Case Report

rare tumors

Rare Tumors
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Choriocarcinoma metastatic to the skin: A rare occurrence associated with dismal outcome

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Abstract

Germ cell tumors (GCTs) are a histologically heterogeneous group of tumors that arise from the primitive germ cell of the embryonic gonad. Choriocarcinoma is a variant of GCTs that is prone to hematogenous metastasis to the liver, lung, and brain. Cutaneous metastasis in choriocarcinoma is rarely encountered with only a few cases reported in literature. We report the case of a 28-year-old male presenting with lower back pain that, upon further work-up, was diagnosed with pure choriocarcinoma of the testes. Around 9 months after his initial presentation, he developed a cutaneous back lesion. Microscopic examination confirmed the presence of choriocarcinoma composed of mononuclear cytotrophoblasts which interweave with multinucleated syncytiotrophoblasts. The patient passed away 3 weeks after the onset of cutaneous metastasis.

Keywords

Choriocarcinoma, cutaneous, metastasis, dermatology, testicular cancer

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Introduction

Germ cell tumors (GCTs) are a histologically heterogeneous group of tumors that arise from the primitive germ cell of the embryonic gonad.[1] Germ cell tumors can be benign or malignant.[2] Testicular germ cell tumors are the most common type of solid tumor in men in reproductive age group, usually arising between the ages of 20 and 40, with an incidence of up to 10 in 100,000 men.[3] Choriocarcinoma is a variant of GCT that is acknowledged to be perfused by fragile vessels and is thus prone to develop hematogenous metastasis most commonly to the liver and lung.[4] Cutaneous metastatic choriocarcinoma is a rare encounter with a few cases reported in literature.[5] In this case, we present a patient with testicular choriocarcinoma that progressed to develop metastatic cutaneous lesion.

Case presentation

A 28-year-old previously healthy male presented with recurrent lower back pain of 2 months duration that was moderate in severity, dragging in nature, and radiating to the lower abdomen with no change in bowel habits or urinary tract symptoms. The pain was partially responsive to pain killers; however, over time it progressed to become more intense and was associated with nausea, general weakness, and malaise. The patient reported a history of an undescended right testicle that was surgically corrected when he was 3 years old. While growing up he noticed that his right testis was relatively smaller

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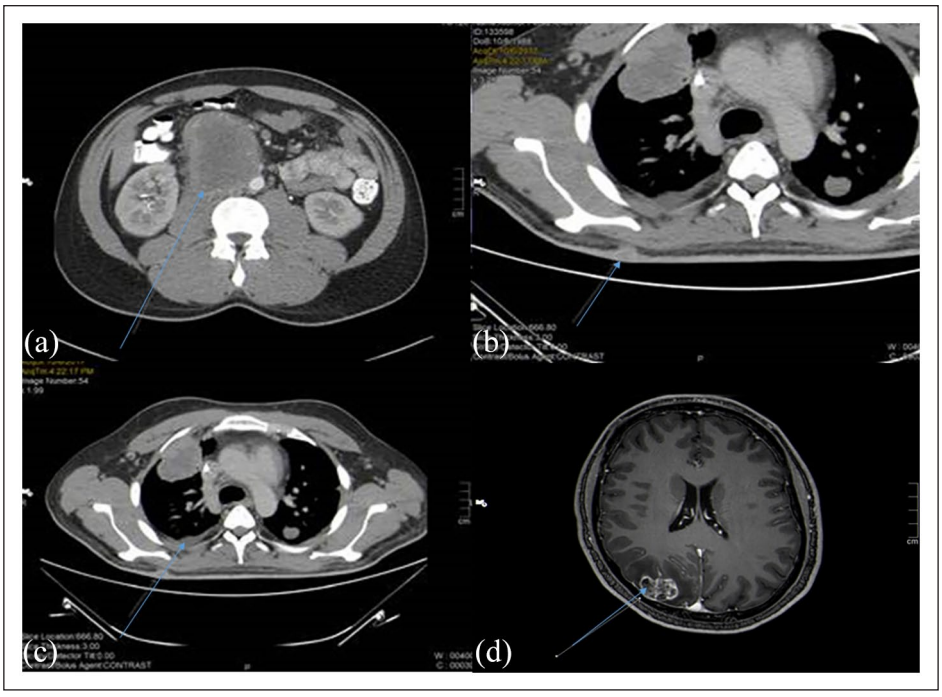

Figure 1. (a) Abdomen CT scan with contrast shows large retroperitoneal soft tissue mass lesion associated with right psoas muscle involvement consistent with the known choriocarcinoma, (b) CT-scan shows a right dorsal skin metastatic nodule, (c) chest CT scan with contrast shows metastatic pulmonary, pleural based, and right skin dorsal nodules, and (d) brain MR scan, T1-weighted images with contrast show hemorrhagic heterogeneous contrast enhancing metastatic lesion in the right parieto-occipital region.

