ABSTRACT

**Background:** Most germ cell tumors eg. choriocarcinomas are located in the gonads, however about 2–5% arise from extragonadal regions, such as the mediastinum, retroperitoneum, and central nervous system. Non-gestational choriocarcinoma in mediastinum without a detectable primary in the gonads is termed primary mediastinal choriocarcinoma.

**Materials and method:** Contrast-enhanced whole body computed tomography scan and correlated with tumour markers such as beta human chorionic gonadotropin are used to assess the mediastinal mass. Confirmation of diagnosis was made with image guided biopsy, histopathological examination and special staining.

**Results:** Primary mediastinal choriocarcinoma was confirmed by lack of testicular lesion on ultrasound examination and presence of mediastinal mass with multiple metastatic lesions. Confirmation by CKAE1/AE3 (immunohistochemical study) positive which showed presence of multinucleated epithelial cells.

**Conclusion:** Contrast-enhanced computed tomography is useful tool to diagnose this condition as also provide image guided access for biopsy. In correlation with tumour markers investigation and special immunohistochemical studies can help to clinch the diagnosis.

**Keywords:** primary mediastinal choriocarcinoma, computed tomography, elevated beta human chorionic gonadotropin
1.0 Introduction:

Choriocarcinoma is an aggressive germ cell tumour usually associated with pregnancy known as secondary choriocarcinoma / gestational choriocarcinoma or in absence of pregnancy known as primary non-gestational choriocarcinoma. Non-gestational choriocarcinoma (NGC) usually occurs in the gonads ie. in the ovary of females and in the testes of males. Most germ cell tumors (GCTs) are located in the gonads, although about 2–5% arise from extragonadal regions, such as the mediastinum, retroperitoneum, and central nervous system. (Macchiarini, 2004) Choriocarcinoma in mediastinum without a detectable primary in the gonads or metastatic disease in the retroperitoneal lymph nodes is termed primary mediastinal choriocarcinoma. (Moran, 1997) It is a very rare form of non-gestational extra-gonadal germ cell tumour and occurs in both sexes, mostly in young males. (Zhang, 2014)

2.0 Material and methods/ case report:

We report a case of a 26-years-old single Malay male, who presented to our emergency department with shortness of breath and fever for 3 days. He also gave a history of cough for more than 2 months and episodes of hemoptysis for two weeks duration. He did not have fever with chills and rigor nor night sweats. He also had right sided pleuritic chest pain, loss of weight of 6kg in the past month.

Laboratory test such as full blood count was non significant. Initial workup was to rule out pulmonary tuberculosis, however sputum cultures for acid fast bacilli (AFB) and Mantoux test were negative. Plain chest radiograph revealed multiple rounded, cannon ball lesions as well as an irregular widening of the anterior mediastinum suspicious of a mass [Figure 1]. In view of our centre being a tertiary referral centre for cardiothoracic cases, it is standard protocol to perform tumour markers investigation for all patients presenting with a thoracic mass. This patient’s special blood test to check for tumour markers revealed markedly elevated levels of serum beta-HCG of 93,409 mIU/mL (normal value: 0–3 mIU/mL). Serum alpha fetoprotein was within normal limits of 1.73 ng/mL (normal value: 0 – 20 ng/mL).

Subsequently, patient had contrast-enhanced computed tomography (CT) scan of the thorax and abdomen, which revealed a large, lobulated anterior mediastinal mass and multiple canal both lesions scattered in both lungs [Figure 2]. These lung nodules and the mediastinal mass were enhancing and had hypodense, necrotic centres. There were also multiple enhancing hypodense liver lesions, right renal lesion and retroperitoneal lymphadenopathy [Figure 3]. Provisional diagnosis of metastatic sarcomatous renal cell carcinoma (sRCC) was made. Differential diagnoses included lymphoma and metastatic germ cell tumour. The patient was then planned for a renal biopsy, however in view of the mediastinal mass being more accessible; therefore, he was subjected to CT guided percutaneous biopsy of the anterior mediastinal mass.

Ultrasound of bilateral testes was also performed to exclude testicular origin of the mediastinal mass. However, no lesion was indentified in the gonads. He was given supportive treatment while awaiting the histopathological results. Nevertheless, his condition
deteriorated dramatically and he succumbed to chest infection and died within three days of admission.

Pathological diagnosis of primary mediastinal choriocarcinoma was made later when the histopathological report of the specimen from the anterior mediastinal mass was obtained. Hematoxylin and eosin (H&E) staining revealed hemorrhagic necrotic tissue and large cytoplasm-rich cells demonstrating nuclear pleomorphism [Figure 4]. The nuclei were either vesicular or hyperchromatic with few prominent nucleoli. Special immunohistochemical staining showed the cells were strongly positive for CKAE1/AE3, CK7 and beta-human chorionic gonadotropin (beta-HCG); but negative for alpha fetoprotein and CK20. It was negative for alpha fetoprotein. In cases of renal malignancy, it is expected that CK7 and CK20 are usually positive.

3.0 Result and Discussion

Primary choriocarcinoma of the mediastinum is an extremely rare condition. It is commoner in men and is most often seen in the second and third decades of life.(Fine, 1962) It is relatively uncommon for germ cell tumours of testicular origin to metastasize exclusively to the mediastinum. They usually metastasize to retroperitoneal lymph nodes, often bypassing the mediastinum via the thoracic duct (Moran, 1997).

