

Extragonadal Germ Cell Tumor in an Older Patient, Not Every Mass is a “Lung Cancer”



Harjot Kaur¹, Konstantinos Arnaoutakis^{2*}

¹Department of Hospital medicine, Cleveland Clinic Campus, Cleveland, Ohio, USA

²Division of Hematology and Oncology, University of Arkansas, Little Rock, Arkansas, USA

***Corresponding author:** Konstantinos Arnaoutakis, MD, FACP, Assistant Professor of medicine- Division of Hematology and Oncology/ Associate Program Director, Hematology/Oncology Fellowship, Winthrop P. Rockefeller Cancer Institute, University of Arkansas for medical sciences, 4301 West Markham Street, Slot # 508, Little Rock, Arkansas 72205, United States; Tel: 501-526-6990 x 8064/ Fax: 501-686-6342; E-mail: KArnaoutakis@uams.edu

Abstract

Background: Extragonadal germ cell tumors are rarely diagnosed beyond the fourth decade of life. Here, we present an unusual case of an older patient with a rapidly growing lung mass and a significantly elevated beta-HCG consistent with an extragonadal germ cell tumor.

Case presentation: A 69 year old male was found to have multiple brain lesions and a lung mass. He was initially diagnosed with stage IV poorly differentiated non-small cell lung cancer. A germ cell tumor was suspected due to its rapid growth and a highly elevated serum beta-HCG was found. Testicular ultrasound was negative for a gonadal mass. AFP was not elevated. There was no isochromosome 12p but there was hyperdiploidy of chromosome 12. He was treated with platinum based chemotherapy. He had an initial transient decline in the beta-HCG levels along with radiographic improvement but the disease progressed rapidly.

Conclusion: Extragonadal germ cell tumors should be suspected in older patients with a lung mass and a rapid tumor progression.

Received date: October 09, 2015

Accepted date: December 12, 2015

Published date: December 18, 2015

Citation: Arnaoutakis, K., et al. Extragonadal Germ Cell Tumor in an Older Patient, Not Every Mass is a “Lung Cancer”. (2016) Intl J Cancer Oncol 3(1): 95- 98.

DOI: 10.15436/2377-0902.15.024

Keywords: Lung cancer; beta-HCG; Extragonadal germ cell

Introduction

Extragonadal germ cell tumors (EGCTs) account for 1–5% of germ cell tumors^[1]. The most common site is in the anterior mediastinum and are typically diagnosed in the third and fourth decade of life^[2]. It has been hypothesized that EGCTs are either a consequence of a mismigration of germ cells along the urogenital ridge during embryogenesis or they arise from germ cells that are physiologically distributed^[3,4]. These are fast growing and clinically may present as chest pain, shortness of breath, cough, weight loss, fever, superior vena cava syndrome or as a mass causing compression of mediastinal structures. The characteristic genetic abnormality that is found is isochromosome 12p^[5,6]. EGCTs are positive for tumor markers such as alpha-fetoprotein (AFP) and beta-Human Chorionic Gonadotropin (HCG)^[7,8].

Beta-HCG elevation is also seen secondary to ectopic secretion by non-trophoblastic tumor cells^[9]. It has been reported as a paraneoplastic phenomenon in about 10% of primary lung cancer case^[10-14]. Lung cancers with elevated beta-HCG are more resistant to chemotherapy and have poor prognosis.

We present here a case of a lung mass with multiple brain lesions and visceral metastasis in a patient with a significantly elevated beta-HCG suggestive of an extragonadal germ cell tumor.

Case Presentation

A 69 year old male smoker presented with headache, unsteadiness, disorientation and was found to have a lung mass with multiple brain lesions. His CT scan chest at presentation was significant for a right apical mass of 3.2 cm x 3.5 cm x 3.8 cm size adjacent to mediastinum, contiguous with mediastinal lymphadenopathy (Figure 1). He had enlarged pretracheal, right paratracheal and



precarinal nodes and bulky right hilar and subcarinal adenopathy (Figure 2). He underwent resection of the largest brain tumor. Final pathology showed poorly differentiated carcinoma. CK 7 was strongly positive. CK 20 was weakly positive. Cytokeratin 5/6, TTF-1 and synaptophysin were negative. He was diagnosed as stage IV non-small cell lung cancer. Following whole-brain radiation he had a restaging scan that showed progression. CT chest showed increasing right apical soft tissue mass with extensive mediastinal lymphadenopathy and hepatic, renal, and skeletal metastases (Figure 3-4). He had a markedly elevated beta-HCG level at 21651.0 mIU/mL (0.0-9.9 mIU/mL) and serum AFP was 7.2 ng/ml (0-8.0 ng/ml). The testicular ultrasound was negative for gonadal mass. There was no isochromosome 12p but 76% of cells had additional copies of chromosome 12, without apparent gain of 12p.

