Case Report

Primitive neuroectodermal tumor in a mixed germ cell tumor - A rare case report

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ABSTRACT

A rare case of testicular tumor in a 20-year-old male with Primitive Neuroectodermal Tumor (PNET) was reported. Imaging studies showed a large heterogenous mass in the right scrotal sac and a large retroperitoneal mass with metastasis in the lung and liver. Serum alpha fetoprotein (AFP) was markedly elevated with moderate increase in serum β-human chorionic gonadotropin (hCG) levels. After orchidectomy, a histological diagnosis of mixed germ cell tumor-teratoma with primitive neuroectodermal, embryonal, and yolk sac components was made. Some scattered embryoid bodies representative of primitive germ cell tumor were also present. Morphological diversity including PNET prompted the authors to report this case as PNET points toward a poor prognosis.

Key words: Mixed germ cell tumor, primitive neuroectodermal tumor, teratoma

INTRODUCTION

Mixed germ cell tumor (MGCT) of the testis is the second most common testicular germ cell tumor (GCT) next to seminoma.[1] A varied combination of neoplastic elements in MGCT can occur; teratoma with embryonal carcinoma (EC) being the commonest.[2] Teratomas may show partial transformation into malignant somatic type tumors and are classified as "teratomas with somatic type malignancy (TSMC)".[3]

A rare case of MGCT of right testis in a young male is reported. The tumor comprised teratoma with somatic type malignancy (PNET)-50%, EC-25%, yolk sac tumor (YST)-25%, with syncytiotrophoblasts and embryoid bodies. This patient was in Stage IV at the time of presentation as the tumor had already metastasized to the liver and lungs.

CASE REPORT

A 20-year-old male presented with swelling of right scrotal sac for seven months and a lump in the abdomen for one month duration. On examination, the right testis was enlarged measuring 12 × 5cm, hard in consistency, and tender on palpation. In addition, there was an abdominal lump in the epigastrium, measuring12 × 8 cm, which was hard in consistency, not tender, not moving with respiration, and non-ballotable. Bilateral inguinal lymphadenopathy was also present.

Contrast-enhanced computed tomography scan (CECT) of abdomen confirmed a large heterogenous mass in the right scrotal sac with few specks of calcification and hemorrhage. A lymph node mass of size 9.3 × 8.3 × 9.3 cm in the right paracentral region compressing the right inferior vena cava and right ureter causing hydronephrosis of the right kidney was observed. A hypodense lesion in the liver measuring 1.5 × 1 cm in segment IV, suggestive of metastasis was also reported [Figure 1]. CECT of chest showed three well-defined parenchymal lesions in the right lung, the largest measuring 2.2 × 1.9 cm, suggestive of metastasis [Figure 2]. Serum AFP level was markedly elevated (3786ng/ml). Serum lactate dehydrogenase (LDH) and β-human chorionic gonadotropin (hCG) were 1136U/L and 186mIU/ml, respectively.

The patient underwent radical orchidectomy. The excised specimen measured 12 × 8 × 8cm and the testis was completely replaced by tumor tissue. The cut surface had a variegated appearance consisting of intermixed firm and soft areas along with areas of hemorrhage and necrosis. The firm areas had a glistening, mucoid appearance. Tunica

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albuginea was found to be adherent to the underlying mass in many areas [Figure 3]. Spermatic cord could not be identified in the specimen.

Microscopically, 50% of the tumor comprised a variety of teratomatous elements including nodules of cartilage, glands lined by mucus-secreting columnar epithelium, squamous islands, adipose tissue, skeletal as well as smooth muscle, and undifferentiated mesenchymal tissue. Multiple thyroid follicles, adjacent to the tunica albuginea were also observed[Figure 4]. Immature neuroepithelial tissue composed of small, round blue cells with high nucleo-cytoplasmic ratio and inconspicuous nucleoli arranged in rosette-like pattern, suggestive of PNET was present. On immunohistochemistry, these cells were positive for neuron-specific enolase (NSE), synaptophysin, S100, and cytoplasmic Wilms tumor 1(WT1) and negative for CD99, confirming the presence of PNET. Interspersed amidst the teratomatous component were embryonal carcinoma (EC) and YST, each covering 25% of the tumor area. Nodules of EC with prominent zones of necrosis showed tumor cells in glandular and solid patterns. Large multinucleate syncytiotrophoblastic giant cells were scattered in the EC areas and were negative for β-hCG immunostaining. These tumor cells and syncytiotrophoblastic giant cells were positive for CD30. Most of the areas of YST demonstrated a reticulo-microcystic pattern. Areas of endodermal sinus pattern with Schiller Duval bodies, enteric YST, and even sarcomatoid YST were present. Embryoid bodies showing a central core of EC cells, associated with an amnion-like cavity lined by flattened cells on one side and YST showing a reticulo-microcystic pattern on the other side were also observed [Figure 5]. A diagnosis of MGCT composed of TSMC-PNET (50%) with EC (25%) and YST (25%) was made.

