

A Case of a Beta-Human Chorionic Gonadotropin Secreting Sinonasal Teratocarcinosarcoma

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Abstract

Background and Importance Sinonasal teratocarcinosarcoma (SNTCS) is an unusual and aggressive neoplasm characterized by the combination of teratoma and carcinosarcoma features that is often misdiagnosed based on a biopsy sample. Approximately 60 cases have been reported in the English literature, but none have been associated with serum tumor markers. We report a case of SNTCS with elevation of serum β -human chorionic gonadotropin (hCG) level.

Clinical Presentation The patient was a 22-year-old pregnant woman at diagnosis, and her β -hCG level was appropriately elevated. Her initial treatment was a surgical resection followed by radiation therapy (RT). Two years later, the patient had a pregnancy work-up after a sexual assault. Her serum β -hCG was elevated, but a nonpregnant uterus was seen on ultrasound. Magnetic resonance imaging (MRI) of the head revealed an intracranial tumor recurrence in the right frontal lobe. During salvage RT, β -hCG decreased rapidly to normal levels, with a complete tumor response on MRI. Retrospective examination of the initial surgical specimen showed expression of β -hCG associated with the anaplastic mesenchymal component.

Conclusion This is the first reported case of a β -hCG secreting SNTCS. The source of β -hCG production was traced to a neoplastic smooth muscle component of the tumor.

Keywords

- ▶ teratocarcinosarcoma
- ▶ β -hCG
- ▶ gonadotropin
- ▶ serum
- ▶ intracranial

Background and Importance

Sinonasal teratocarcinosarcoma (SNTCS) is a very unusual and aggressive neoplasm first characterized as a separate entity by Heffner and Hyams in 1984.¹ It is currently defined by the World Health Organization as “a complex malignant sinonasal neoplasm combining features of teratoma and carcinosarcoma” that typically includes benign and malignant epithelial, mesenchymal, and neuroepithelial elements including immature tissue with blastomatous features.² Unlike other malignant mixed germ cell tumors (GCTs), SNTCS lacks embryonal carcinoma, yolk sac tumor, choriocarcinoma,

and seminoma components. Based on an inadequate sample, this heterogeneous tumor can be misdiagnosed as olfactory neuroblastoma, squamous cell carcinoma, undifferentiated carcinoma, adenocarcinoma, malignant salivary gland-type tumors, or adenosquamous carcinoma.² A recent comprehensive review of the literature by Wei et al revealed < 60 cases reported in the English literature.³ The primary treatment in 82% of the cases reviewed was surgery, with or without adjuvant radiation therapy (RT). The remainder received definitive RT. Many patients in both groups received some form of chemotherapy as well. There were high rates of recurrence and metastasis overall, although no clear

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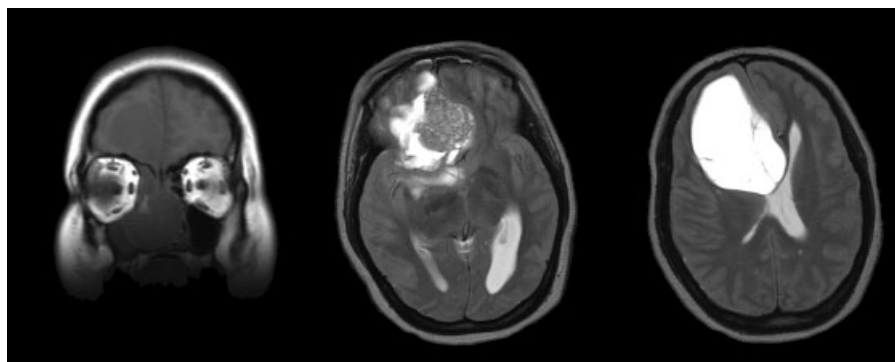


Fig. 1 Noncontrast magnetic resonance imaging of the head showing a large cystic mass in the paranasal sinuses and frontal lobe.

prognostic factors were identified. Overall, 1-year and 3-year survival rates were 36% and 25%, respectively, for those patients with reported outcomes.³ Of all the reported cases of SNTCS, only one has shown any hormone secretion: antidiuretic hormone, causing hyponatremia.⁴ In that case, sodium levels were a reliable marker of tumor control and were an early postoperative indicator of tumor recurrence. To date, no SNTCS with elevated GCT markers has been reported. We present a case in which a highly radiosensitive SNTCS was associated with elevated β -hCG.