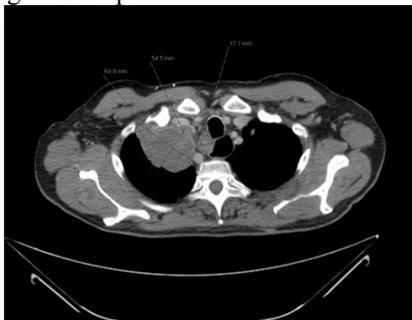


Figure 1: CT scan Chest with oral and intravenous contrast. A large soft tissue mass is present in the right apex measuring 7 x 5.5 cm with moderate compression of the superior vena cava and multiple metastatic nodules

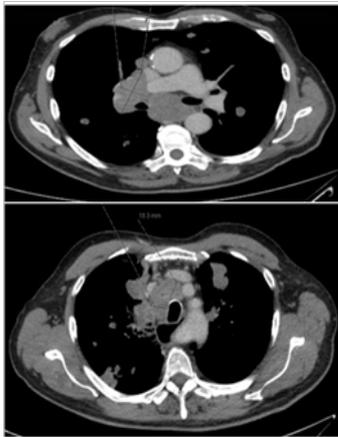


Figure 2: Extensive mediastinal lymphadenopathy is seen. Multiple paratracheal nodes, subcarinal and conglomerate of nodes in the right and left hilum is seen

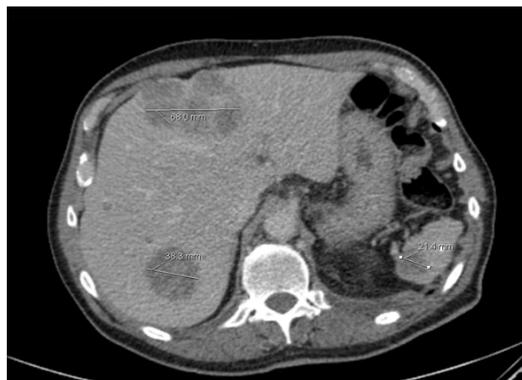


Figure 3: Multiple peripherally enhancing hypodense mass lesions seen throughout the liver with heterogenous densities in the kidneys

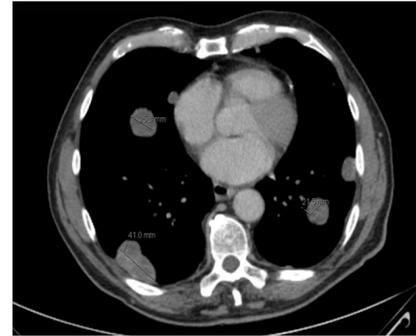


Figure 4: Large satellite nodules present throughout the lungs measuring between 2 and 4 cm

He completed 4 cycles of platinum based chemotherapy. Follow up CT scan showed significant interval improvement in the mediastinal lymphadenopathy, with decrease in pulmonary and visceral lesions. His beta-HCG decreased to 35.4 mIU/ml after the fourth cycle. However, he continued to have significant burden of residual disease and his beta-HCG started rising. He failed second line treatment with gemcitabine and oxaliplatin and later with gemcitabine and paclitaxel. His beta-HCG level continued to rise despite ongoing chemotherapy with elevation to >1,000,000 mIU/ml. Repeat CT scan showed innumerable bilateral pulmonary metastatic lesions with largest up to 3.8 cm with marked progression of metastasis. Due to progressive disease, worsening performance status and multiple co-morbidities, palliative care was recommended. The patient passed away 11 months after his initial presentation.

Discussion

The encountered clinical scenario shared many similarities with a primary mediastinal non-seminomatous germ cell tumor (PMNSGCT) except for the patient’s age. The reported median age for PMNSGCT is 30 years^[6,13]. The rapid clinical progression in this patient raised the suspicion of a non-conventional case of non-small cell lung cancer which further prompted beta-HCG evaluation. Beta-HCG can be elevated with both trophoblastic and non-trophoblastic tumors. Ectopic secretion of beta-HCG is reported in 20-40% of non-trophoblastic tumors such as gastric, liver, ovarian and lung cancers. It acts as an autocrine or paracrine growth factor by inhibiting apoptosis and probably contributes to tumor progression, chemo-resistance and therefore poor prognosis^[11]. Elevation of beta-HCG in lung cancer is rare. It has a reported incidence of 14% in small cell lung cancer and 28% in non-small cell lung cancer^[12-19]. The reported elevation of beta HCG in lung cancer is about 20-3000 mIU/ml only. The persistent and very highly elevated beta-HCG in this patient raised a strong possibility of a germ cell tumor even without a traditional isochromosome 12p^[20]. The hyperdiploidy for chromosome 12 in germ cell tumors is rare but has been described before^[21].