Postoperatively, the patient received chemotherapy. Retroperitoneal lymph node dissection could not be performed because of the close proximity to large vessels and reluctance of the patient at the time of informed consent. The

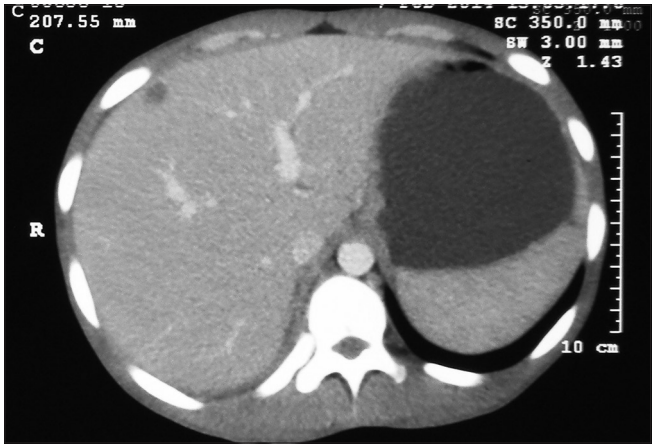

Figure 1: CECT Abdomen showing hypodense lesion measuring 1.5 x 1 cm in segment IV of liver suggestive of liver metastasis

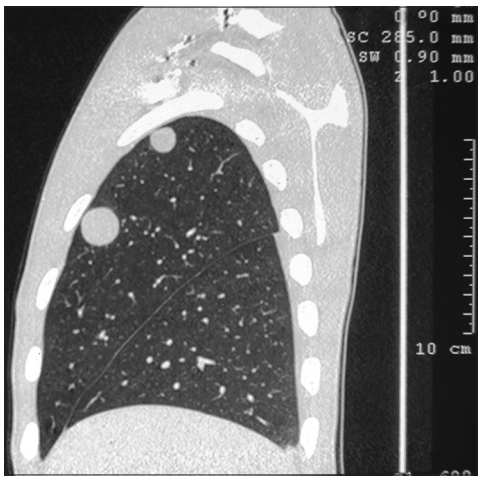

Figure 2: CECT chest showing two well-defined parenchymal lesions in right lung with smooth margins, largest measuring 2.2 x 1.9 cm suggestive of lung metastasis

Figure 3: Gross examination - completely replaced right testis by tumor, having a variegated appearance with intermixed firm areas having a glistening, mucoid appearance, and soft areas, along with areas of hemorrhage and necrosis

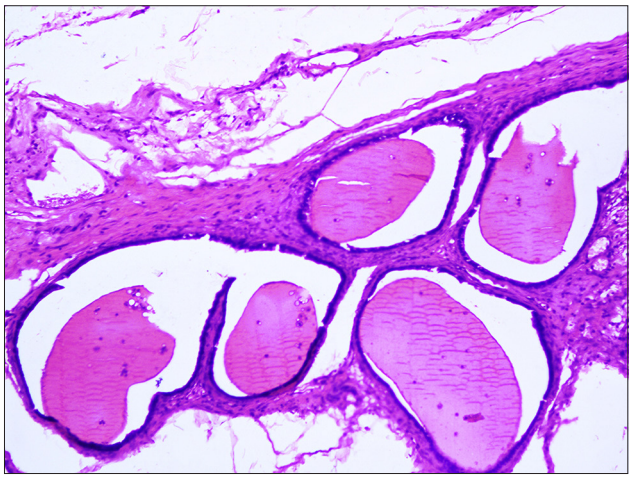

Figure 4: Photomicrograph showing thyroid follicles at the periphery of the tumor (H and E ×10)

