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A 24-Year-Old Man Presenting with Lung Metastases from a Primary Retroperitoneal Extragonadal Choriocarcinoma

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Male, 24-year-old
Final Diagnosis: Retroperitoneal choriocarcinoma
Symptoms: Left sided • pleuritic chest pain and back pain radiating down his left leg of one year duration
Medication: —
Clinical Procedure: —
Specialty: General and Internal Medicine

Objective: Rare disease

Background: Primary retroperitoneal choriocarcinoma is a rare form of extragonadal germ cell tumor that is highly aggressive and responds poorly to chemoradiation. Extragonadal choriocarcinomas are notoriously challenging to diagnose, and have often progressed to advanced disease by the time of diagnosis. The survival rate for extragonadal choriocarcinoma is approximately 30%, which is much lower than that of extragonadal non-seminomatous germ cell tumors (GCT) in general.

Case Report: A 24-year-old man with no significant past medical history presented with left-sided, pleuritic chest pain and back pain radiating down his left leg, of 1-year duration. Computed tomography (CT) of the chest revealed multiple bilateral pulmonary nodules and a CT of the abdomen and pelvis showed a large heterogeneous soft tissue mass measuring 9.3×8×10.5 cm. A CT-guided core needle biopsy of a lung nodule was performed and the findings were consistent with the diagnosis of metastatic choriocarcinoma. Magnetic resonance imaging (MRI) of the brain was negative for metastatic disease. Tumor markers were significant for a markedly elevated beta human chorionic gonadotropin (B-hCG) of 104 712 mIU/mL. He was diagnosed with a stage IIIC germ cell tumor, further classified as a primary retroperitoneal choriocarcinoma with lung metastasis, and was started on urgent inpatient chemotherapy.

Conclusions: Due to the poor outcomes associated with extragonadal choriocarcinoma, it is important to promptly and correctly identify this malignancy in order to initiate treatment in a timely manner. The following case report explores the histopathologic characterization of this malignancy and describes the clinical course and outcomes from treatment for this patient.

Keywords: Choriocarcinoma, Non-Gestational • Neoplasm Metastasis • Neoplasms, Germ Cell and Embryonal

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/936288

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Background

Germ cell tumors (GCT) account for 95% of testicular cancers and most commonly affect adolescent and young adult males ages 15-39 years old. Choriocarcinoma is a rare malignant GCT most commonly seen in females and represents less than 5% of all GCTs in males [1]. In male patients, germ cell tumors mainly present in the testes, however, but they occasionally present primarily in an extragonadal location, most commonly in midline regions such as the anterior mediastinum, retroperitoneum, or pineal gland [2]. Extragonadal choriocarcinoma in males is especially rare, with an incidence rate of approximately 0.022 per 100, 000 people [3]. The pathogenesis of extragonadal choriocarcinoma is poorly understood and an accurate diagnosis is critical for correct management. The diagnosis requires imaging and histology [4,5].

Extragonadal choriocarcinoma in an adult male typically yields a poor prognosis, with a 5-year overall survival (OS) rate of around 30% [6], which is significantly lower compared to retroperitoneal nonseminomas in general, which have an associated 62% 5-year OS rate [6]. Extragonadal choriocarcinoma in a male is an aggressive malignancy, and first-line therapy includes multiagent chemotherapy followed by surgical resection of the residual tumor. As extragonadal choriocarcinoma is very rare in males and yields a poor prognosis, increased awareness of this tumor type in males can facilitate earlier diagnosis and treatment and thus improve survival rates [7]. Here, we present a case of an otherwise healthy 24-year-old man who was diagnosed with a high-risk primary retroperitoneal choriocarcinoma with metastatic disease to the lungs.

Case Report

A 24-year-old man with no significant past medical history presented with a chief concern of left-sided, pleuritic chest pain and back pain radiating down his left leg. The pain started approximately one1 year prior to admission, but progressively worsened over the past few weeks, prompting the patient to seek medical attention at an urgent care facility. A recent chest radiograph and radiograph of the lumbar spine were reported as normal and the patient was treated with pain medication. However, the pain failed to resolve and he returned to the emergency room 2 weeks later. The patient was a nonsmoker and did not use alcohol or illicit drugs. Initial vital signs revealed mild tachypnea but were otherwise normal. On physical examination, there were scattered rhonchi noted on pulmonary auscultation bilaterally. His back was nontender to palpation. Pertinent laboratory results were: hemoglobin 8.8 g/dL [normal 12.6-16.7 g/dL], D-dimer 3155 ug/mL [normal 0.27-0.49 ug/mL], lactate dehydrogenase (LDH) 409 U/L [normal 140-271 U/L], and normal leukocyte count and differential. Computed tomography (CT) of the chest (**Figure 1**) revealed innumerable bilateral pulmonary nodules measuring up to 4.5 cm, concerning for pulmonary metastasis. CT of the abdomen and pelvis (**Figure 2**) showed a large heterogeneous soft tissue mass measuring 9.3×8×10.5 cm that was compressing the bladder, consistent with a possible primary neoplasm arising from the left iliopsoas muscle. Magnetic resonance imaging (MRI) of the brain was negative for intracranial metastasis. A CT-guided core needle biopsy of a lung nodule was performed. Tumor markers were significant for a markedly elevated beta human chorionic gonadotropin (B-hCG) of 104 712 mIU/mL. Alpha fetoprotein (AFP) was normal. Subsequent physical examination of the testes was negative