In patients with extragonadal tumors, the presence of liver, lung and brain metastasis, a primary mediastinal location, a non-seminomatous histology, and elevated beta-HCG have been recognized as the negative predictors for both progression free survival and overall survival. In the International Germ Cell Cancer Collaborative Group (IGCCCG) database, mediastinal NSGCTs have lower complete remission rate, higher relapse rate

and failure of salvage chemotherapy^[8]. The studies identified the characteristics such as age older than 30 years, beta-HCG elevation at presentation, metastasis to liver, brain and lung, to independently contribute to the poor overall survival in these patients. Most of these characteristics were identified in this case and have probably contributed to rapid deterioration in our patient.

Treatment for PMNSGCTs usually entails cisplatin-based combination chemotherapy regimens followed by post-chemotherapy surgical resection in cases with radiographic evidence of residual disease. Standard treatment involves four cycles of BEP (Bleomycin, Etoposide, Cisplatin), or alternatively VIP (Vinblastine, Ifosfamide, Cisplatin). Chemotherapy regimens using cisplatin have improved the median survival to 29 months^[7]. The median survival in patients untreated with cisplatin is reported as 4.0-6.5 months^[23,24]. In a study by Hartmann et al^[24], it was observed that the long-term disease-free survival after second-line chemotherapy was only 11% and a mediastinal origin of the NSGCT independently predicted failure of second-line chemotherapy. Patients with rising post-chemotherapy serum tumor markers values have median survival of 9.7 - 11.5 months and overall 1- and 5-year survival rates of 41% and 36%, respectively^[25,26]. In the advanced cancers, salvage chemotherapy has achieved only 7% long-term disease-free survival and 39-42% 2-year overall survival from the initial clinical presentation^[27,28].

Considering persistent and highly elevated post chemotherapy beta HCG, rapid tumor progression with pulmonary lesions with bulky mediastinal involvement and extra pulmonary metastasis, elderly age and the poor survival despite chemotherapy, the given clinical scenario is less likely to be a case of lung tumor with paraneoplastic syndrome. This case probably represents an unusual manifestation of an extragonadal germ cell tumor in a patient in the 7th decade of life.

Conclusion

The germ cell tumors should be suspected while encountering any predominantly mediastinal mass with a rapid progression, and elevated serum beta-HCG or AFP, to be able to initiate early appropriate therapy and discuss prognosis.

Financial disclosure: None

Conflict of Interest: None

References

- Moran, C.A., Suster, S. Primary germ cell tumors of the mediastinum: I. Analysis of 322 cases with special emphasis on teratomatous lesions and a proposal for histopathologic classification and clinical staging. (1997) *Cancer* 80(4): 681-690.
- Collins, D.H., Pugh, R.C. Classification and frequency of testicular tumours. (1964) *Br J Urol* 36(Suppl): 1-11.
- Willis, R.A. The borderland of embryology and pathology. (1950) *Bull N Y Acad Med* 26(7): 440-460.
- Friedman, N.B. The function of the primordial germ cell in extragonadal tissues. (1987) *Int J Androl* 10(1): 43-49.
- Chaganti, R.S., Houldsworth, J. Genetics and biology of adult human male germ cell tumors. (2000) *Cancer Res* 60(6): 1475-

1482.

