Published in final edited form as:

J Clin Oncol. 2007 June 10; 25(17): 2482–2484. doi:10.1200/JCO.2007.11.1419.

Persistent Positron Emission Tomography–Positive Liver Lesions After Successful Chemotherapy in Mediastinal Seminoma

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A 27-year-old Filipino man with no known past medical history presented with a 2-week history of progressive symmetric facial and neck swelling. On physical examination, the neck and anterior chest wall veins were engorged and distended. The examination was otherwise unremarkable, including a lack of lymphadenopathy in the cervical, axillary, or inguinal regions. Computed tomography (CT) of the chest showed a large mediastinal mass ($10 \times 6.5 \times 8$ cm) that had almost completely compressed the superior vena cava (Fig 1A). Additionally, several enlarged mediastinal lymph nodes were identified. A transthoracic biopsy of the mediastinal mass was performed, and the histology and immunostains were consistent with seminoma. Testicular ultrasound did not reveal a gonadal mass. Alpha fetal protein and beta-human chorionic gonadotropin levels were within normal limits. Lactate dehydrogenase was slightly elevated at 266 IU/L (0 to 200 U/L). A diagnosis of extragonadal seminoma presenting as superior vena cava syndrome was made. Interestingly, an abdominal CT showed three ill-defined hypodensities in the liver, with the largest measuring 1.5 cm in diameter. These lesions (Fig 1C; arrows), in addition to the mediastinal mass and one right hilar node, all demonstrated intense 2- $[^{18}\text{F}]$ fluorodeoxyglucose ($[^{18}\text{F}]$ FDG) uptake (Figs 1A and 1C). The patient underwent standard chemotherapy with three cycles of bleomycin, etoposide, and cisplatin, and one cycle of etoposide and cisplatin. He had a dramatic clinical response to the chemotherapy, with complete resolution of symptoms and physical examination findings. After completing four cycles of chemotherapy, whole-body positron emission tomography (PET)/CT showed almost

complete resolution of the mediastinal mass, with insignificant standard uptake value levels. However, the previously described liver lesions and the one right hilar node (Fig 1B, arrow) did not change in size or number and continued to show intense [^{18}F]FDG uptake. Six weeks later, a repeat PET/CT remained unchanged.

Germ cell tumors account for approximately 1% of all malignancies, but are the most common tumors in men between the ages of 15 to 35 years.¹ Small subsets of these tumors (2% to 5%) are of extragonadal origin.² Liver has been a rarely described site for metastatic extragonadal seminoma. In the largest case series of patients with extragonadal germ cell tumors, liver metastasis was only described in one of 51 patients.³ Residual masses found in patients with bulky seminoma after chemotherapy are commonly reported in approximately 56% to 78%⁴; however only a small fraction of these lesions were found to actually harbor viable tumor cells. There is a disagreement on whether the size of residual masses after chemotherapy predicts for the presence of active disease. Although not proven, there is postulation that the size of the residual mass may be a predictor for residual disease as a large residual mass may have a higher potential to contain tumor cells. One study⁵ determined that there was a higher likelihood of finding viable tumor tissue within residual lesions that were 3 cm or larger, whereas another study⁶ did not see such a correlation. Based on the experience from Memorial Sloan-Kettering Cancer Center (New York, NY), patients with residual masses of 3 cm or larger are recommended to undergo surgical excision of the lesion.⁵ In contrast, the experience of the Indiana University group (Indianapolis, IN) suggests that an initial period of observation is a plausible option, regardless of the size of the residual mass, and further therapy is reserved for patients with progressive disease.⁶ PET imaging has been assessed for its validity in predicting persistent disease in patients with residual mass after apparent successful chemotherapy for testicular cancer. The largest prospective study showed that this imaging modality was highly sensitive and specific in predicting residual disease, particularly in patients with residual mass larger than 3 cm. From the 56 scans performed in 51 patients, the sensitivity, specificity, positive predictive value, and negative predictive value were determined to be 80%, 100%, 100%, and 96%, respectively. In this series of patients, PET imaging was more accurate in predicting residual disease than size determination of the residual mass (>3 cm v 3 cm) by CT.⁴ In a retrospective analysis looking at 24 scans from 19 patients, PET imaging demonstrated a high negative predictive value (100%), but a significantly lower positive predictive value (67%).⁷ Given the unusual location of the residual lesions, we felt compelled to pursue additional work-up, especially with the discrepancy in the response to chemotherapy between the mediastinal mass and the residual lesions. We were concerned for the potential of a mixed tumor with nonseminomatous component in the residual lesions. A CT-guided biopsy of one of the hepatic lesions showed rare noncaseating granulomata in benign liver parenchyma without evidence of tumor. A second CT-guided liver biopsy showed benign appearing hepatocytes with portal fibrosis and chronic inflammation. The liver biopsy was stained for acid fast *Bacillus* and sent for viral, fungal, mycobacterial, and bacterial cultures, all of which were negative. Current data on management of postchemotherapy residual mass in seminoma is still quite limited. This case demonstrates the complexity in interpreting positive PET images in a patient with apparent response to chemotherapy, and it highlights the necessity to tailor the medical management to each

individual whose disease does not follow the expected course. Fortunately, this patient continues to have stable findings on serial follow-up CT imagings and remains in remission 2 years after successful chemotherapy.

References

1. Jemal A, Siegel R, Ward E, et al. Cancer Statistics, 2006. *CA Cancer J Clin.* 2006; 56:106–130. [PubMed: 16514137]
2. Collins DH, Pugh RCB. Classification and frequency of testicular cancer. *Br J Urol.* 1964; 36(suppl 1):1–11. [PubMed: 14184707]
3. Bokemeyer C, Nichols CR, Draz JP, et al. Extragonadal germ cell tumors of the mediastinum and retroperitoneum: Results from an international analysis. *J Clin Oncol.* 2002; 20:1864–1873. [PubMed: 11919246]
4. De Santis M, Becherer A, Bokemeyer C, et al. 2-18fluoro-deoxy-D-glucose positron emission tomography is a reliable predictor for viable tumor in postchemotherapy seminoma: An update of the prospective multicentric SEMPET trial. *J Clin Oncol.* 2004; 22:1034–1039. [PubMed: 15020605]
5. Puc HS, Heelan R, Mazumdar M, et al. Management of residual mass in advanced seminoma: Results and recommendations from the Memorial Sloan-Kettering Cancer Center. *J Clin Oncol.* 1996; 14:454–460. [PubMed: 8636757]
6. Schultz SM, Einhorn LH, Conces DJ, et al. Management of postchemotherapy residual mass in patients with advanced seminoma: Indiana University experience. *J Clin Oncol.* 1989; 7:1497–1503. [PubMed: 2778480]
7. Lewis DA, Tann M, Kesler K, et al. Positron emission tomography scans in postchemotherapy seminoma patients with residual masses: A retrospective review from Indiana University Hospital. *J Clin Oncol.* 2006; 24:e54–e55. [PubMed: 17135635]

Fig. 1.