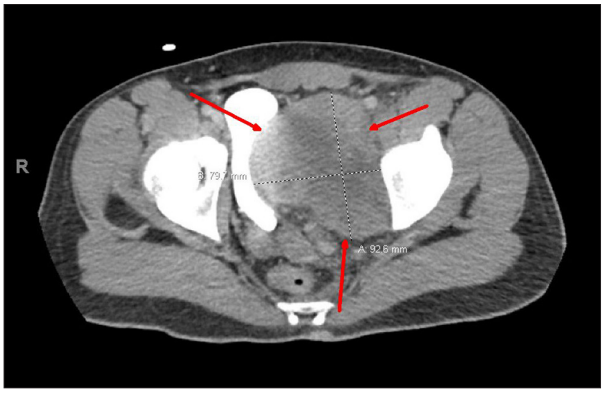
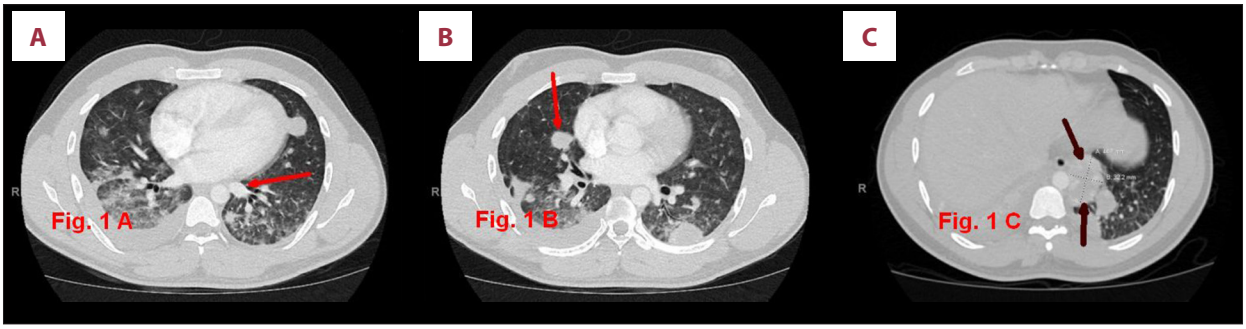


Figure 2. Computed tomography (CT) of the pelvis showing a large heterogeneous soft tissue mass compressing the bladder (red arrow).



Figures 1. (**A-C**) Computed tomography (CT) of the chest showing diffuse bilateral pulmonary nodules (red arrow).

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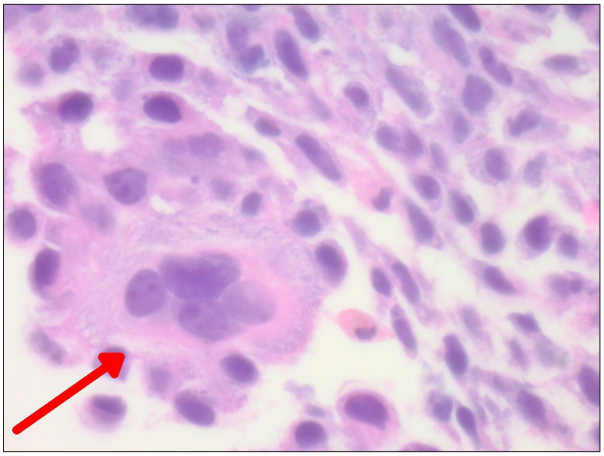

Figure 3. The tumor cells strongly express Cytokeratin AE1/3 (60×).

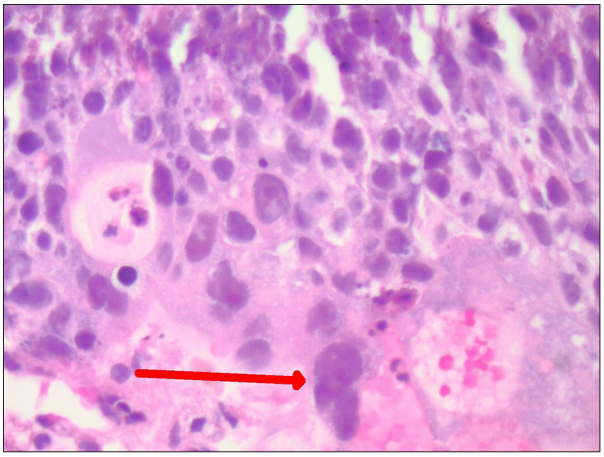

Figure 4. Lung tissue histology illustrates a nest of highly pleomorphic cytotrophoblasts admixed with syncytiotrophoblasts (red arrow), mitotic figures, and necrosis.

