OLGU SUNUMU CASE REPORT

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Anterior Mediastinal Mass: Large Cell Neuroendocrine Tumour of the Thymus

Anterior Mediastinal Kitle: Timusun Büyük Hücreli Nöroendokrin Tümörü

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ABSTRACT This is a rare case of thymic large cell neuroendocrine tumour with a unique method of vascular reconstructions using polytetrafluoroethylene (PTFE) and bovine pericardial graft. 51-y-o gentleman had an incidental finding of a mediastinal mass. Computed tomography showed a locally advanced anterior mediastinal thymic mass. The brachiocephalic trunk was involved and there was the presence of tumor thrombus at superior vena cava. We performed sternotomy, en-bloc resection of tumour with brachiocephalic trunk conduit (PTFE) and left brachiocephalic vein conduit (bovine pericardium graft). Bovine pericardium patch, fashioned into a conduit to reconstruct the transacted innominate vein. Thymic neuroendocrine tumours constitutes 5% of all thymic tumours. Large cell neuroendocrine carcinomas (LCNEC) is considered to have a poorer prognosis and to be aggressive in nature. Immunohistochemistry staining showed positive for chromogranin, CKAE1/AE3 and was negative for TTF-1. Hence, this was likely thymic LCNEC instead of lung LCNEC. In accordance to Masaoka-Koga stage classification for thymic tumours, this tumour would represent Stage Iva.

Keywords: Thymic malignancies; neuroendocrine tumours; vascular reconstructive surgery

ÖZET Bu, politetrafloroetilen (PTFE) ve sığır perikardiyal grefti kullanılarak benzersiz bir vasküler rekonstrüksiyon yapılan nadir bir büyük hücreli nöroendokrin tümördür. Elli bir yaşında bir erkekte tesadüfi olarak mediastinal kitle saptandı. Bilgisayarlı tomografide lokal olarak ilerlemiş anterior mediastinal timik kitle görüldü. Brakiyosefalik trunkus tutulmuştu ve superior vena kavada tümör trombusu vardı. Sternotomi, brakiyosefalik yolla en-blok tümör rezeksiyonu (PTFE) ve sol brakiyosefalik ven kanalı (sığır perikardı grefti) yaptık. İşlem görmüş innominat veni rekonstrükte etmek için bir kanal şeklinde biçimlendirilmiş sığır perikard yaması kullanıldı. Timik nöroendokrin tümörler, tüm timik tümörlerin %5'ini oluşturur. Büyük hücreli nöroendokrin karsinomların (Large cell neuroendocrine carcinomas-LCNEC) daha kötü prognoza sahip olduğu ve doğası gereği agresif olduğu kabul edilir. İmmünohistokimya boyaması, kromogranin, CKAE1/AE3 için pozitif bulundu ve TTF-1 için negatifti. Bu nedenle, bu muhtemelen akciğer LCNEC yerine timik LCNEC idi. Timik tümörler için Masaoka-Koga evre sınıflandırmasına göre, bu tümör Evre Iva'ya uymaktadır.

Anahtar Kelimeler: Timik maligniteler; nöroendokrin tümörler; vasküler rekonstrüktif cerrahi

In 1972, Rosai and Higa first described primary neuroendocrine tumours of the thymus (NETT). Prior to that, all epithelial tumours of the thymus were referred as epithelial thymomas.[1] These tumours are considered rare and constitute approximately 0.4% of all carcinoid tumours. Surveillance, Epidemiology and End Results (SEER) database shows the incidence of NETT to be 0.02/100,000 person per year.[2] According to the World Health Organization classification of thymic tumours 2015, these tumours are divided into 2 major groups which are well differentiated and neuroendocrine carcinomas. They are fur-

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ther subdivided to well differentiated represented by typical and atypical and neuroendocrine group represented by small-cell and large-cell types.[3] We report a case of advanced thymic large cell neuroendocrine tumour with multiple vascular structure reconstructions using bovine pericardial patch and polytetrafluoroethylene (PTFE) grafts.

