumour of testis in a 28-year-old male who presented with right sided scrotal swelling since 6 months associated with loss of appetite and weight. Trans- illumination positive, fluctuation positive. No engorged veins. Penis & opposite scrotum - normal. No gynaecomastia or cryptorchidism was noticed clinically. Alpha-Fetoprotein (AFP) and beta-HCG values were found to be abnormal. USG of the scrotum revealed a right sided testicular mass. The CT scan of abdomen and pelvis was normal. The patient underwent right-sided high orchidectomy. Grossly, grey white to yellow enlarged testicular mass measuring 10 X 6 X 5 cm, firm-to-hard in consistency was found. Cut-section revealed a variegated mass of solid and cystic areas with hemorrhage and necrosis. Microscopically,a mixed germ cell tumor with seminoma, embryonal carcinoma, yolk sac tumor and immature teratoma & syncytiotrophoblast components was found. Immunohistochemistry showed immuno-positivity for PLAP, CD 117, Alfa feto-protein (AFP) and OCT 3/4, betaHCG, confirming the diagnosis of Mixed Germ cell tumour.

KEYWORDS: Testicular mixed germ cell tumor, classical seminoma, with syncytiotrophoblastic cells, embryonal carcinoma, yolk sac tumour and immature teratoma.

INTRODUCTION: Testicular mixed germ cell tumours are composed of two or more types of germ cell tumours. They are considered to be part of non-seminomatous germ cell tumours, as it is that component which dictates prognosis and treatment.

- Overall they account for over 10% of all testicular cancers (15% of all testicular germ cell tumours which account for 90% of all testicular cancers).[1]
- Epidemiology, clinical presentation and radiographic features will therefore reflect the underlying components. Similarly treatment and prognosis will be dictated by the the most malignant component.
- Testicular neoplasms are divided into two major categories: germ cell tumors and sex cord–stromal tumors. Approximately 95% of testicular tumors arise from germ cells. Germ cell tumors are subdivided into seminomatous and non-seminomatous germ-cell tumor (NSGCT) types. The non-seminomatous tumors may be composed of undifferentiated cells that resemble embryonic stem cells, as in embryonal carcinoma, but can differentiate into various lineages generating yolk sac tumors, choriocarcinomas and teratomas.[2]

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- Mixed germ cell tumors contain more than one germ cell component and are much more common than any of the pure histologic forms representing 32%-60% of all germ cell tumors. The composition of these tumors varies.[3]
- Germ cell tumors may have a single tissue component, but in approximately 60% of cases, contain more than one tumor type: seminoma, embryonal carcinoma, yolk sac tumor, polyembryoma, choriocarcinoma and teratoma. The age of the patient provides a clue to the most likely type of tumor present. Most germ cell tumors occur between the ages of 20 and 50 years. Before puberty, seminoma is extremely uncommon, while yolk sac tumor and the better differentiated types of teratoma are the usual germ cell tumors. Spermatocytic seminoma and malignant lymphoma usually occur in older patients, although both may also occur in younger individuals.[4]
- Testicular mixed germ cell tumor, having classical seminoma, with syncytiotrophoblast cells, embryonal carcinoma, yolk sac tumour, immature teratoma is quite rare.

CASE REPORT: A 28 years old male presented with history of right-sided scrotal swelling since 6 months. It was a right sided painless swelling which was progressively increasing in size. It was associated with history of loss of appetite and weight. General Physical, & systemic examination and vital parameters were normal. On local examination, a large right -sided scrotal swelling was found. Trans- illumination positive, fluctuation positive. No engorged veins, Penis & Opposite scrotum - normal. The scrotal skin was normal. Gynaecomastia or cryptorchidism was not seen clinically. Per-abdominal examination did not reveal any abnormality. Virchow's nodes were negative. Serology was carried out which showed increased levels of serum Alpha-Fetoprotein (AFP): 1805 ng/ml, Beta-HCG: 512 IU/ml. USG of the scrotum revealed a large right sided testicular swelling measuring 10 X 6 X 5 cm consisting of solid and cystic areas. The vasculature was normal. The Chest X-Ray and CT scan of abdomen & pelvis were normal. The patient underwent right-sided high orchidectomy. On gross pathological examination, a solitary, un-encapsulated grey black to yellow enlarged testicular mass was found measuring 10 X 6 X 5 cm, firm to hard in consistency [Fig. 1(a)]. The cut-section revealed a variegated mass of solid and cystic areas punctuated by foci of haemorrhage and necrosis [Fig. 1(b)].

