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CASE REPORT

Lymphoma with superimposed tuberculosis and fungal infection mimicking parapharyngeal abscess complicated with recurrent neurocardiogenic syncope: a case report

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Abstract

Introduction: Lymphoma of parapharyngeal space (PPS) is a rare condition. The clinical presentations may vary and often masquerades as infection or an inflammatory condition. A misdiagnosis will lead to a delay in treatment of the disease. Due to the complex anatomy of PPS, any attributed pressure from masses can lead to a life-threatening event such as cardiac syncope. *Case Report:* We report a rare case of PPS B-cell non-Hodgkin lymphoma with superimposed Tuberculosis (TB) and fungal infection that presents with several episodes of syncope and hemodynamic depression. *Discussion:* The clinical entities in PPS lesions syncope and its associated syndromes, pathophysiology, and differential diagnosis together with possible managements are further discussed.

Keywords: Lymphoma, tuberculosis, fungal, neurocardiogenic, syncope

INTRODUCTION

Parapharyngeal space (PPS) is one of the potential facial planes for neoplasms and infections; however, the incidence is uncommon and the neoplasms are mostly benign. Tumours of parapharyngeal space accounts for less than 1% of all head and neck neoplasms.[1] The most common neoplasms are salivary followed by neurogenic in origin.[2] Only one-third of the neoplasms are malignant, lymphoma being the top four on the list. Reactive nodes in response to infections are the most common findings. Parapharyngeal space abscess is the second most common of the deep neck abscesses.[1] We report a rare case of B-cell non-Hodgkin lymphoma with superimposed Tuberculosis (TB) and fungal infection masquerading as an abscess. He also presented with several syncopal attacks and hemodynamic depressions, initially triggered while dressing his neck wound and eventually became spontaneous.

CASE REPORT

A 58-year-old Malay gentleman presented to otorhinolaryngology outpatient department with increasing painful left neck swelling for 3 weeks. His only complaint was a fluctuating fever with no other symptoms from ear, throat and nose nor was there any constitutional symptom. Clinical examination showed a firm tender upper left neck swelling measuring 8x7cm. Except for trismus, other examinations including flexible nasal endoscopy were unremarkable. An initial Contrast Enhanced Computer Tomography (CECT) imaging revealed a fluid collection with septations within, occupying the left parapharyngeal space (Fig. 1A). The internal and common carotid arteries, as well as the internal jugular vein, were displaced medially. No filling defects were seen within these vessels. There was no splaying of the carotid bifurcation by any enhancing mass. A diagnosis of parapharyngeal abscess was made. However, the incision and

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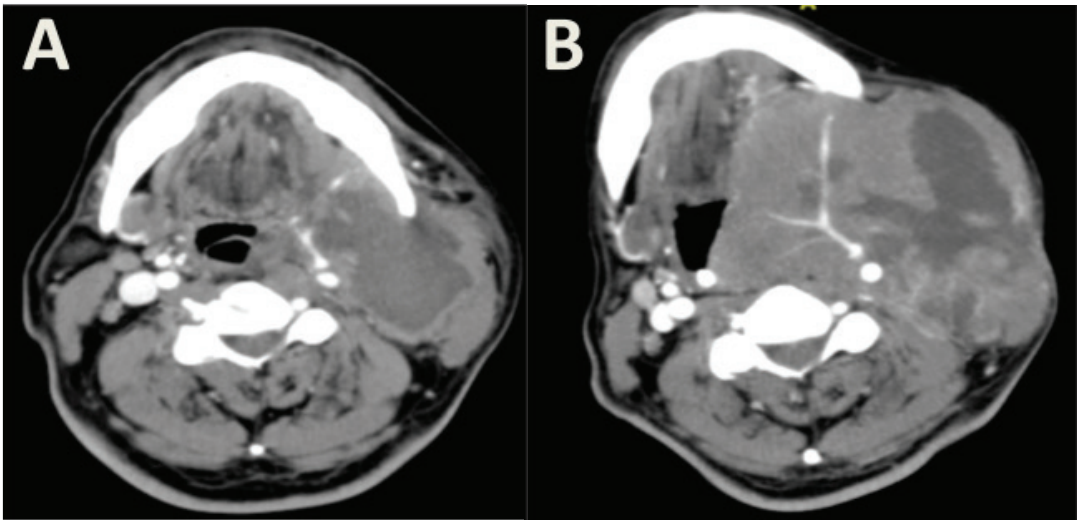

