Uterine leiomyosarcoma associated with high levels of serum beta-hCG

Elias Tsakos[1], Emmanouil M. Xydias[2], Apostolos C. Ziogas[2], Angelos Sioutas[3], Kanelina Bimpa[1], Georgios Tampakoudis[4]

1: EmbryoClinic, Thessaloniki, Greece, 2: University of Thessaly, School of Health Sciences, Faculty of Medicine, Larissa, Greece, 3: Private practice, Thessaloniki, Greece, 4: Consultant in Maternal-Fetal Medicine and Obstetrics, Saint Luke's Hospital, Thessaloniki, Greece

Introduction

Leiomyosarcomas of the are rare, constituting 3% of all uterine and more commonly appear in 40-60 year-old women. The clinical outcome is generally poor, with frequent distant metastases and 5-year survival rates varying between 0%-73%, but usually being on the lower side of the spectrum. Diagnosis is facilitated by clinical and imaging findings and ultimately confirmed by histopathologic evaluation. Treatment includes total abdominal hysterectomy with lymph node dissection and adjuvant chemotherapy. In this report we present the rare case of a β-hCG producing uterine leiomyosarcoma and discuss the hormone's application as a prognostic factor or as an evaluator of treatment effectiveness.

Case presentation

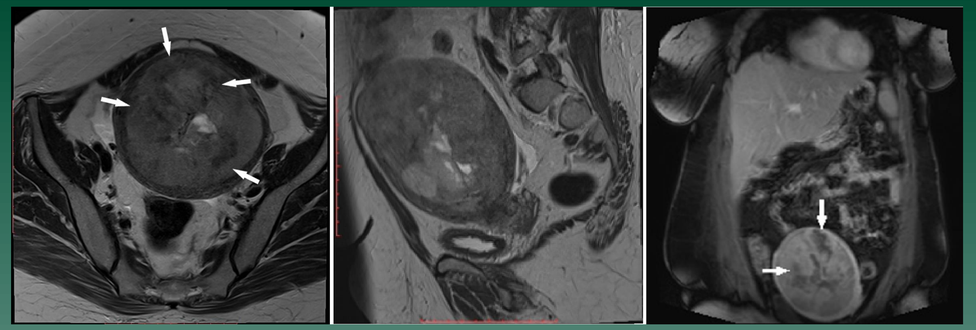
A 53-year-oldA 54-year-old Greek, Caucasian, nulligravida and nullipara presented to our clinic with gradually worsening intermittent meno-metrorrhagia and ultimately anemia that had begun two years prior. The patient had no personal or family history of gynecological cancer, rejected blood transfusions, had a BMI)of 41.5 and type 2 diabetes under inadequate control (HbA1c: 6.8%) via oral medication and diet. During those two years, a benign uterine mass had been diagnosed, which after further examination by D&C at our clinic was shown to be malignant and leiomyosarcoma was diagnosed. Oncological staging showed a large mass (14.5X10.2X9 cm) and multiple lung metastases. Furthermore, the serum blood test results revealed largely elevated β-hCG levels at 383.3 IU/L (reference normal levels < 5 IU/L) but all the other serum tumor markers (CEA, Ca-125, Ca 15.3, Ca 19.9, a-FP) were within normal levels.

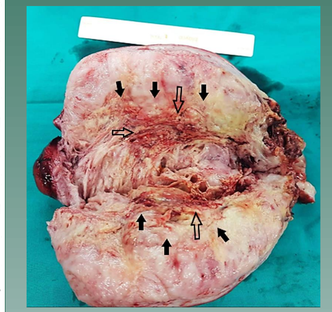
A total abdominal hysterectomy with bilateral salpingo-oophorectomy, bilateral pelvic lymph node dissection, cytology examination of peritoneal washings and subcolic omentectomy was performed. The uterus weighed 1.3 kg and was deformed, with the mass infiltrating the myometrium at the fundus and extending down to the endocervix. Macroscopic examination revealed a solid, white/yellowish tumor, while microscopic examination revealed a dense neoplastic population of spindle cells, with intense nuclear atypia and deeply stained nuclei with a high number of mitoses. Immune-histochemical studies showed positive SMA staining and lymphnodes along with peritoneal washings were clear of cancerous cells. Three weeks later, the β-hCG levels had returned to normal levels, at 2.2IU/L. The patient made an uneventful recovery, proceeded with further Oncology board evaluation and underwent chemotherapy, however ultimately died 6 months later due to pulmonary embolism.