Clinical Presentation

A 22-year-old African American woman presented to the emergency department at ~ 16 weeks of gestation with a 2- to 3-month history of worsening headaches and a 3-week history of increasing somnolence, nausea, vomiting, weight loss, and personality changes.

A magnetic resonance imaging (MRI) of her head revealed an 11-cm right frontal mass with a 7-cm cystic component causing significant compression of the right frontal and temporal lobes, mild herniation of the right uncus, and mild hydrocephalus. The tumor extended through the anterior cranial base to the nasal cavity and paranasal sinuses (**Fig. 1**).

On day 2 of admission, she had rapid mental status decline and underwent an emergent decompressive craniotomy. The tumor was extra-axial, and the cyst expressed a dark fluid

“similar to crankcase oil.” The small biopsy specimen taken during this procedure revealed neoplastic cells with squamous and basaloid differentiation and necrosis, leading to the impression of basaloid squamous cell carcinoma.

She subsequently underwent a combined endoscopic transnasal and cranial resection of the entire anterior cranial fossa and nasal cavity mass on day 28 of admission. The surgical specimen consisted of a 9.0 × 8.5 × 3.5-cm aggregate of tan-brown soft tissue and bony fragments. Histologically, the tumor consisted of a heterogeneous mixture of malignant epithelial, mesenchymal, and primitive neuroepithelial elements. Tumor infiltration of brain tissue was observed. The epithelial component included squamous and basaloid carcinoma features (**Fig. 2**). The mesenchymal component included areas of hypercellular smooth muscle, ranging from mildly anaplastic to overtly malignant, with focal areas of osteoid deposition (**Fig. 3**). The neuroepithelial component included neuroblastoma-like and primitive neuroectodermal tumor-like areas (**Fig. 4**). Immunohistochemical staining revealed expression of vimentin, pancytokeratin, and 34 β E12, with focal positivity for CD99 and synaptophysin among the heterogeneous tumor components. After internal and external review, a diagnosis of sinonasal teratocarcinosarcoma was made.

Postoperative RT was recommended after surgery but was delayed for 5 months due to a complicated hospital course and family concerns about her pregnancy. The radiation planning MRI showed some residual soft tissue thickening

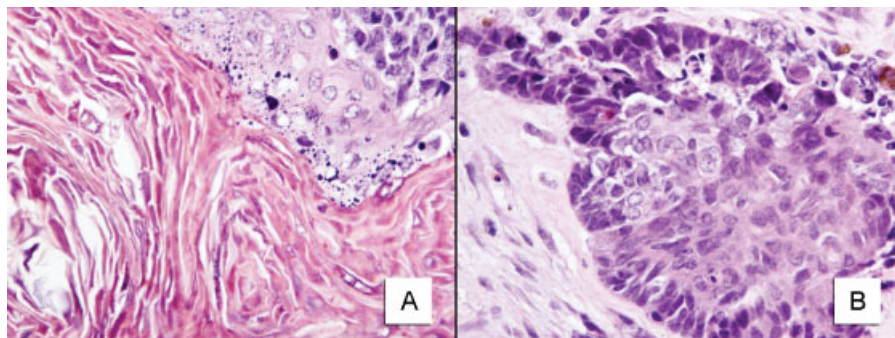


Fig. 2 Epithelial component. (A) Squamous epithelium (hematoxylin and eosin [H&E]). (B) Basaloid epithelium (H&E).

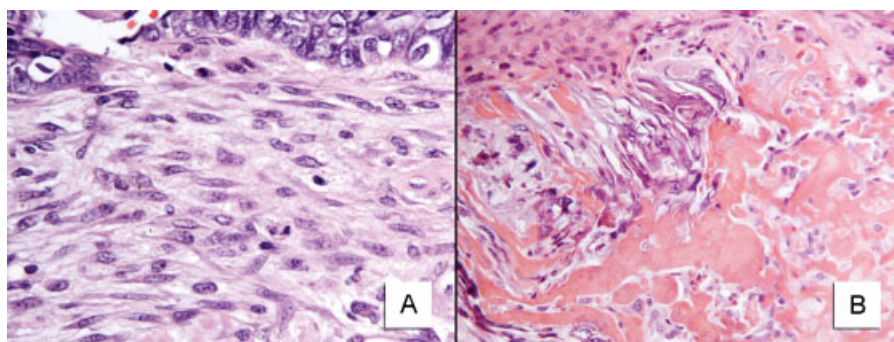


Fig. 3 Mesenchymal component. (A) Stromal smooth muscle with mitoses (hematoxylin and eosin [H&E]). (B) Osteoid (lower right) admixed with epithelial component (upper left) (H&E).