CASE REPORT

A fit 51-years-old gentleman presented with shortness of breath for 2 weeks associated with chest discomfort. He had loss of 5 kg in the past 2 weeks. He had no haemoptysis, no history of tuberculosis contact or family history of malignancy. Clinical examinations was unremarkable, but the chest radiograph showed a widened mediastinum. Further investigations with contrasted computed tomography (CT) showed an anterior mediastinal mass measuring 8.8x7.2x8.9 cm (APxWxCC). The mass appeared heterogeneously enhancing with multiple punctate calcifications within. The superior vena cava (SVC) and the left brachiocephalic vein are displaced anteriorly. We performed an ultrasound-guided biopsy of the mass and the histopathological examination revealed a large cell neuroendocrine tumour of the thymus. He was then planned for 6 cycles of EP (etoposide and cisplatin) and was given radiotherapy. The reassessment CT showed mass to have increased in size 9.7x10.7x10.8cm and progressive compression onto the left brachiocephalic vein with near total occlusion. The tumour increasingly compressing onto the SVC with the presence of tumour thrombus within.

We performed sternotomy and tumour en-bloc resection. Intra-operatively, we found a large mediastinal tumour measuring 10x8cm. The relation of the tumour was anterior: left brachiocephalic vein, inferior: pericardium and base of heart, inferior-medial: ascending and arch of aorta, superior-medial: brachiocephalic trunk, posterior: medial aspect of the right upper/middle lobe of lung and posterior-lateral: encasing the SVC and proximal of right brachiocephalic vein. The tumour was densely adherent to the structures mentioned above. The patient sustained iatrogenic injuries to the aortic arch and brachiocephalic trunk. The aortic arch was repaired, and the brachiocephalic trunk was anastomosed to the ascending aorta with a PTFE graft conduit. The left brachiocephalic vein was transacted and removed as en-bloc with the tumour. We used bovine pericardium patch, fashioned into a conduit, to reconstruct the transacted innominate vein. There were some lung and pleural tissue which had to be compromised for en-bloc tumour removal. He was closely monitored and was extubated on day 2 post-operation. He had right pleural effusion which required a longer hospital stay than expected (12 days) but resolved with treatment. Although the patient was counselled for both targeted therapy with pembrolizumab versus, he preferred conventional chemotherapy with cisplatin and etoposide.

The required ethical approval and consent to participate has been obtained from the patient. The patient consented information to be for publication purposes (Figure 1, Figure 2a, Figure 2b, Figure 3, Figure 4, Figure 5, Figure 6).

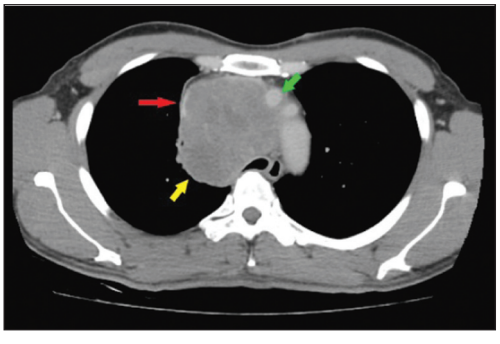

FIGURE 1: First contrasted CT (transverse plane) demonstrating a mediastinal with compression to the SVC and close proximity with brachiocephalic trunk (Red arrow: shows the compressed SVC, yellow arrow shows the tumour and the green arrow shows the brachiocephalic trunk). CT: Computed tomography; SVC: Superior vena cava.

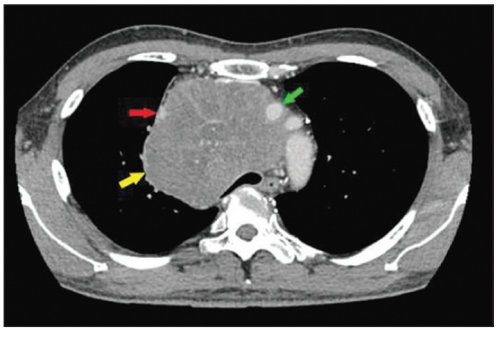

FIGURE 2a: Contrasted CT (axial plane) prior to surgery with a mediastinal mass that has increased in size and the presence of local invasions.
CT: Computed tomography.