Histopathology studies showed the mixed germ tumor containing components 1) seminoma with syncytiotrophoblast component, 2) embryonal carcinoma, 3) yolk sac tumor and 4) immature teratoma.

Embryonal carcinoma (EC) was characterized by large anaplastic cells, with hyperchromatic nuclei, prominent nucleoli, amphophillic cytoplasm & increased atypical mitosis [Fig. 1(e)].

Yolk sac tumor (YST) was characterized by medium sized cuboidal and elongated cells with small nuclei, forming papillary visceral and parietal layers of cells (Schiller-Duval Bodies) [Fig. 1(c)].

Immature teratoma (IT) composed of neuro-epithelium, immature glandular epithelium and immature mesenchyme [Fig.1 (d)].

The other areas show classical seminoma with syncytiotrophoblast component [Fig. 1(f)].

Immunohistochemical studies were performed which exhibited immune-positivity for CD 117 / PLAP for seminoma and OCT 3 / 4 [Fig. 2 (d)] & alpha-feto protein emphasizing yolk sac tumor [Fig. 1 (b)] and beta HCG for syncytiotrophoblastic cells [Fig. 2 (c)]. CD30, cytokeratins, for Embryonal carcinoma [Fig. 2 (a)]. The patient underwent adjuvant chemotheraphy and he has survived without any evidence of recurrence or metastasis for last 3 years of follow up.

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DISCUSSION: Mixed germ cell tumors contain more than one germ cell component are much more common than any of the pure histologic forms representing 32%-60% of all germ cell tumors. Minor foci of yolk sac tumor are common, although it is usually overshadowed by other components, such as embryonal carcinoma. The average age of presentation for patients with mixed germ cell tumors is 30 years.

Embryonal carcinomas usually occur admixed with other germ cell tumor types. The combination of positivity for placental alkaline phosphatase and negativity for epithelial membrane antigen can assist in the distinction of embryonal carcinomas from somatic carcinomas.

AFP is normally synthesized by fetal yolk sac and also the liver and intestine. It is elevated in 50-70% of testicular germ cell tumors and has a serum half-life of 4-5 days.[4][5]

In embryonal carcinoma (EC), the expression of this cytokine receptor has been demonstrated only by immunohistochemistry. Testicular germ cell tumors with EC differentiation have been described to react with the CD30 antibodies Ki-122 and Ber-H2.[6]

The immune reactivity of germ cell tumors for PLAP was as follows: 98% of cases with seminomatous elements were PLAP positive. 21% of pure embryonal carcinomas (EC), 25% of EC components in mixed tumors, all yolk sac tumour (YST) components, 20% of pure teratomas (T) and 47% of T components were AFP positive.[7] In EC and YST the immunohistochemical staining depicted characteristic previously unrecognized histological structures, presumably representing patterns of further differentiation.[8]

The most frequent combination is that of embryonal carcinoma, yolk sac tumor, teratoma, and choriocarcinoma, which constitutes 14% of testicular germ cell tumors. Choriocarcinomas are highly malignant and carry a poor prognosis. Grossly, they are small, red-brown, friable lesions with extensive hemorrhage and necrosis. Microscopically, choriocarcinomas contain both multinucleated syncytiotrophoblasts and polygonal cytotrophoblasts. The syncytiotrophoblasts stain positively with human chorionic gonadotropin (HCG). Intratubular germ cell neoplasia, unclassified type, represents the common precursor to most testicular germ cell neoplasms. The majority of germ cell neoplasms stain positively with placental alkaline phosphatase (PLAP) and negatively with epithelial membrane antigen (EMA).[9]

