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Case Report

Primary retroperitoneal choriocarcinoma with lung metastasis: Case report

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ABSTRACT

Extragonadal germ cell tumor with choriocarcinoma in males is a rare tumor. Usually, Choriocarcinoma occurs in the midline of the body, such as the retroperitoneum and mediastinum. The B-hCG is used for diagnosis and monitoring treatment response. It is an aggressive and highly metastatic tumor with poor outcome.

A 24-year-old male patient was admitted in our hospital with abdominal pain that had progressively worsened over two months and was associated with a weight loss of 7 Kg over 2 months. Patient had no significant medical, personal, and family histories.

The ultrasound abdomen showed mild hepatosplenomegaly and hepatic hemangioma. A CT scan of the thorax and whole abdomen showed multiple bilateral lung lesions with areas of arterial phase hyperenhancement. The largest lesion measured 60 x 42 mm in the left basal lung, and abdominal images showed an 86 x 68 x 90 mm lobulated left para-aortic lesion in the infrarenal location.

An excision of the right lower lobe lung with nodule was done, and the histopathological findings were consistent with those of a germ cell tumor with a component of choriocarcinoma.

Tumor markers, particularly serum beta human chorionic gonadotropin (B-hCG) was significantly raised with level of 917950 mIU/mL. Other tumor markers done were Lactate dehydrogenase (LDH) - 725 U/L and Alpha feto protein (AFP) -0.762 IU/ml.

Patient was diagnosed with a primary retroperitoneal choriocarcinoma with metastasis to lungs and was started on urgent inpatient chemotherapy.

Extragonadal choriocarcinoma always has a late presentation when these bulky tumors cause compression symptoms and metastasize to other places. Diagnosis of extragonadal choriocarcinomas requires the exclusion of metastatsis from a primary tumor in the testes and distinguishing an extragonadal GCT from another poorly differentiated cancer via histopathological and immunohistochemical examination.

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1. Introduction

Extragonadal germ cell tumors (EGGCTs) are group of neoplastic germ cell tumors arising from extragonadal anatomical locations without any evidence of primary gonadal tumors.[1] Testicular germ cell tumors comprise of approximately 95% of testicular cancers and is most commonly seen between 18 to 45 years of age.[2]

Predominantly testis is the site of origin of Germ cell tumors, but a subset of germ cell tumors is extragonadal in origin. All germ cell tumors with nongonadal site of origin, particularly in the retroperitoneum and mediastinum constitute approximately 1% to 5%.[3] Pure choriocarcinoma represents less than 1% (0.19%) of testicular germ cell tumors; choriocarcinoma is admixed with other germ cell tumor elements in 8% of testicular germ cell tumors.[4]

Extragonadal choriocarcinoma is rarely seen in males, with an incidence of about 0.022 per 100,000 people.[5]

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The pathogenesis of extragonadal choriocarcinomas is poorly understood. Extragonadal choriocarcinoma in an adult male typically yields an aggressive malignancy and poor prognosis, with a 5-year overall survival (OS) rate of approximately 30%.[6]

Here, we present a rare case of retroperitoneal mass with lung metastasis. Primary retroperitoneal choriocarcinoma is a rare form of extragonadal germ cell tumor that is highly aggressive and responds poorly to chemoradiation.

2. Case Report

A 24-year-old male patient admitted in our hospital with abdominal pain that had progressively worsened over two months, associated with a weight loss of 7 kg over 2 months. Patient had no significant medical, personal, and family histories.

The ultrasound abdomen showed mild hepatosplenomegaly and hepatic hemangioma. A CT scan of the thorax and whole abdomen showed multiple bilateral lung lesions with areas of arterial phase hyperenhancement. The largest lesion measured 60 x 42 mm in the left basal lung, and abdominal images showed an 86 x 68 x 90 mm lobulated left para-aortic lesion in the infrarenal location. The lesion showed multiple arterial-phase-enhancing areas within. Lesion adherent with DJ flexure. The lesion was adherent to the aorta up to its bifurcation and adherent to the left psoas muscle. The left superior and anterolateral parts of the lesion are close to small bowel loops. There was an active leak or intravenous contrast from the tumor vessels surrounding jejuna loops in the left upper-mid abdomen, with mild hyperdense collection extending significantly surrounding spleen up to the left subdiaphragmatic region.