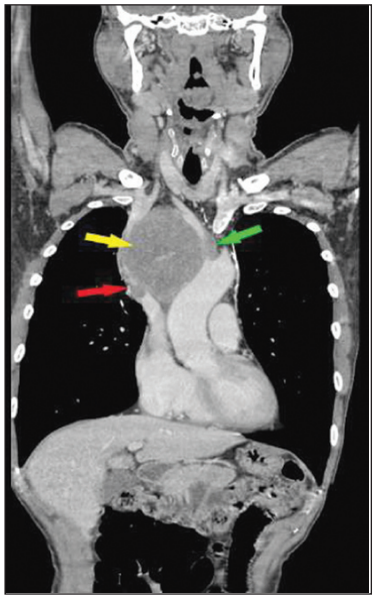

FIGURE 2b: Contrasted CT (coronal plane) prior to surgery with local invasion of the tumor and the presence of tumour thrombus. CT: Computed tomography.

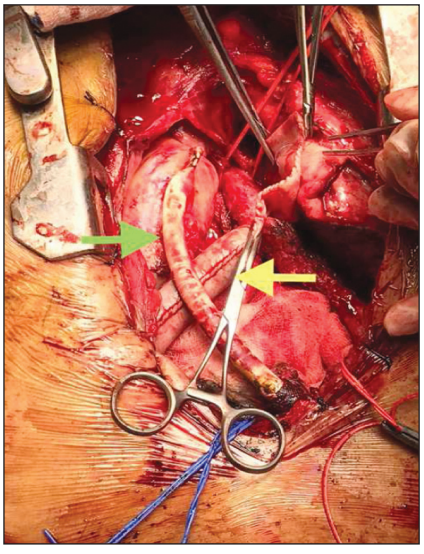

FIGURE 4: The extensive vascular reconstruction (PTFE graft between brachiocephalic trunk and ascending aorta (green arrow), and brachiocephalic vein conduit with bovine pericardium). PTFE: Polytetrafluoroethylene.

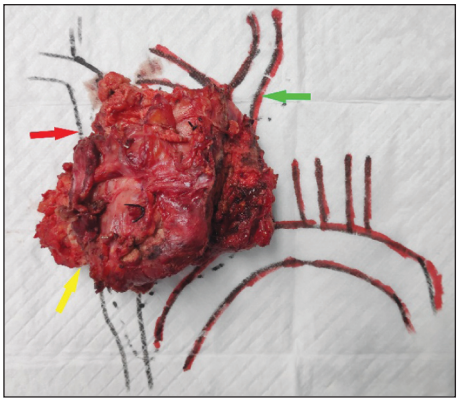

FIGURE 3: Resected specimen of tumour in relation to adjacent vascular structures.

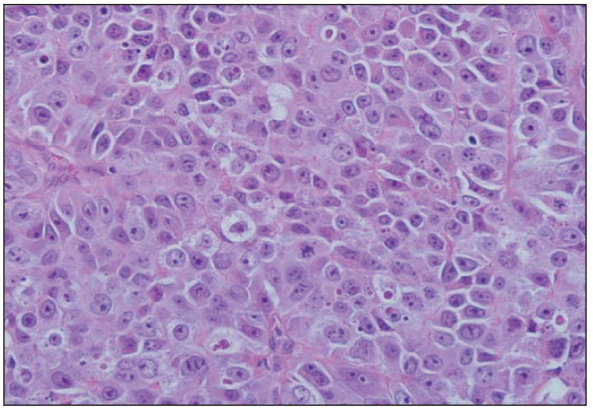

FIGURE 5: H&E staining: Large tumour cells, predominantly polygonal in shaped with prominent nucleoli (x400).