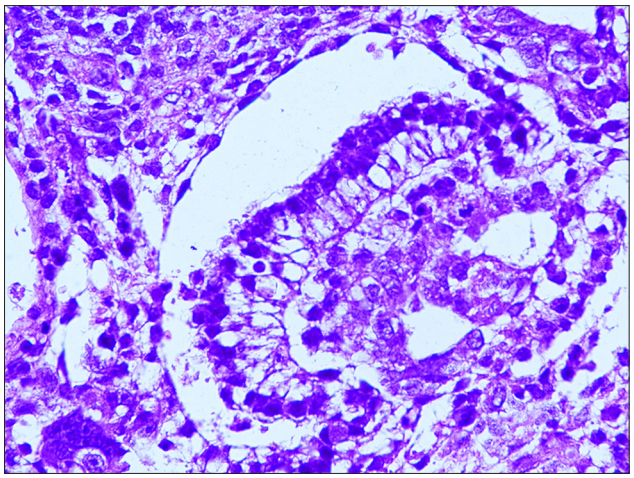

Figure 5: Photomicrograph showing embryoid body (H and E ×40)

size of the retroperitoneal mass increased steadily despite four cycles of chemotherapy. The patient is presently on follow up.

DISCUSSION

Testicular neoplasms comprise 1% of all the tumors in males, of which 94 – 96% are GCTs.[1] MGCTs constitute 40 – 45% of all testicular GCTs[3] and 69 – 91% of non-seminomatous GCTs (NSGCTs).[2] Excluding seminomas, a combination of different neoplastic types rather than pure forms are more commonly reported in the literature.[4] Therefore, to arrive at a correct diagnosis, appropriate sampling and correlation with serum tumor markers is mandatory.[1] Serum AFP and β-hCG elevations occur in 60 and 55% of patients with MGCTs, respectively.[5] Serum elevation of β-hCG indicates the presence of syncytiotrophoblastic cells in the tumor, whereas the elevated AFP levels are observed in YST.[5] Our patient had markedly elevated serum AFP because of the YST component along with moderate elevations in β-hCG because of the presence of syncytiotrophoblasts.

Mixed germ cell tumors are characteristically variegated on gross appearance with cystic and solid areas indicating the various components, as was also observed in the present case. Ideally, at least one section per centimeter of tumor with inclusion of differently appearing areas is a must to make a correct histopathological diagnosis.[1]

An estimate of the relative proportions of various components is important as is of immense prognostic value. Teratoma is present in approximately 50% of MGCTs and EC in 87% of NSGCTs,[4] as was also seen in the present case. Tumors having both EC and teratoma are less aggressive than pure EC.[6] Component of YST is present in about 40% of MGCTs[2] and favorably alters the behavior of GCTs.[6] This was not so in the present case. Although seen in only 16% of MGCTs, choriocarcinoma is most aggressive.[4] Approximately 40% of MGCTs, especially those with a seminomatous component, contain syncytiotrophoblasts raising concern for the presence of choriocarcinoma.[7] Demonstration of cytotrophoblasts is essential to diagnose choriocarcinomatous component. Most ECs also show syncytiotrophoblasts accounting for serum β-hCG elevations in 60% of the cases.[5] Degenerating cells in EC with multinucleation and dark smudged chromatin can be differentiated from syncytiotrophoblasts by immunostaining for β-hCG. Embryoid bodies are the most immature components of teratomas[8] and were also observed in the present case.

Although teratomas are common, a malignant transformation is uncommon. Resistance of TSMC to current chemotherapeutic regimens highlights the need for its recognition.[9] The most commonly arising malignancy is a sarcoma followed by nephroblastoma and PNET.[2,9] PNET arising as a part of testicular GCTs resembles central PNET. Morphologically and immunohistochemically, PNET in our case resembled neuroblastic tumor with abundant neuropil and true rosettes as described by Ulbright *et al*.[10] Testicular GCTs with PNET metastasize or relapse more frequently than MGCT without PNET.[11] The present case also presented with metastasis to abdominal lymph nodes, the liver, and the lung at the time of diagnosis.

CONCLUSION

In conclusion, MGCT represents the entire spectrum from the most primitive GCTs (EC) to the most differentiated GCTs (teratoma).The accompanying central PNET confers a poor prognosis as evidenced by multiple metastasis in the present case at the time of first presentation.

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