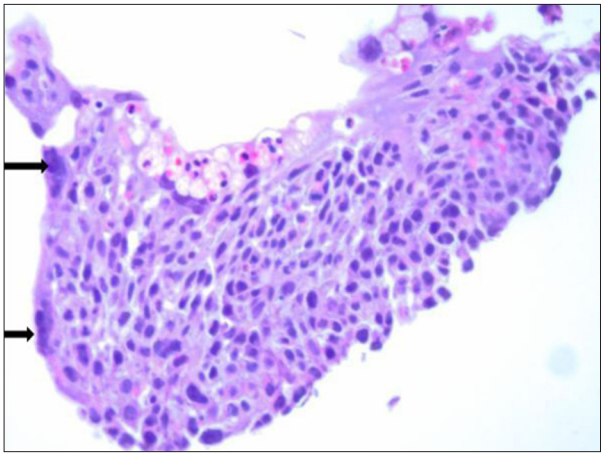

Figure 5. H&E high-power highlights the multinucleated syncytiotrophoblasts (black arrows) and the smaller cells with pale cytoplasm and hyperchromatic nuclei are the intermediate and cytotrophoblasts.

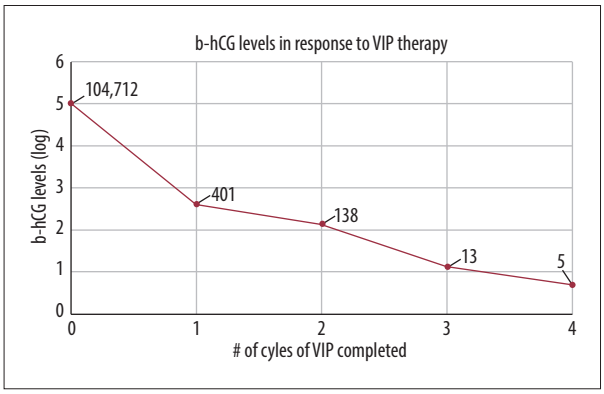

Figure 6. Beta human chorionic gonadotropin (B-hCG) levels.

for any anomaly and testicular ultrasound was negative for a mass. Pathology revealed tumor cells that strongly and diffusely expressed CK AE1/3 (anti-cytokeratin monoclonal antibodies, AE1 and AE3) (**Figure 3**), Cam 5.2 (Anti-Cytokeratin), CK7 (Cytokeratin 7), GATA-3, and HCG. The morphologic and immunophenotypic findings were consistent with the diagnosis of metastatic choriocarcinoma (**Figures 4, 5**). Oncology was consulted for evaluation of a high-risk, stage IIIC germ cell tumor, further classified as a primary retroperitoneal choriocarcinoma with lung metastasis. A primary testicular tumor was excluded because of the examination and scrotal imaging. A primary retroperitoneal extragonadal choriocarcinoma and not a primary lung or mediastinal extragonadal choriocarcinoma was considered likely considering his clinical presentation and abdominal and retroperitoneal imaging. Due to the bulky nature of his disease, the patient was started on urgent inpatient chemotherapy with cisplatin, etoposide, and ifosfamide (VIP). He successfully completed 4 cycles of chemotherapy with good response. His B-hCG decreased to 5 mIU/mL (**Figure 6**) and re-staging CT scans showed response to therapy with a decrease in the size of pulmonary nodules and a smaller but persistent left pelvic sidewall mass. The patient subsequently underwent retroperitoneal lymph node dissection with urology and pathology revealed no viable tumor cells. The patient is currently asymptomatic and will continue to follow up with Oncology and Urology as needed.

Discussion

Approximately 95% of male germ cell tumors originate in the testes [1]. Germ cell tumors are categorized as either seminomatous or non-seminomatous. Non-seminomatous GCTs consist of embryonal tumors, yolk-sac tumors, teratomas, and choriocarcinomas. Choriocarcinomas are the rarest of the non-seminomas and are associated with the worst overall survival rate [3]. When there is no evidence of a primary testicular

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tumor, GCTs are classified as extragonadal germ cell tumors (EGCT). When they do arise, EGCT tend to present along the midline, most commonly the anterior mediastinum, retroperitoneum, and pineal gland. Presentation along midline structures suggests a diagnosis of a primary EGCT rather than metastatic disease from a primary testicular tumor [10]. As of 2018, 27 cases of retroperitoneal choriocarcinoma have been reported in the literature [3].