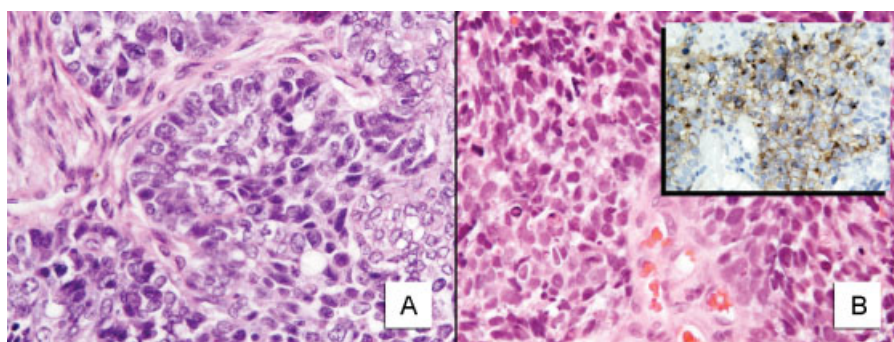


Fig. 4 Neuroectodermal component. (A) Neuroblastoma-like area. (B) Primitive neuroectodermal tumor-like area; hematoxylin and eosin; synaptophysin (inset).

and gyral enhancement in the floor of the craniotomy site but no gross tumor. After delivery of a healthy infant, she underwent a 2-month course of RT to the surgical bed to a total dose of 60 Gy. The follow-up MRIs showed no evidence of recurrent disease for 18 months post-RT.

Two years (27 months) after finishing her postoperative RT, she was admitted for evaluation through the emergency department following an alleged sexual assault by a family member. Her quantitative serum β -human chorionic gonadotropin (hCG) was elevated (60 U/L; normal nonpregnant range: 0–3) but did not rise as would be expected for pregnancy. Pelvic and transvaginal ultrasound studies showed a normal-appearing nongravid uterus. MRI of the

head showed a recurrent intracranial mass in the right frontal lobe (**Fig. 5A**). She was deemed a high surgical risk, so reirradiation of the tumor was recommended. Serum β -hCG was monitored throughout the admission. Radiation was delayed by 45 days, and the planning MRI showed significant interval growth of the tumor with further elevation of β -hCG to 130 U/L (**Fig. 5B**), but there were no new masses in the brain.

Because of clinical concern over the origin of the serum β -hCG elevation, the previous tumor tissue was examined with additional immunohistochemical staining for smooth muscle actin and β -hCG expression. β -hCG was found in areas of anaplastic smooth muscle (**Fig. 6**).

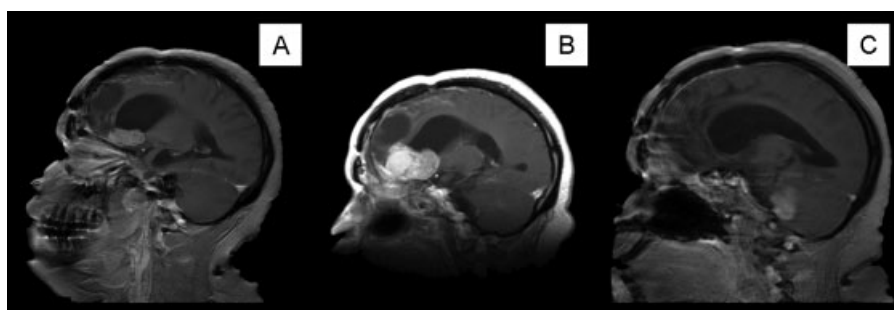


Fig. 5 (A) Magnetic resonance imaging (MRI) showing frontal lobe recurrence 27 months after radiation therapy. (B) MRI showing tumor growth 45 days later, before reirradiation. (C) MRI showing complete response of frontal lobe mass (and new posterior fossa disease) 1 month after reirradiation.