The patient underwent angioembolization for tumor rupture.

Tumor markers, particularly serum beta human chorionic gonadotropin (B-hCG) was significantly raised with level of 917950 mIU/mL. Other tumor markers done were Lactate dehydrogenase (LDH) - 725 U/L and Alpha feto protein (AFP) -0.762 IU/ml.

Table 1:

Day	Serum beta hCG levels(mIU/mL)
On admission	917950
After 1st chemotherapy cycle	11036
After 2^{nd} chemotherapy cycle	299.93
After 3rd chemotherapy cycle	67.59

A wedge of right lower lobe lung measuring 60 x 40 x 15 mm was excised and submitted to the histopathology department. On evaluation, the specimen showed a hemorrhagic solid mass measuring 40x25x15 mm.

The lung parenchyma has markedly pleomorphic cytotrophoblasts with disseminated multinucleated syncytiotrophoblasts, and areas of necrosis and hemorrhages are present.

The tumor cells express pancytokeratin (AE1+ 3), B-hCG, SALL 4, GATA 3, and PLAP (few cells) and were negative for OCT3/4, CD117, D2 40, and AFP, with features consistent with those of germ cell tumors with a component of choriocarcinoma.

Examination of the urogenital system and scrotum was normal, hence primary testicular tumor was excluded.

Pt was diagnosed as a case of primary retroperitoneal choriocarcinoma with metastasis to lung and underwent treatment, and his B-hCG dropped to 67.59 mIU/mL.

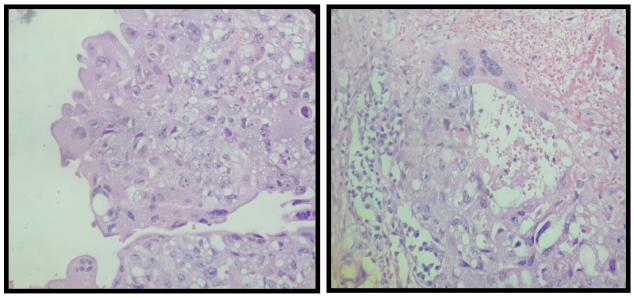

Figure 1: Lung parenchyma has markedly pleomorphic cytotrophoblasts with disseminated multinucleated syncytiotrophoblasts with area of necrosis and hemorrhages. (Hematoxylin and eosin, magnification 400×)

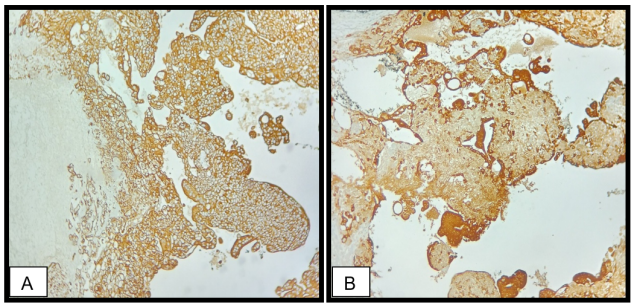

Figure 2: A): AE1+3 show strong membranous staining. (Magnification 100×); **B)**: Beta hcg show strong cytoplsmic staining; (Magnification 100×)

3. Discussion

Choriocarcinoma is a malignant trophoblastic tumor which can be gestational or non-gestational on the basis of site of origin. Davidson eat al. first reported the rare phenomenon of extragonadal choriocarcinoma arising in the midline without a primary testicular tumor in the German literature.[7]

Germ cell tumors include the germinoma family of tumors and nonseminomatous germ cell tumors. The germinoma family of tumors consists of seminoma, and