Rarely, generalized metastases of a testicular neoplasm are found without a viable or identifiable primary source in the genital organs. In such cases the metastases are not confined to the mediastinum. When a germ cell tumor presents in the mediastinum in the absence of a detectable testicular primary and in the absence of metastatic disease in the retroperitoneal lymph nodes, one may consider it a primary mediastinal tumour.

Mediastinal choriocarcinoma is frequently associated with lung metastasis. However, presence of concurrent liver and spleen metastasis are rare. Renal involvement is extremely rare. Hepatic involvement is not common, affecting only (10%) of patients, occurring late in the course of the disease. Rare sites include gastrointestinal tract, spleen, and kidneys.(Hillard, 1993) Normally the diagnosis of choriocarcinoma is made clinically, guided by a high beta-HCG titer (>100,000 IU/L). In actual practice, the majority of patients are treated without the benefit of a histopathologic diagnosis (Soper, 1995).

Management of choriocarcinoma, as well as with all germ cell tumours, requires careful staging and initiation of chemotherapy. There are multiple prognostications scoring available which also helps in treatment stratification and optimization of chemotherapy regimes. The commonly used scoring systems include WHO scoring for prognosis of trophoblastic disease (Committee on Gynecologic Oncology, 2009) and the Charing Cross Hospital scoring system (Kelechi, 2013). According to the WHO scoring system this patient’s staging falls into Stage IV: total score 11), whereby a score of 7 and above carries high risk.

In this case, the patient presented at a late stage with extensive lung and abdominal metastases. Given his initial presentation, he was treated as having active pulmonary tuberculosis. Elevated serum beta-HCG was the only indication that we were dealing with a possible mediastinal germ cell tumour. Patient also did not have gynaecomastia at time of presentation despite raised beta-HCG levels. In view of right renal lesion and small
retroperitoneal lymph nodes, differential of squamous type of renal cell carcinoma (sRCC) and testicular choriocarcinoma were more likely initial differential diagnoses.

Figure 1: Chest X-Ray taken on admission showing multiple cannon ball lesions (straight arrow) seen in bilateral lung fields. There is an irregular opacity causing widened mediastinum (notched arrow).
Figure 2: Axial contrast enhanced computer tomography (CECT) image of the thorax at mediastinum level in soft tissue window, showing an irregular anterior mediastinal mass (straight arrow). There are multiple cannon ball lesions scattered in both lungs (notched arrow).
Figure 3: (a) MPR Coronal image of CECT thorax, abdomen and pelvis revealing mediastinal mass (notched arrow), intrapulmonary enhancing nodules (line arrow) and peripherally enhancing irregular hypodense liver lesion (straight arrow). (b) Axial CT image revealing hypodense liver (notched arrow) and renal lesion (straight arrow). (c) Axial CT image showing retroperitoneal lymph nodes (straight arrow).
Figure 4: (a) H & E low power (x40) showing area of haemorrhage (line arrow). (b) H & E high Power (x200) demonstrating biphasic pattern with pleomorphism and focal multinucleation (straight arrow). (c) CKAE1/AE3 (immunohistochemical study) with presence of multinucleated epithelial cells positive in choriocarcinoma (straight arrow). (d) Beta - HCG – positive for malignant cells indicating diagnosis of choriocarcinoma (arrow).

4.0 Conclusion and Recommendation

The diagnosis of mediastinal choriocarcinoma needs to be considered in a young male presenting with cough, hemoptysis and progressive shortness of breath guided by imaging findings of anterior mediastinal mass and multiple lung nodules and elevated beta-HCG tumour marker. As illustrated by this case primary mediastinal choriocarcinoma can be rapidly fatal. Clinical outcomes can be improved with early presentation to hospital, high clinical index of suspicion and quick initiation of chemotherapy.
Acknowledgement

Ethical approval was waived, as this is a retrospective case report. No grants or sponsorship were made available for this report. We acknowledge Hospital Serdang, Selangor, Malaysia and National Medical research Register, Malaysia for permission to access the materials required for this report.

Declaration

The authors declare that there is no conflict of interest in the preparation of this article and for publication in this journal. This article has not been previously published in any other journal or conference proceeding. No grant funding or sponsor affiliation for this publication.

Authors’ contribution

Author 1: Dr. Dhayal Balakrishnan, Radiologist, Hospital Serdang, Malaysia.
Email: dhayal2@yahoo.com

Author 2: Dr. Subapriya Suppiah, Senior Medical Lecturer and Radiologist, Centre for Nuclear Diagnostic Imaging, Universiti Putra Malaysia.
Email: subapriya@upm.edu.my

Author 3: Dr. Shahrin Md. Sidek, Consultant Radiologist, Hospital Serdang, Malaysia.
Email: sagilboyan@yahoo.com

Author 4: Dr. Noriah Othman, Consultant Pathology, Hospital Serdang, Malaysia.
Email: drnoriah75@yahoo.com

References:

Committee on Gynecologic Oncology (2009). Stage Information for Gestational Trophoblastic Tumors and Neoplasia at The National Cancer Institute (NCI), part of the National Institutes of Health (NIH), in turn citing: FIGO Committee on Gynecologic Oncology: Current FIGO staging for cancer of the vagina, fallopian tube, ovary, and gestational trophoblastic neoplasia. Int J Gynaecol Obstet 105 (1): 3 – 4