FIG. 1: (A) Thick wall collection occupying the left parapharyngeal space measuring 8.9 x 5.2 x 7.4cm with septation extending to the submandibular and cervical spaces. (B): Heterogenous enhancing collection measuring 10.2 x 9.2 x 12.0cm with a mixed solid cystic component within which encased the carotid arteries.

drainage performed yielded only serous fluid. A polymerase chain reaction (PCR) performed on the tissue taken from the abscess wall confirmed a tuberculous lesion (TB) and histological examination revealed some atypical cells. He was started on an anti-tuberculous regime.

In addition, dressing of the wound triggered multiple episodes of syncopal attacks whereby the blood pressure dropped to a range of 70-92/50-57 mmHg associated with bradycardia of 50 beats per minute. Each episode was accompanied by urinary incontinence and a spontaneous regain in consciousness after a few minutes. Electrocardiogram (ECG) showed sinus bradycardia but no acute ischemic changes were seen. His ejection fraction was normal, which was 56%. There were only mild mitral regurgitation and trivial tricuspid regurgitation. Holter monitoring was not indicated. He was managed as syncopal attack caused by carotid body stimulation secondary to the mass effect.

A few weeks later, he presented again with increasing neck swelling involving the facial and lower four cranial nerves palsy. The subsequent syncopal attacks occurred spontaneously without provocation, in one of which episodes he fainted while driving. A repeat CECT imaging revealed a progressively enlarging lesion with a thicker wall, which encased the carotid arteries (Fig. 1B). A repeated tissue biopsy was taken from the similar left neck swelling and the histological examination revealed sheets of medium to large, malignant lymphoid cells exhibiting round pleomorphic vesicular nuclei with a prominent single to multiple nucleoli and clear cytoplasm. Immunohistochemical staining was positive for CD20, BCL2 and BCL6 and negative for CD3 and CD10 which confirmed the diagnosis of diffuse large B-cell lymphoma (DLBCL) (Fig. 2). In addition, Candida parapsilosis was also isolated from the same tissue biopsy.

The patient had received concomitant 6 cycles of chemotherapy, 5 cycles of RCHOP (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone) and 1 cycle of R- EPOCH (Etoposide phosphate, Prednisone, Vincristine sulfate, Cyclophosphamide, and Doxorubicin hydrochloride) as well as an anti-fungal therapy and anti-tuberculosis (TB). However, anti-TB was stopped after 6 weeks of treatment in view of patient develop anti-TB induced hepatitis. He responded well to the treatment as shown by the regressing neck swelling with no further syncopal attack reported.

DISCUSSION

The treatment of parapharyngeal lymphoma is often delayed due to a misdiagnosis.[1] The associations of TB or fungal infection with Non-Hodgkin lymphoma (NHL) have been reported in several cases.[2-5] However, this is the first case of DLBCL with dual concomitant infections by both TB and fungus, to be reported.

In 2016, WHO reported that 10.4 million people suffered from TB of which 64 percent

