Oncology

Case report: Extragonadal mixed germ cell tumor in the thigh

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1. Introduction

Germ cell tumors (GCTs) in males predominantly arise from testicular tissue, but 2–5% arise in extragonadal sites with no evidence of a primary testicular tumor, thus called extragonadal germ cell tumors (EGCTs). They mostly arise in the mid-axis of the body; 50–70% in the mediastinum, 30–40% in the retroperitoneal space, and fewer arise in the pineal gland and the suprasellar region. Few occurrences in the prostate and the liver have been reported.1

GCTs are divided into seminomatous, which make up 20–24% of EGCTs, and non-seminomatous that form the majority of EGCTs and have a worse prognosis.2 Extragonadal localization of germ cell tumors is rare; to the best of our knowledge, a location in the soft tissue of the thigh has never been previously reported in literature.

2. Case report

A 25-year old male patient presented complaining of a 3-year history of a progressively enlarging painless left thigh mass, with no other associated symptoms. Examination revealed a mass in the medial aspect of the left mid-thigh of about 15 × 10 cm, with no erythema nor tenderness on the overlying skin.

An MRI showed a large irregular heterogeneous mass located in the superficial subcutaneous tissue, measuring 11.8 × 10.9 × 8.6 cm in the AP, craniocaudal and transverse dimensions, respectively. The overlying skin is significantly thickened (Fig. 1).

The mass is predominantly hypointense on T1-weighted images with focal areas of T1 hyperintensity. It is of intermediate to high signal intensity on T2 and STIR images. After contrast administration, there is heterogeneous mainly peripheral nodular contrast enhancement with central non-enhancing component (Fig. 2). There is another satellite soft tissue nodule proximal to this mass measuring around 2 cm. In addition, there were two enlarged T1 hypointense/T2 hyperintense lesions in the left inguinal region.

A biopsy of the mass showed the tumor to be composed of 85% yolk sac component, 14% immature teratomatous component in the form of neuroepithelium, and 1% embryonal carcinoma component. SALL4 immunostain is positive in the germ cell components. Glypican 3, alpha-feto protein, and CK(MNF) highlighted the yolk sac component. CD30 is positive in the embryonal carcinoma. S100 and synaptophysin are positive in the immature neuroepithelium. Vimentin and CD34 are positive in the stroma. OCT3/4 is non-contributory (Fig. 3).

Scrotal ultrasound showed no abnormality in the testis except for bilateral microlithiasis. Chest CT showed no abnormalities or metastasis.

Initial levels of alpha fetoprotein (AFP) were 100 ng/ml, and Beta human chorionic gonadotropin was 4.2 mIU/ml.

He was started on 2 cycles of BEP chemotherapy. The tumor markers were normalized, repeat cross sectional scan showed variable response in the inguinal lymph nodes and stable pelvic lymph nodes, and MRI showed progression of the thigh mass. Since the mass was hard to resect, second line chemotherapy of two cycles of TIP was given.

Five months later, the patient underwent left hip disarticulation. Two tumor nodules were found in the thigh, the larger nodule expanding beyond the skin and measuring 30 × 30 × 20cm, and the smaller one measuring 12 × 12 × 12cm. The resection margins were free. Pathology showed mixed non-seminomatous germ cell tumor with extensive necrosis. The viable tumor comprised 40% of the lesions. The lesions were composed almost entirely of...
teratomatous elements mostly immature. Focal maturations in the form of glial tissue and cartilage were seen. Minimal elements of yolk sac tumor were also seen.

The patient was kept on follow up, and CT scans showed disease progression, with new lung metastases to the left upper and right lower lobes, and an increase in the size of pelvic lymphadenopathy. AFP was 16.9, LDG 336, and B-HCG was normal. He was started on 3rd line chemotherapy VeIP. CT afterwards showed mild regression in the size of the bilateral large lung nodules, accompanied with regression in the size of metastatic lymph nodes in the left side of the pelvis from about 9.2 cm to approximately 8.5 cm. Tumor markers were normalized.

After two more cycles of VeIP, he received palliative care.

3. Discussion

This case is, to the best of our knowledge, the first reported case of an EGCT arising in the soft tissue of the thigh.

There are multiple theories regarding the development of EGCTs. One explains them by a disturbance of the migration of primordial germ cells along the urogenital ridge, which then undergo malignant transformation under the influence of their microenvironment. Another theory suggests that EGCTs develop when germ cells that have regularly spread during embryogenesis into the liver, bone marrow and brain undergo malignant transformation.1
A biopsy is required for the definitive diagnosis of EGCTs. Most patients present with clear evidence of germ cell features, but a minority could present with a poorly differentiated tumor with no distinctive germ cell features. In our patient’s case, the diagnosis was clear as a mixed EGCT with a combination of yolk sac tumor as the primary component, immature teratoma and embryonal carcinoma.

If an extra-gonadal GCT is found, it is considered metastases from an occult or “burned out” gonadal cancer until a primary testicular tumor is ruled out. An ultrasound should always be performed to exclude a testicular tumor. Taking a gonadal biopsy to rule out intra-tubular neoplasia is controversial, but not recommended.3

Presence of a non-pulmonary visceral metastasis or primary tumor location other than testicle and retroperitoneum automatically places a patient in the International Germ Cell Cancer Collaboration Group (IGCCCG) classification of poor prognosis. This group has a 5-year survival rate of 48%.4

A multimodality approach starting with chemotherapy followed by surgery for residual masses is considered the best course of action. The standard first line approach for a poor-prognosis GCT is BEP chemotherapy. 5–15% of these patients will have persistent marker elevation or disease progression afterwards, thus managed with second-line chemotherapy, conventionally VeIP or TIP. If tumor markers normalize but there is a residual mass >1cm, like our patient, surgery is performed.5

Our patient had viable malignancy after the surgery, which is considered a poor prognostic factor, so he is expected to have a dismal outcome, with reported five-year survival rates of 45–77% in similar patients.7

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eucr.2017.11.012.

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