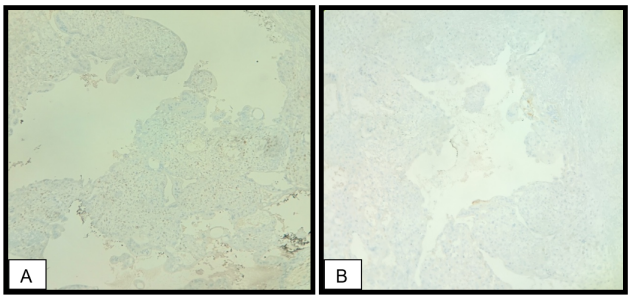

Figure 3: A): SALL4 show nuclear positivity (Magnification 100×); **B**): PLAP show focal membranous and cytoplasmic staining (Magnification 100×)

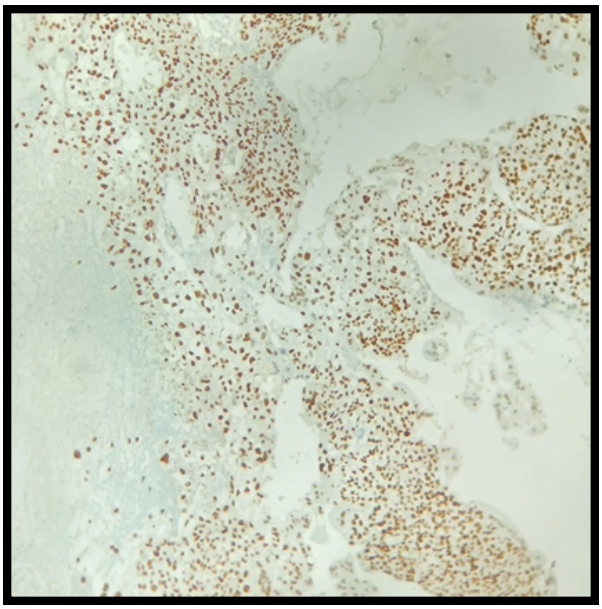

Figure 4: GATA3 show nuclear positivity (Magnification 100×)

nonseminomatous germ cell tumors including embryonal carcinoma (EC), teratoma (post pubertal type and teratoma with somatic type malignancy), yolk sac carcinoma (YST), placental site trophoblastic tumor, epithelioid trophoblastic tumor, cystic trophoblastic tumor and choriocarcinoma.[4] Choriocarcinomas are the rarest nonseminomas germ cell tumors and are associated with poor survival rate.[5]

Choriocarcinoma affects all sexes and arises in gonadal and nongonadal sites, particularly in the mediastinum, retroperitoneum, and pineal gland. Rare cases with site of origin in the bladder, prostate, paratesticular adnexa, vulva, placenta, pelvis, uterus, kidney, nasal sinuses, and other sites have also been reported.[1]

Choriocarcinoma disseminates through both hematogenous and lymphatic pathways. Studies have shown that retroperitoneal lymph nodes, adrenal glands (56%), gastrointestinal tract (71%), liver (86%), and spleen, brain, and lungs (100%) are commonly involved.[4]

The pathogenesis of EGCT is not well defined, but three prominent hypotheses have been proposed to explain its origin: 1) The tumor may result from abnormal primordial germ cell migration during embryonal development; 2) the tumor might be a testicular choriocarcinoma metastasis with spontaneous regression of the primary testicular tumor; 3) the tumor may originate as a nontrophoblastic neoplasm that mutated into a choriocarcinoma.[8]

Histopathology of choriocarcinoma has an admixture picture with varying proportions, of cytotrophoblastic, syncytiotrophoblastic and intermediate trophoblastic cells. These cells are arranged in different patterns, against necrotic and hemorrhagic background. All the patterns show vascular invasion. The syncytiotrophoblastic cells are usually deeply staining with eosinophilic to amphophilic cytoplasm; they typically have several irregularly shaped, large, hyperchromatic and smudged appearing multinuclei. The cytotrophoblastic cells have irregularly shaped, single nucleus with one or two nucleoli and pale to clear cytoplasm. Intermediate trophoblastic cells have single nuclei and eosinophilic to clear cytoplasm.[4]

