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The Contentious Management of Anaplastic Thyroid Carcinoma with Acute Airway Obstruction during COVID-19 Pandemic

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Abstract

There are many important concerns and issues raised in managing acute airway obstruction cases with regards to the current COVID-19 pandemic. As a further matter, a patient with a huge thyroid mass in anaplastic thyroid carcinoma (ATC) presenting with impending airway obstruction poses treatment challenges, as immediate active intervention is necessary despite the risk of spreading of COVID-19 viruses. The unknown status of COVID-19 of the patient will add additional concerns during active assessment and treatment as patients with this undifferentiated thyroid carcinoma commonly deteriorate fast. This carcinoma may also invade the trachea and result in upper airway

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obstruction leading to a fatal outcome. Therefore, an appropriate treatment strategy is essential. This report highlights a case of an ATC patient who presented with diffuse cemented-hard anterior neck, whereby the whole management of ATC with acute airway obstruction during this COVID-19 pandemic is purely contentious and challenging. The issue of providing artificial ventilation either via intubation or tracheostomy is made more complicated as the patient presents with an acute upper airway obstruction whilst the COVID-19 status is unknown. While endotracheal intubation approach was not easy, the trachea was also difficult to be identified externally due to the huge 'cemented-hard' mass plastered over the compressed trachea. Due to the advanced disease, surgical intervention was not an option.

Keywords: *Coronavirus disease 2019, thyroid cancer, upper airway obstruction, Malaysia*

1. Introduction

The World Health Organization (WHO) characterized the novel coronavirus disease 2019 (COVID-19) as an infectious disease caused by a newly discovered strain of coronavirus in human. It was unknown before December 2019, until the outbreak of a pneumonia of unidentified cause emerged in Wuhan, China (Chan et al., 2020). The first case of COVID-19 in Malaysia was detected on 24 January 2020 (World Health Organization, 2020). As of 19 May 2021, Malaysia had a total of 485,496 of cases with 2040 deaths (Ministry of Health, Malaysia, 2021). With the increasing trend of COVID-19 outbreak in Malaysia, the Ministry of Health (MOH) warrants all healthcare providers to adapt and adopt the recommended Infection and Prevention Control guiding principles.

Anaplastic thyroid carcinoma (ATC) is one of the most aggressive forms of solid tumours in human, with an average survival of 3-5 months. Although it contributes to only 1-3% of all thyroid cancers, the mortality is very high with up to 14-50% of death cases reported (Nagaiah et al, 2011; Perri, 2011). As the disease is rapidly progressing, most of the cases were diagnosed at the advanced stage. Rapid progression of the anteriorly enlarged neck mass often requires prompt airway management due to the acute airway obstruction. This can lead to an inevitable mortality by suffocation and patient with poorly differentiated to undifferentiated thyroid carcinoma commonly have a fast deterioration and fatal outcome (Yang et al., 2012).

The difficult airway has always posed varying degrees of challenges to both the anaesthesiologists and otolaryngologist. Even the established treatment algorithm of difficult airway management needs to be modified to a varied extent taking into consideration the risks posed during normal intubation and ventilation in potential COVID-19 patients (Bajwa et al., 2020). These risks are further amplified in the case of difficult airway as presented in ATC patients. In this report, we highlight the challenges in managing an elderly patient with anaplastic thyroid carcinoma, who presented with acute upper airway obstruction, during the pandemic.

2. Case Presentation

A 66-year-old lady, with underlying hypertension and history of cerebrovascular accident associated with dysarthria, presented with progressive worsening shortness of breath for one week duration which was aggravated by cough. It was associated with intermittent noisy breathing.

She had noticed the presence of a painless anterior neck swelling since past two years which turned to be rapidly increased in size in one-month duration. She also complained of difficulty in swallowing solid food for two-week duration as well as worsening of the pre-existing dysarthria. She denied any fever, hemoptysis, loss of appetite, loss of weight or night sweats. There was no family history of malignancy, negative contact history with any case of tuberculosis or COVID-19 patients. There were no symptoms of hypothyroidism or hyperthyroidism. Due to her worsening breathiness and intermittent stridor without known COVID-19 status, she was triaged to Severe Acute Respiratory Infection (SARI) Suite, a dedicated consultation room for such symptomatic patients, in the casualty unit itself.

On general examination, she appeared tachypneic with respiratory rate of 25 breaths per minute at rest, spoke with a weak voice, only able to speak 1-2 words in a single breath. There was no apparent stridor heard and she was pink and alert. There were subcostal and intercostal recessions seen. There were no facial asymmetry and no sign of thyroid ophthalmopathy noted. Her vital signs were stable with SpO_2 of 96% via nasal prong oxygen 2 L/min.