than the left, but he denied feeling any masses in the testis or scrotum. On physical examination, his right testis was atrophic with no palpable masses, his left testis was normal, and there were no scrotal or penile lesions. He had a palpable, ill-defined mass occupying the periumbilical area that prevented a proper abdominal examination due to pain upon palpation. The patient underwent computed tomography (CT) scan that showed a retroperitoneal mass (Figure 1(a)) involving the psoas muscle with liver and lung lesions. He underwent biopsy from the mass which was diagnosed as a pure choriocarcinoma. Scrotal ultrasound showed bilateral testicular microlithiasis more prominent on the right side. In addition, the right testis showed a cystic mass located in the lower pole, and a small epididymal cyst. His blood tests showed a markedly elevated Beta-hCG (308,098 mIU/ml) and LDH (652 U/l) levels. All other markers were within normal ranges. A diagnosis of testicular choriocarcinoma was consequently rendered.

The patient started on chemotherapy consisting of VIP (Cisplatin, Etoposide, and Ifosfamide) regimen for four cycles over a period of 3 months. On completion the chemotherapy course, his serum Beta-hCG was at the lowest reported level (26.65 mIU/ml) and LDH was within the normal range (169 U/l). However, soon afterwards, his serum markers started to rise again, it was therefore decided to start the patient on a salvage TIP (paclitaxel, ifosfamide, and cisplatin) chemotherapy regimen supplemented with bone marrow transplantation.

Almost 9 months after his initial presentation, the patient developed a cutaneous lesion on his back. Radiological examination showed a skin nodule that was suspicious for metastasis (Figure 1(b)). In addition, there was evidence of a new small bowel mass located in the mid abdomen, new mild ascitic fluid and innumerable variably-sized liver masses compatible with metastases, occupying most of the liver parenchyma, which had dramatically progressed since the previous CT scan. Multiple splenic masses and bilateral renal masses were noted along with a new right paraumbilical anterior abdominal wall mass. A progression of his bilateral metastatic pulmonary nodules was also seen (Figure 1(c)).

An excisional biopsy from the cutaneous nodule consisted of an ellipse of skin with underlying subcutaneous tissue bearing a hemorrhagic central nodule. Microscopically, there was a biphasic tumor composed of hyperchromatic mononuclear cells that interweaved with multinuclear cells surrounding a large area of necrosis (Figure 2(a) and (b)). Lymphovascular invasion was also seen (Figure 2(c)). Immunostain for Beta-HCG was positive in the tumor cells (Figure 2(d)), supporting the diagnosis of metastatic choriocarcinoma to the skin.

Three weeks later, the patient presented to the Emergency Department with loss of consciousness and hemodynamic

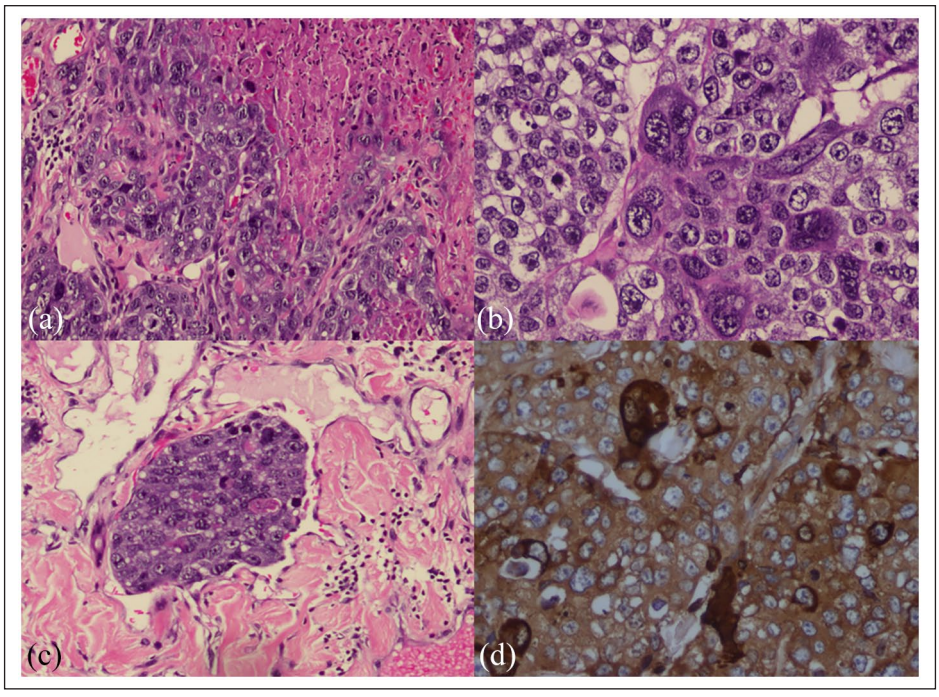

Figure 2. (a) The tumor is composed of hyperchromatic mono- and multinuclear cells surrounding a large area of necrosis (H&E X20), (b) a higher power magnification of both components, in which the mononuclear cytotrophoblasts interweave with the multinucleated syncytiotrophoblasts (H&E X40), (c) lymphatic invasion is seen (H&E X40), and (d) beta-HCG immunostain is positive in the tumor cells (X40).

instability. MRI imaging of the brain showed right parieto-occipital brain metastasis (Figure 1(d)). His condition deteriorated dramatically and he passed away later that day, almost 10 months since his initial diagnosis.