Syncytiotrophoblast cells can be seen in other types of germ cell tumors; however, their presence as isolated elements or even as syncytial clusters (with or without accompanying hemorrhage) in a testicular germ cell tumor is not sufficient for a diagnosis of choriocarcinoma. It is only when these cells are intimately mixed with cytotrophoblastic elements in a biphasic pattern that the diagnosis of choriocarcinoma is justified. It should also be mentioned that in exceptional circumstances one can find a trophoblastic testicular tumor formed almost exclusively of cytotrophoblasts (so-called monophasic choriocarcinoma), but this is more common in the post-treatment setting.[9]

Immunohistochemically, choriocarcinoma cells are positive for hCG and keratin. They may also be reactivity for hPL, SP1 and CEA.[9] Trophoblastic associated markers such as hCG and hPL are ex- pressed mainly by the syncytiotrophoblasts, but a few cytotrophoblasts are also positive. The syncytiotrophoblasts also express inhibin, GATA3, and glypican- 3 (GPC3). The cytotrophoblasts express SALL4, GDF3, p63, and GATA3. The intermediate trophoblasts may weakly label for HPL. Serum β-hCG is signicantly raised in a majority of the choriocarcinoma cases approximate 50% to 90% and in seminoma patients up to 10%.[10]

Serum tumor markers are frequently raised in extragonadal germ cell tumors and are useful for diagnosis and follow-up. The most commonly raised serum tumor markers include αFP, β-hCG, and lactate dehydrogenase (LDH) in extragonadal germ cell tumors. In choriocarcinoma patients B-hCG is particularly used to diagnose, monitor the treatment response, and predict recurrence of disease.[1]

The etiopathogenesis of testicular GCTs have got a deeper insight with the advent of genetic studies. In postpubertal testicular GCTs the most frequent genetic aberrations observed is chromosome 12 abnormalities with 12p overexpression being most oftenly observed.[11] Differential diagnosis of choriocarcinoma includes placental site trophoblastic tumor, epithelioid trophoblastic tumor, and cystic trophoblastic tumor. These tumors are very rare. These tumors are particularly seen in metastatic sites with mildly raised serum beta-hCG levels and are frequently seen in post treatment phase.[4]

The final diagnosis of an extragonadal choriocarcinoma requires the exclusion of metastatic disease from a primary testicular tumor and distinguishing an extragonadal germ cell tumor from other poorly differentiated cancer via histopathological and immunohistochemical examination. Extragonadal choriocarcinomas usually have late presentation when these bulky tumors causes compression symptoms. Clinical manifestations of EGCTs are due to a large tumor burden causing compression of surrounding structures leading to various symptoms including back pain, abdominal pain, obstructive uropathy and lower-extremity edema.[12]

The choriocarcinoma in males has high mortality, poor prognosis, and limited treatment measures.[13] Extragonadal choriocarcinoma in a male is an aggressive malignancy, and first-line therapy includes multiagent chemotherapy followed by surgical resection of the residual tumor.

Immunotherapy with immune check point inhibitors (ICIs) have recently shown a key role to treat choriocarcinomas.

Ancillary technique to assist histopathology diagnosis is available during recent years where various immunohistochemical markers and molecular techniques are used, while serum beta hCG level for monitoring patients.[14]

4. Conclusion

Extragonadal choriocarcinoma usually have late presentation when these bulky tumors causes compression symtoms and metastasized to other places. Diagnosis of extragonadal choriocarcinomas are require exclusion of metastatsis from a primary testicular tumor and distinguishing an extragonadal germ cell tumor from other poorly differentiated cancer via histopathological and Immunohistochemical examination.

5. Source of Funding

None.

6. Conflict of Interest

None.

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