Discussion

Elevated serum β-hCG is most commonly indicative of pregnancy, however it could also indicate malignancy, mainly trophoblastic tumors, with β-hCG having been hypothesized to act as an autocrine growth factor inhibiting apoptosis and thus facilitating tumor proliferation. Mesenchymal tumors are an exceedingly rare cause of increased β-hCG, leiomyosarcomas in particular, with only a handful of cases reported and only two that arose in the uterus in particular in the available literature. Liang et al [1] were the first to document the case of a 49-year-old woman with abnormal uterine bleeding and a history of uterine fibroids, who on examination had elevated β-hCG levels, uterine leiomyosarcoma, and extensive peritoneal metastases in subsequent weeks. Krishnan et al [2] documented a 33-year-old woman with a 4 month history of vaginal bleeding and elevated β-hCG caused by pleomorphic, high-grade sarcoma. After surgery, serum β-hCG levels dropped however at a 6-month follow-up, multiple lung metastases were discovered. Cases of similar tumors in different locations are inconsistent with regard to β-hCG level response and change following treatment, as well as regarding initial levels.

To our knowledge this is world's third documented case of β-hCG producing leiomyosarcoma located in the uterus. Similar to the aforementioned cases, as well as the majority of such leiomyosarcomas documented, our patient developed distant metastases. Thus, it could be argued that elevated β-hCG could be indicative of a more adverse outcome, as was hypothesized by other researchers as well. However, β-hCG level response after treatment is inconsistent, thus not always accurately reflecting the underlying pathology. This was observed in our case as well, with β-hCG levels dropping, despite our initial hypothesis of the opposite due to the lung metastases. Further studies and reports of similar cases are needed to provide further insight on this extremely scarce pathology and ascertain the validity of this correlation of β-hCG with more adverse prognosis.





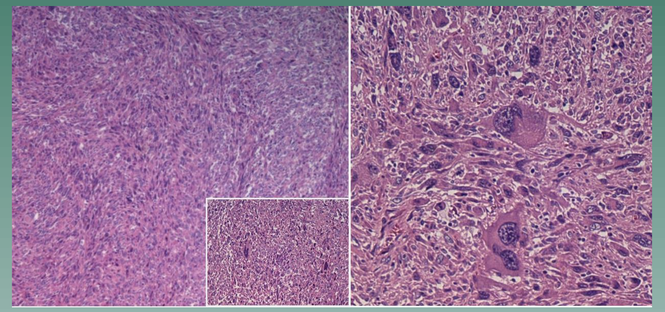


Figure 1 (up): Intrauterine non-homogenous mass detected in the MRI scan.
Figure 2 (down, left): Leiomyosarcoma was shown to be soft and large relative to the total uterine volume, with irregular borders noted to be invading the myometrium (block arrows) with a hemorrhagic center (line arrow). The ruler next to the uterus measures 15 cm.
Figure 3 (down, right): Areas of the dedifferentiated component, comprising of cells with various eosinophilic cytoplasm.

References

1. Liang S, Stone G, Chalas E, Pearl M, Callan F, Zheng W. A high-grade uterine leiomyosarcoma with human chorionic gonadotropin production. Int J Gynecol Pathol. 2006;25(3):257-61.
2. Krishnan V, Sauthier P, Provencher D, Rahimi K. Pleomorphic Undifferentiated Uterine Sarcoma in a Young Patient Presenting With Elevated Beta-hCG and Rare Variants of Benign Leiomyoma: A Case Report and Review of the Literature. Int J Gynecol Pathol. 2020;39(4):362-6.
3. Weiss SW, Goldblum JR. Enzinger and Weiss's Soft Tissue Tumors. 4th ed. Philadelphia: Mosby-Harcort; 2001.
4. Bell SW, Kempson RL, Hendrickson MR. Problematic uterine smooth muscle neoplasms. A clinicopathologic study of 213 cases. Am J Surg Pathol. 1994;18(6):535-58.
5. Kapp DS, Shin JY, Chan JK. Prognostic factors and survival in 1396 patients with uterine leiomyosarcomas: emphasis on impact of lymphadenectomy and oophorectomy. Cancer. 2008;112(4):820-30.
6. Russell MJ, Flynt FL, Harroff AL, Fadare O. Dedifferentiated Liposarcoma of the Retroperitoneum with Extensive Leiomyosarcomatous Differentiation and beta-Human Chorionic Gonadotropin Production. Sarcoma. 2008;2008:658090.