Non-seminomatous germ cell tumors, including mature and immature teratomas, have a varigated appearance and often display hemorrhage and necrosis. These tumors are biologically more aggressive and radioresistant. These tumors still carry a relatively high rate of remission with aggressive chemotherapy, including 60-75% remission with clinical stage III disease. The histologic subtype does not influence prognosis. Biologic markers, including AFP, HCG, PLAP, and lactate dehydrogenase (LD) are valuable in continued follow up of the patient.[10]

CONCLUSION: Mixed Germ Cell Tumors of the testis are rather rare and most commonly occur in young men. It continues to be diagnostically challenging issue, as its biological behavior, clinical management and prognosis vary with its different histological elements. Therefore accurate pathological diagnosis is essential and immunohistochemistry plays an important role in the diagnosis and differential diagnosis of various elements of testicular MGCT. In the present case, the immunohistochemistry for CD30, AFP, cytokeratin and placental alkaline phosphatase was helpful to accentuate each GCT component.

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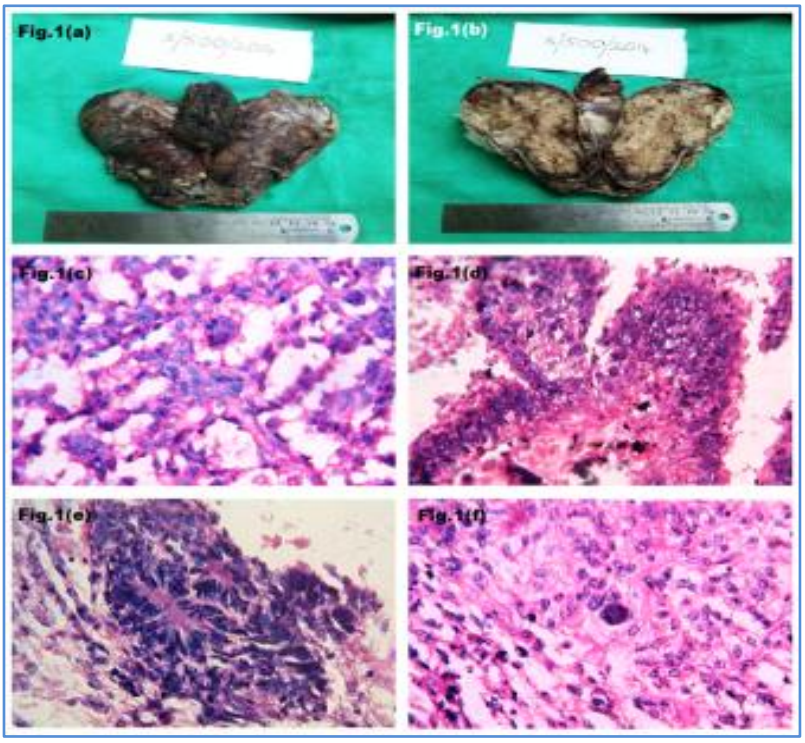

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Fig. 1 (a): Gross-External surface showing a solitary, un-encapsulated grey black to yellow enlarged testicular mass measuring 10 X 6 X 5 cm.
Fig. 1 (b): Gross-Cut section showing yellowish, variegated right testicular mass.

Fig. 1 (c): Photomicrograph under H&E stain (x45) of yolk sac tumour showing (YST) showing medium sized forming papillary visceral and parietal layers of cells (Schiller-Duval Bodies).

Fig. 1 (d): Photomicrograph under H&E stain (x45) of Immature teratoma (IT) showing neuro-epithelium, immature glandular epithelium and immature mesenchyme.

Fig. 1 (e): Photomicrograph under H&E stain (x45) of embryonal carcinoma (EC) showing large anaplastic cells forming embryoid bodies.

Fig. 1 (f): Photomicrograph under H&E stain (x45) of classical seminoma with syncytiotrophoblast component.