Neck examination revealed: a huge anterior neck mass measuring 15 cm x 7 cm, extending from right sternocleidomastoid muscle (SCM) to the left posterior neck triangle; horizontally, superiorly at the level of cricoid cartilage and inferior border was not palpable (Figure 1). The mass was cemented-hard in consistency, fixed to the underlying structure, no skin changes or pus discharge seen. The thyroid cartilage was pushed to the right, with no trachea or cricoid cartilage palpable.

Intra-oral examination was normal. Bedside flexible nasopharyngolaryngoscopy revealed a distorted larynx being pushed to the right side, partially obscuring the glottic opening with left vocal cord appeared to be immobile. Otherwise, there were no obvious mass seen in both vocal cords and surrounding laryngeal structure. Larynx was not edematous and there was no pooling of the saliva seen. Both nasal cavities and nasopharynx were unremarkable. There were transmitted sounds with crepitations on auscultation of the lungs bilaterally.

Her blood investigation showed moderate anemia with thrombocytopenia and leucocytosis. The arterial blood gas (ABG) under nasal prong oxygen was within normal limits. Other blood investigations were normal except the erythrocyte sedimentation rate (ESR) was slightly raised (36mm/h). Thyroid function test and COVID-19 test were performed on her and the results needed 1-2 working days to be ready. Her chest radiograph showed widened mediastinum, deviated trachea to the right, with presence of opacities more prominent in the right lung (Figure 2).

Figure 1: Clinical photograph showing a diffuse cemented-hard anterior neck mass extending from right SCM (black arrow) to the left posterior triangle of neck (red arrow).

Our working clinical diagnosis as the patient was having multiple comorbidities, include respiratory distress with upper airway obstruction secondary to community-acquired pneumonia with unknown COVID-19 status, extensive anterior neck mass, most likely thyroid malignancy with left vocal cord immobility. The differential diagnoses were metastatic neck lymphadenopathy, thyroid lymphoma, and mediastinal lesions such as lymphoma, malignant thymoma, soft tissue sarcoma and tuberculous lymphadenitis with pulmonary involvement.

The patient was then transferred to a designated COVID-19 ward while waiting for the COVID-19 screening result, and family members consented for emergency tracheostomy due to anticipating difficult intubation. In the ward, her condition deteriorated hence the intubation was planned by the intensivist in the operating theatre with otolaryngologist on standby for emergency tracheostomy under full personal protective equipment (PPE) (Figure 3). Despite the huge cemented-hard anterior neck mass and distorted larynx, the endotracheal tube was successfully inserted under nasal flexible endoscopy, hence tracheostomy was abandoned.

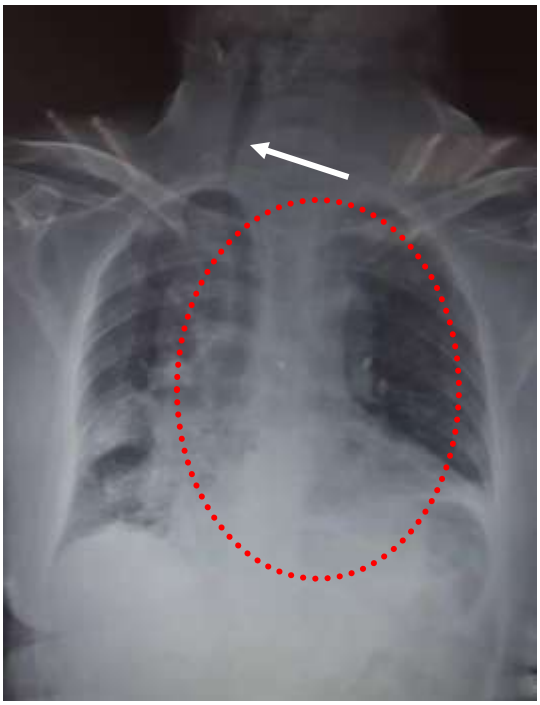

Figure 2: Chest radiograph (AP view) showing a large mediastinal mass (red circle) with deviated trachea (white arrow) to the right side.

The patient was kept intubated and sedated. On the next day, the COVID-19 test result came back as negative. Thus, urgent contrast enhanced computed tomography (CECT) neck and thorax were performed and revealed a huge ill-defined solid cystic heterogeneously enhancing left hemithyroid mass measuring approximately 6.6 x 9.0 cm extending from C3 to T2 level, causing deviation of trachea to the right. There was presence of coarse calcifications within. Inferiorly it extended to the retrosternal region (Figure 4). There were also local invasion (left phrenic nerve palsy), nodal and distant metastasis (lung). Fine needle aspiration for cytology (FNAC) was performed over the anterior neck mass and both smears and cellblock showed singly dispersed malignant cells admixed with necrotic debris at the background. These malignant cells were pleomorphic and composed of multinucleated cells, spindle cells and plasmacytoid cells (Figure 5). They were negative for Thyroid Transcription Factor-1 (TTF-1) and Calcitonin immunohistochemistry. The interpretation of FNAC was ATC and the diagnosis of Stage IVC ATC was confirmed, however patient succumbed to the illness on day 4 of admission due to worsening respiratory failure.