EGCTs share the same tumor markers and histological subtypes as their gonadal germ cell tumor counterparts. The serum tumor markers alpha fetoprotein (AFP), human chorionic gonadotropin (B-hCG), and lactate dehydrogenase (LDH) are measured in GCTs and are primarily used to monitor treatment response and detect disease recurrence. In particular, B-hCG is used to monitor treatment response and disease recurrence in patients with choriocarcinoma [9]. The pathogenesis of EGCT is not well defined, but 3 prominent hypotheses have been proposed to explain the 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 [10,11]. Non-seminomatous GCTs are highly invasive masses and radiographically appear inhomogeneous due to necrosis and hemorrhage within the tumor [10]. Histologically, choriocarcinoma presents as solid sheets and clusters of syncytiotrophoblasts and cytotrophoblasts with occasional hemorrhage and necrosis. Immunohistochemically, tumor cells express keratin and hCG. Our patient's tumor pathology was consistent with these findings. Differential diagnoses include other germ cell tumors such as seminoma with scattered syncytiotrophoblasts, non-small cell carcinoma of the lung, and embryonal carcinoma [11].

The definitive diagnosis of an extragonadal GCT requires both exclusion of metastatic disease from a primary tumor in the testes and distinguishing an extragonadal GCT from another poorly differentiated cancer via biopsy and histopathological examination. Retroperitoneal GCTs are typically bulky at the time of presentation because patients tend to seek medical attention only once the tumor is large enough to compress surrounding organs and cause symptoms. Clinical manifestations of EGCTs are often related to compression of surrounding structures due to a large tumor burden, including abdominal pain, back pain, lower-extremity edema, and obstructive uropathy [11].

Treatment of extragonadal choriocarcinoma consists of a cisplatin-based chemotherapy followed by surgical resection of the residual mass [10]. Proper histological classification, anatomical location, tumor marker levels, and patient demographics are all important factors that determine prognosis and guide therapy of EGCT. Risk factors that stratify patients into intermediate- and high-risk groups include mediastinal or retroperitoneal location, visceral metastases, and elevated tumor markers [11]. In these groups, 4 cycles of chemotherapy are recommended, as opposed to the 3 cycles for lower-risk individuals. First-line therapy is a cisplatin-based regimen with either BEP (bleomycin, etoposide, and cisplatin) or VIP (etoposide, ifosfamide and cisplatin). BEP is the standard therapy, while VIP can be considered in those with underlying pulmonary disease [12]. For patients in the low-risk category, a reasonable but slightly less effective regimen with EP (etoposide and cisplatin) can be considered to avoid the adverse effects of bleomycin. In non-seminomatous EGCT, surgical removal of the residual mass is recommended after the completion of chemotherapy [13].

In our patient, a primary retroperitoneal choriocarcinoma with significantly elevated B-hCG levels and the presence of metastatic disease placed him in the high-risk category, and he was subsequently started on 4 cycles of cisplatin-based chemotherapy. According to the National Comprehensive Cancer Network (NCCN) guidelines, both BEP and VIP are considered to be first-line therapy [14]. VIP was chosen over BEP as the preferred treatment regimen in our patient to avoid the possibility of bleomycin-induced lung toxicity given the presence of pulmonary metastatic disease. After 4 cycles of VIP, our patient showed a significant response as evidenced by a marked reduction in B-hCG levels from 104 712 mIU/mL to 5 mIU/mL, and decreased tumor burden on re-staging CT scans. Routine measurement of B-hCG levels and regular re-staging PET/CT scans (positron emission tomography) are essential for monitoring disease regression. Additionally, long-term follow-up of these patients may be required to more accurately measure treatment response and monitor for disease recurrence.

Extragonadal choriocarcinoma is an extremely rare tumor that usually presents in young males. Extragonadal choriocarcinomas are notoriously challenging to diagnose, and have often progressed to advanced disease by the time of diagnosis. The survival rate for extragonadal choriocarcinoma is approximately 30%, which is much lower than that of other extragonadal non-seminomatous GCTs [4,15]. Although a diagnosis of extragonadal choriocarcinoma yields a poor prognosis and this tumor type typically responds poorly to chemoradiation, treatment can potentially be lifesaving. Our patient, in particular, has experienced significant improvement in symptomatic disease and tumor burden after treatment with chemotherapy and post-chemotherapy retroperitoneal lymph node dissection.

Conclusions

Due to the poor outcomes associated with extragonadal choriocarcinoma, it is important to promptly and correctly identify

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this malignancy in order to initiate treatment in a timely manner. However, given the rarity of extragonadal choriocarcinoma, there are not many actively enrolling clinical trials available to patients. Therefore, it is imperative to conduct more randomized clinical trials to better establish treatment guidelines and improve survival rates.

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