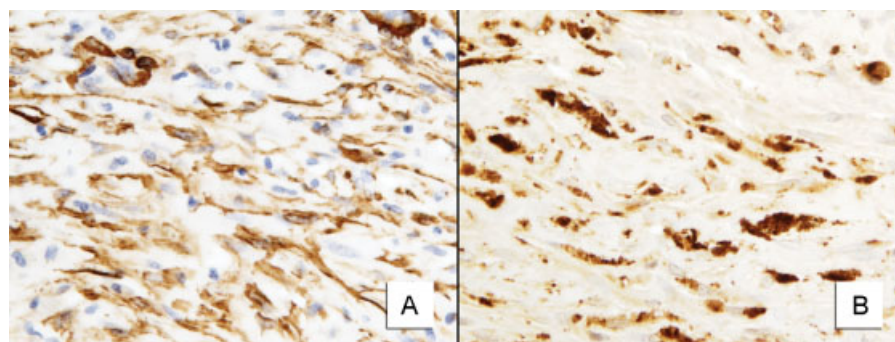


Fig. 6 Smooth muscle component. (A) Smooth muscle focus; smooth muscle actin. (B) β -human chorionic gonadotropin.

The patient received 48 Gy (of a planned 50 Gy) of RT to the recurrent mass in 24 fractions. She missed many appointments but finished most of her prescribed course in a 6-week period with no acute morbidity. Computed tomography scan after the 10th fraction showed significant tumor response, and the treatment was replanned to account for the smaller tumor volume. Her serum β -hCG level dropped from a peak of 130 U/L, measured at the start of RT, to 6 U/L (almost within normal limits) at the end of treatment (**Fig. 7**).

One month later she was admitted to the hospital again for increasing ataxia and falls. A brain MRI showed resolution of the enhancing frontal lobe mass (**Fig. 5C**) but revealed at least five intracranial masses in the posterior fossa, outside of the prior RT fields. Serum β -hCG level was in the normal range. The decision was made to palliate with 30 Gy of RT to the posterior fossa in 10 fractions. There was no biopsy or follow-up imaging. She was discharged to hospice and died a month later. An autopsy was not performed.

Discussion

By definition, SNTCS do not contain areas of embryonal carcinoma, choriocarcinoma, yolk-sac tumor, or seminoma. They are hypothesized to arise from primitive pluripotent olfactory epithelial cells rather than germ cells. Thus they are traditionally believed to be incapable of producing GCT markers including β -hCG or α -fetoprotein, although they have rarely been noted to produce pituitary hormones.⁴

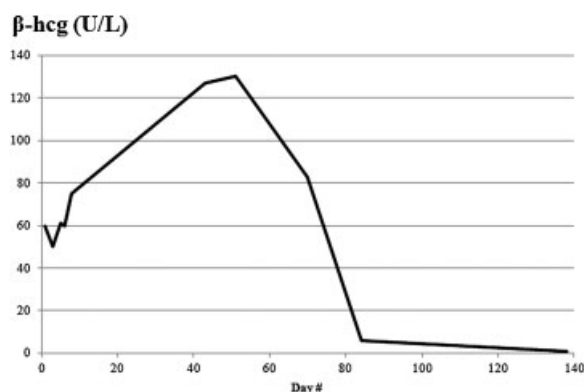


Fig. 7 Serum β -human chorionic gonadotropin levels before and after radiation therapy (RT) for recurrence in frontal lobe. RT was started on day 45.

These tumors comprise varying combinations of epithelial, mesenchymal, and neuroectodermal components exhibiting varying maturation. The mesenchymal component may appear along a continuum from benign to malignant and can include mature components such as cartilage, bone, and striated or smooth muscle. Malignant sarcomatous transformation is also documented.^{1,5-7}

In this case, smooth muscle actin highlighted an anaplastic smooth muscle component in this heterogeneous tumor. There are rare reports of pure leiomyosarcomas secreting β -hCG in the literature.⁸⁻¹⁰ In the absence of the GCT components just mentioned, the neoplastic smooth muscle component of the tumor with expression of β -hCG was the likely source for the elevated serum β -hCG levels.

Because this patient was pregnant on initial presentation, any tumor-related β -hCG production at that time was masked by the elevated serum levels associated with pregnancy. However, on recurrence, tumor production of β -hCG was confirmed with elevation of serum β -hCG, expression of β -hCG on the smooth muscle component of the tumor tissue, and correlation of serum β -hCG levels with changes in tumor size seen on imaging.

This patient's recurrent tumor initially showed a complete response to RT by both serum marker and imaging criteria. Subsequent tumor growth outside of the RT field was not associated with elevation of serum β -hCG.

Conclusion

SNTCS is a rare and unusual neoplasm that lacks embryonal carcinoma, yolk sac tumor, choriocarcinoma, and seminoma components. This is the first reported case of a β -hCG secreting SNTCS. The source of β -hCG production was traced to a neoplastic smooth muscle component of the tumor. Serum levels of this hormone were a reliable tumor marker during the patient's first recurrence and subsequent RT.

Acknowledgments

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