Figure 3: Intensivist and otolaryngology team were on full PPE, preparing for difficult intubation procedure with emergency tracheostomy standby.

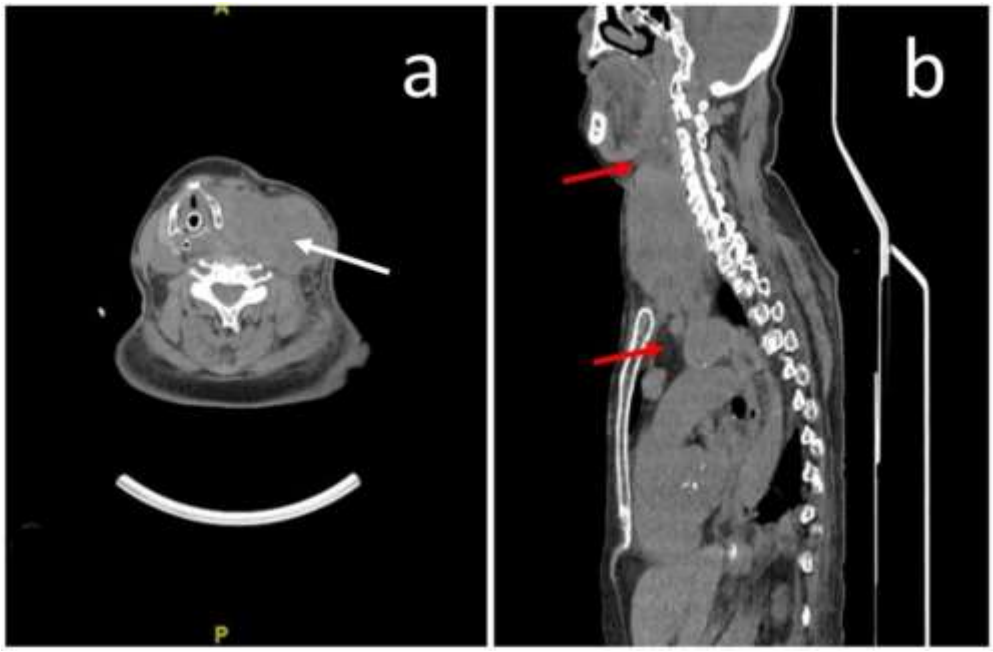

Figure 4: The CECT neck and thorax of patient in axial (4a) and lateral (4b) views. 4a) The white arrow showing a huge, ill-defined left hemithyroid mass compressing and pushing the whole larynx to the right side. 4b) The mass extended from lower part of mandible (C3) to the retrosternal space (T2) as indicated by red arrows.

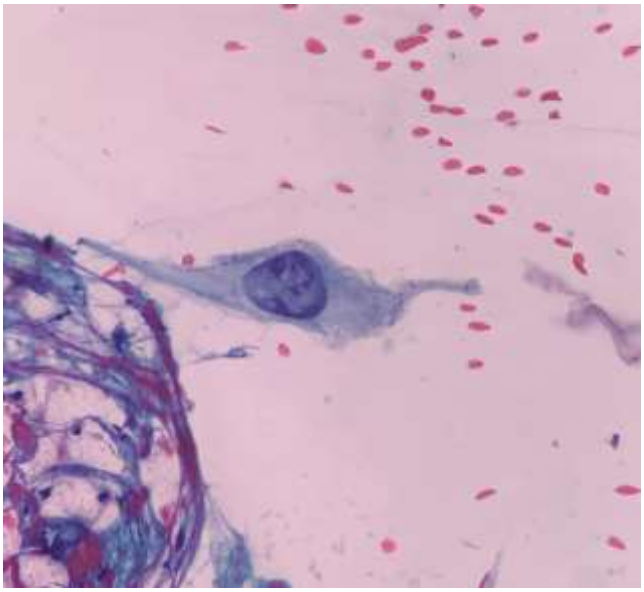

Figure 5: Cytologic smear of the neck mass demonstrates giant spindle cells with the nucleus is almost 20 times larger in comparison with the red blood cell (PAP stain, x 40 magnification).