Discussion

The 2016 WHO classification system categorizes testicular germ cell tumors (TGCTs) into two major entities; those derived from germ cell neoplasia in situ (GCNIS) and non-GCNIS-related TGCTs.[6] TGCTs are further classified into seminomas, which originate in germinal epithelium of the seminiferous tubules, and nonseminomas germ cell tumors (NSGCT) which are composed of embryonal carcinoma, teratoma, yolk sac tumor, and choriocarcinoma, either as pure, or more commonly as mixed tumors. Moreover, seminomatous and NSGCT elements can also be concurrently present.[7] The NSGCT patients usually present between 20 and 30 years of age with a median age of 29.[8]

Choriocarcinoma carries the worst prognosis of all GCT, often exhibiting early hematogenous metastases to multiple locations, most commonly the lungs. Other common sites of metastasis include liver, brain, gastrointestinal tract, spleen, and the adrenal glands. When present, even as a component of mixed GCT, brain imaging should be considered.[9] Periaortic and iliac lymph nodes are also frequently involved.[10] Sites of metastasis such as skin have been rarely reported and are associated with poor prognosis.[11] This applies to our patient as his condition deteriorated shortly after the appearance of the cutaneous lesion.

Metastatic cutaneous choriocarcinoma has been reported in both genders. It has been reported in female patients following gestational choriocarcinoma.[12] In males, there have been <20 cases reported. Most reported metastasizing choriocarcinoma to the skin occurred in young patients in their 20s, with a few cases reported in younger and older patients.[13] Skin is an infrequent metastatic site of malignant neoplasms, and in most cases a primary underlying malignancy has already been diagnosed.[14] In men, most skin metastases originate from lung and colon cancer in addition to melanoma.[15] Due to its high-vasculature, choriocarcinoma cutaneous metastasis usually manifest as hemorrhagic nodules, red papules resembling hemangiomas, or occasionally as asymptomatic subcutaneous nodules,[16] which can be solitary, as in our case, or multiple. Metastasis to unusual skin sites including nasal skin,[17] the lip,[5] or the little finger[18] are on record. Cutaneous metastasis to the back, similar to our case, has only been reported in another case of a 22 year old male patient, albeit, as multiple nodules, and the patient died 3 months later.[16] This may originate from a pure choriocarcinoma or from a mixed GCT.[14]

Due to its rarity, the diagnosis of metastatic choriocarcinoma to skin might warrant histopathologic confirmation supported by immunohistochemical testing.[12] Cytology

can sometimes be used to establish the diagnosis, as cytological smears usually show cyto- and syncytiotrophoblasts. However, cytological examination may be challenging if a primary tumor was not already diagnosed.[19] The elevated serum Beta-hCG levels may aid in establishing and/or confirming the diagnosis. Moreover, the elevated serum levels of Beta-hCG might correlate with prognosis.[20] Our patient's Beta-hCG levels were 308,098 mIU/ml, when he presented with cutaneous metastasis, which is considered elevated. The patients passed away 3-weeks later. An elevated alpha-fetoprotein levels should raise the suspicion for other diagnoses or suggest a mixed germ cell tumor with yolk-sac component.[14]

Treatment for metastatic choriocarcinoma should be individualized based on the extent of disease. Most patients receive at least four cycles of chemotherapy with ongoing monitoring of serum Beta-hCG levels.[21] Our patient received four cycles of VIP chemotherapy regimen followed by a salvage TIP chemotherapy regimen. Despite this, his condition deteriorated and the patient eventually succumbed to his disease.

In summary, a high index of suspicion of metastatic choriocarcinoma to the skin, especially among dermatologists and dermatopathologists, in patients diagnosed with gonadal germ cell tumors should be maintained. Unfortunately, once developed, metastatic cutaneous choriocarcinoma appears to be associated with dismal outcome.

Contributorship

Mousa El-Khaldi; conception of the idea, providing the radiology material as well as drafting and approving the manuscript. Rakan Radi; literature review, helping in drafting the manuscript and final approval. Maysa Al-Hussaini; providing pathology material, helped with literature review. Critical review of the initial draft of the manuscript and final approval.

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Ethical approval

This is a case report on a deceased patient, so a waiver from Ethics Committee approval was granted.

Informed consent

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