- Bokemeyer, C., Nichols, C.R., Droz, J.P., et al. Extragonadal germ cell tumors of the mediastinum and retroperitoneum: Results from an international analysis. (2002) *J Clin Oncol* 20(7): 1864-1873.
- Takeda, S., Miyoshi, S., Ohta, M., et al. Primary germ cell tumors in the mediastinum: A 50-year experience at a single Japanese institution. (2003) *Cancer* 97(2): 367-376.
- International germ cell consensus classification: A prognostic factor-based staging system for metastatic germ cell cancers. International germ cell cancer collaborative group. (1997) *J Clin Oncol* 15(2): 594-603.
- Pelosof, L.C., Gerber, D.E. Paraneoplastic syndromes: An approach to diagnosis and treatment. (2010) *Mayo Clin Proc* 85(9): 838-854.
- Hauber, H.P. Paraneoplastic syndromes in lung cancer. (2011) *Pneumologie* 65(6): 347-358.
- Iles, R.K. Ectopic hCGbeta expression by epithelial cancer: Malignant behaviour, metastasis and inhibition of tumor cell apoptosis. (2007) *Mol Cell Endocrinol* 260-262: 264-270.
- Szturmowicz, M., Slodkowska, J., Zych, J., et al. Frequency and clinical significance of beta-subunit human chorionic gonadotropin expression in non-small cell lung cancer patients. (1999) *Tumour Biol* 20(2): 99-104.
- Vicier, C., Tabouret, E., Tallet, A., et al. Beta HCG secretion by a pulmonary adenocarcinoma. (2013) *World J Surg Oncol* 11: 228.
- Szturmowicz, M., Wiatr, E., Sakowicz, A., et al. The role of human chorionic gonadotropin beta subunit elevation in small-cell lung cancer patients. (1995) *J Cancer Res Clin Oncol* 121(5): 309-312.
- Yoshida, J., Nagai, K., Nishimura, M., et al. Secretion of hCG/beta-hCG by squamous cell carcinoma of the lung in a 31-year-old female smoker. (2000) *Jpn J Clin Oncol* 30(3): 163-166.
- Mehta, H., Bahuva, R., Sadikot, R.T. Lung cancer mimicking as pregnancy with pneumonia. (2008) *Lung Cancer* 61(3): 416-419.
- Taverne, J., Delourme, J., Dhalluin, X., et al. Should elevated beta-HCG levels be an exclusion criteria in clinical trials? A case report of paraneoplastic secretion associated with lung adenocarcinoma. (2013) *Rev Pneumol Clin* 69(1): 36-40.
- Khobta, N., Tomasini, P., Garcia, M.E., et al. Beta-human chorionic gonadotropin (HCG) dosage and lung cancer: A pitfall when screening patients for clinical trials. (2012) *Bull Cancer* 99(11):1065-1068.
- Khattari, S., Vivekanandarajah, A., Varma, S., et al. Secretion of beta-human chorionic gonadotropin by non-small cell lung cancer: A case report. (2011) *J Med Case Rep* 5:19.
- Carter, B.W., Marom, E.M., Detterbeck, F.C. Approaching the patient with an anterior mediastinal mass: A guide for clinicians. (2014) *J Thorac Oncol* 9(9 Suppl 2): S102-S109.
- Castedo, S.M., de Jong, B., Oosterhuis, J.W., et al. Cytogenetic analysis of ten human seminomas. (1989) *Cancer Res* 49(2): 439-443.
- Economou, J.S., Trump, D.L., Holmes, E.C., et al. Management of primary germ cell tumors of the mediastinum. (1982) *J Thorac Cardiovasc Surg* 83(5): 643-649.
- Dulmet, E.M., Macchiarini, P., Suc, B., et al. Germ cell tumors of the mediastinum- A 30-year experience. (1993) *Cancer*

72(6): 1894-1901.

24. Hartmann, J.T., Einhorn, L., Nichols, C.R., et al. Second-line chemotherapy in patients with relapsed extragonadal nonseminomatous germ cell tumors: Results of an international multicenter analysis. (2001) *J Clin Oncol* 19(6):1641-1648.

25. Radaideh, S.M., Cook, V.C., Kesler, K.A., et al. Outcome following resection for patients with primary mediastinal non-seminomatous germ-cell tumors and rising serum tumor markers post-chemotherapy. (2010) *Ann Oncol* 21(4): 804-807.

26. De Latour, B., Fadel, E., Mercier, O., et al. Surgical outcomes in patients with primary mediastinal non-seminomatous germ cell tumours and elevated post-chemotherapy serum tumour markers. (2012) *Eur J Cardiothorac Surg* 42(1): 66-71.

27. Saxman, S.B., Nichols, C.R., Einhorn, L.H. Salvage chemotherapy in patients with extragonadal nonseminomatous germ cell tumors: The Indiana University experience. (1994) *J Clin Oncol* 12(7): 1390-1393.

28. Walsh, G.L., Taylor, G.D., Nesbitt, J.C., et al. Intensive chemotherapy and radical resections for primary nonseminomatous mediastinal germ cell tumors. (2000) *Ann Thorac Surg* 69(2): 337-343.