3. Discussion

ATC is more common in women than in men and peak of occurrence is within sixth to seventh decades of life (Kebebew et al., 2005). The theoretical etiologies of ATC are divided into two: (i) transformation of well-differentiated thyroid tumour and (ii) *de novo* which means it derives from the follicle cells itself without transformation from well-differentiated thyroid tumour, however the exact pathogenesis remains unknown (Sugitani et al., 2012). The risk factors include pre-existing well-differentiated thyroid carcinoma (which accounts to about 25-50% of the cases), history of radiation, goiter, iodine deficiency and female sex (Yamazaki et al., 2019). However, pertaining to the case presented, the patient had no identified risk factors, besides the unmodifiable gender factor.

The clinical manifestation varies depending on the disease progression. Locally, ATC may show rapid anterior neck enlargement, accompanied with dysphagia (40%), hoarseness (40%) and stridor (24%) (Dwipayana et al., 2017). Locoregional symptoms include enlarged lymph nodes and neck pain while systemically the patient may develop shortness of breath with lung metastases and remarkable weight loss (Lo et al., 2020).

As the disease rapidly progress, most cases were diagnosed at advanced stage besides the histologically proven ATC itself has made the thyroid malignancy as stage IV. Approximately 20-50% of patients already have distant metastases (80% to the lung, 6-16% to the bone and 5-13% to the brain (Taccaliti et al., 2012). In our case, the patient complained of worsening of shortness of breath with rapidly growing anterior neck mass for one month, associated with dysphagia and intermittent stridor, may indicate locally advanced thyroid carcinoma with retrosternal extension and lung metastases as evidenced on radiograph and CECT. Hence, the disease was staged as IVC according to AJCC 8th edition (AJCC, 8th Edition 2018).

The fact that airway management is always a difficult issue in ATC especially during this COVID-19 pandemic is indisputable. It is incredibly critical to do pre-testing of COVID-19 status in the patient as she may require either active airway intervention or hospitalization with concern of exposing health care workers (Shaha AR, 2020). Hence, modification of the treatment approaches to a case of suspected thyroid cancer is necessary (Vrachimis A et al., 2020). According to the first ATC guidelines, elective tracheostomy is best avoided; however, it may be necessary if the patient is having acute airway distress (Smallridge et al., 2012). In this case, both intubation and tracheostomy were challenging. The trachea was difficult to be identified due to the large cemented-hard mass covering the trachea, besides it was pushed to the contralateral side. Surgical debulking of the thyroid mass may need to be performed to get the access to the trachea, as well as obtaining the tissue for diagnostic purposes.

The tissue diagnosis of ATC possesses a challenge in cytological smear, as the malignant cells tend to disperse singly instead of any pattern. Based on the pleomorphism of the cells, the possible differential diagnoses are medullary carcinoma of the thyroid, poorly differentiated carcinoma of the thyroid and ATC. The immunohistochemistry play a big role in supporting the tissue diagnosis. The medullary carcinoma will be stained with calcitonin as it is arising from the C cells of the thyroid, whereas the poorly differentiated carcinoma of the thyroid will show positivity towards TTF-1. Both immunohistochemistry are negative in ATC as demonstrated in our case (Cibas and Ali, 2017).

Generally, there is no specific treatment for ATC per se, but there are roles of surgical, radiation, chemotherapy or combination of these modalities, betting on situation. There are 2 criteria used to determine curative surgical resection; (i) distinguishing between locoregional disease and distant metastatic ii) the extent of local invasion and structures involved. In a patient with locoregional disease (Stage IVA/IVB), tumour can be curatively resected depending on structural involvement, whereas in an advanced ATC with metastasis (Stage IVC) treatment option are going to be palliative (Corrigan et al., 2019). However, most of the cases are detected late, at least stage IVB with extrathyroidal spreads, hence tumour is unresectable as it may involve invasion of prevertebral fascia, carotid artery or other large blood vessels and spreads to thorax. In this case, due to the advanced disease with lung metastasis (Stage IVC), surgical intervention is not recommended and best treated with supportive care.

4. Conclusion

Acute airway obstruction is always an emergency, despite the caveat that says, “There is no emergency in pandemic!” (Bowhead Health, 2020). An integrated treatment strategy is crucial when encountering a case of anaplastic thyroid carcinoma (ATC) complicated with airway obstruction in this COVID-19 pandemic. Acute airway obstruction in ATC must be addressed with caution as an emergent intervention regardless of the COVID-19 status with difficult airway, to which requires multidisciplinary team involvement and modification of treatment approach during this deadly pandemic. In this case, artificial airway was instituted via endotracheal intubation in full PPE as COVID-19 status was uncertain at the time of presentation. Nevertheless, once the diagnosis is confirmed, plus the extension of the lesion, supportive management was the best option.

5. Acknowledgement

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