DISCUSSION

Thymic malignancies are rare (0.13 cases per 100,000 population in the United States) but among the most frequent mediastinal primary tumours.[4] Thymic neuroendocrine tumours constitutes approximately 5% of all thymic tumours with a median age of 54 years and predominantly in male population.[5] Amongst NETT, large cell neuroendocrine carcinomas (LCNEC) are considered to have a poorer prognosis and aggressive in nature. They usually present at advanced clinical stage similarly to this case. This patient presented with symptoms due to compression

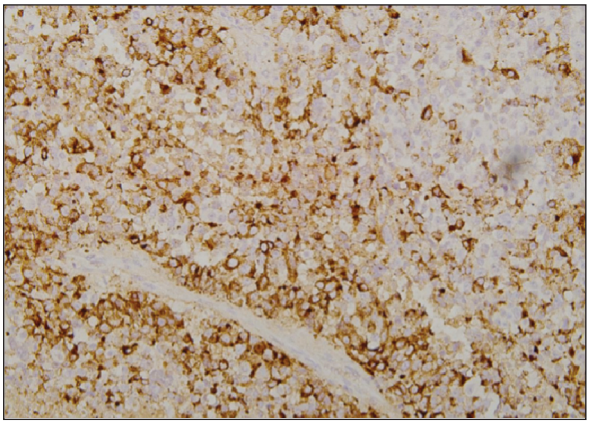

FIGURE 6: Chromogranin staining showed diffuse positivity (x200).

to lung and airway. Despite having CT images, identification of the origins of the mediastinal mass is challenging as it may arise from a primary lung tumour or another mediastinal organ primary neoplasm. In this patient, this issue was addressed with an ultrasonography guided biopsy which showed a NETT.

The mass was in the anterior mediastinum and the histopathological findings showed extensive areas of necrosis and the tumour cells displaying large, polygonal in shape with moderate to abundant cytoplasm and prominent nucleoli with high mitotic count. They are positive for neuroendocrine markers, chromogranin (diffuse) and synaptophysin (patchy) with negative for TTF-1 immunohistochemistry stains. Hence, this was likely thymic LCNEC instead of lung LCNEC.[6] Masaoka-Koga staging system was selected by the International Thymic Malignancy Interest Group (ITMIG) to stage thymic malignancies. In accordance to Masaoka-Koga stage, this tumour would represent Stage IVb. In 2017, American Joint Committee of Cancer proposed a TNM staging for all thymic malignancies. In accordance to it, this patient would be Stage IVb also.[7] According to SEER, the median survival for the patient who had surgical therapy was longer (109 vs 46 months).[4]

The prognosis of the disease is closely related to the staging and according to the European Society of Thoracic Surgeons, the median overall survival was 13.5 years for Stage I and II, 7.3 years for Stage III and 4.2 years for Stage IVb.[7] There were also studies that showed a higher 10-year survival rate in patients with smaller tumour at first presentation. Although there were case reports which demonstrated benefits of neoadjuvant therapy for locally advanced disease, our patient had little improvement from it, therefore its value requires further investigations. Completeness of surgical resection highly influence the overall survival of the patient.[4,7] We were unable to obtain clear margins as the tumour was locally aggressive with close proximity with major vessels. Therefore this is an R2 resection and the survival may be guarded.

CONCLUSION

This is a rare and aggressive form of tumour which require more studies to design a better management plan to yield a better outcome. This was an aggressive tumor which required us to perform an unique vascular reconstruction of the brachiocephalic trunk and brachiocephalic vein with PTFE graft and bovine pericardium.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Ahmad Zuhdi Mamat;* ***Control/Supervision:*** *Ahmad Zuhdi Mamat, Rosnelifaizur Ramely;* ***Data Collection and/or Processing:*** *Harinthiran Vijeyan, Wan Zainira Wan Zain;* ***Literature Review:*** *Andee Dzulkarnaen Zakaria;* ***Writing the Article:*** *Harinthiran Vijeyan.*

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