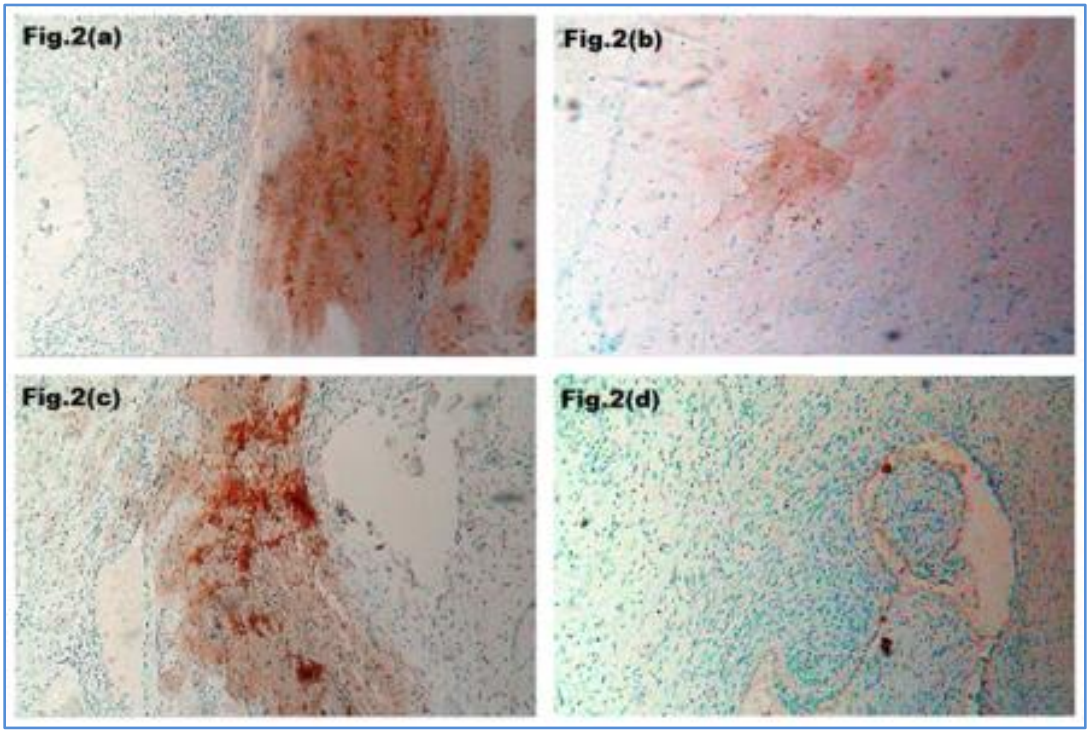

Fig. 2 (a): Photomicrograph under IHC stain (x45) CD30 +ve tumor cells.

Fig. 2 (b): Photomicrograph under IHC stains (x45) AFP +ve tumor cells.

Fig. 2 (c): Photomicrograph under IHC stains (x45) B-HCG +ve tumor cells.

Fig. 2 (d): Photomicrograph under IHC stain (x45) CD117+ve tumor cells. OCT 3/4

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AUTHORS:

1. Ashok M. Patil
2. Sayeed M. Yendigeri
3. Mohammad Arifulla K.
4. Nadia Shafi
5. Sarita Nair

PARTICULARS OF CONTRIBUTORS:

1. Professor & HOD, Department of Pathology, Al Ameen Medical College, Vijayapur.
2. Associate Professor, Department of Pathology, Al Ameen Medical College, Vijayapur.
3. Assistant Professor, Department of Pathology, Al Ameen Medical College, Vijayapur.
4. Post Graduate, Department of Pathology, Al Ameen Medical College, Vijayapur.
5. Post Graduate, Department of Pathology, Al Ameen Medical College, Vijayapur.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Ashok M. Patil,
Professor & HOD,
Department of Pathology,
Al Ameen Medical College,
Vijayapur-586108,
Karnataka.
Email: ashokmp8@gmail.com

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