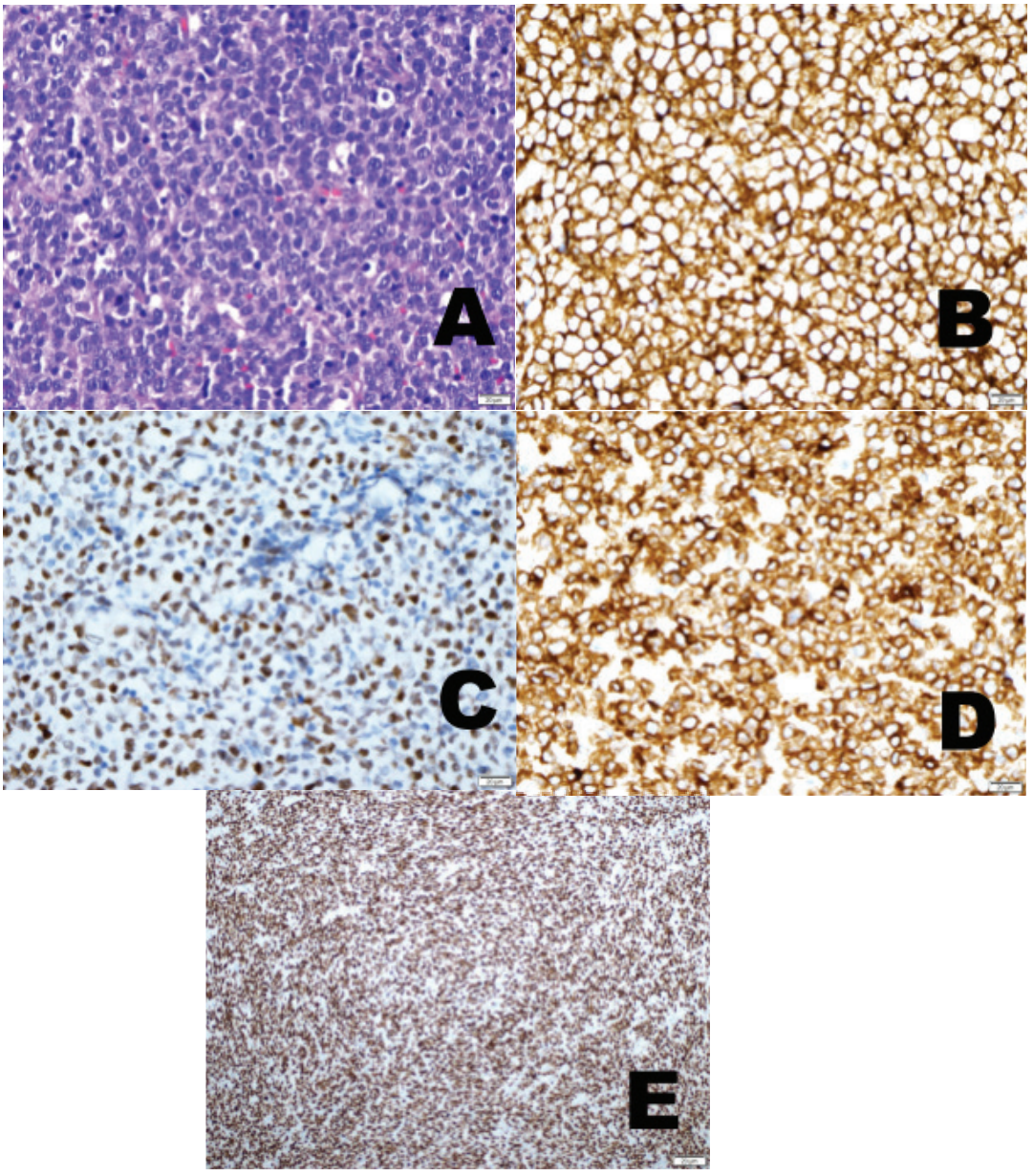

FIG. 2: (A) Diffuse sheets of medium to large malignant lymphoid cells exhibiting round pleomorphic vesicular nuclei with prominent single to multiple nucleoli and moderate amount of clear cytoplasm (H&E, x400). (B) Diffuse positivity for CD20 (CD20, x400), (C) Bcl-6 positive (x400), (D) Bcl-2 Positive (x400), (E) The ki67 proliferative index is 90% (x40).

were from developing countries.[6] In patients with lymphoma, immunosuppression is the main cause that leads to their susceptibility to TB. The lymphoma may have evoked a granulomatous reaction by aberrant cytokine production from the tumour cell.[7] A cohort study by J Askling *et al*. (2001) concluded that patient diagnosed with severe or chronic TB has been linked to increased occurrence of NHL.[8]

Similarly, studies showed that fungal infections are most likely to occur in patients diagnosed with haematologic neoplasms and 10 percent of them had lymphoma. Impairment of immunological function in lymphoma patients either due to the disease progression itself or the therapies involved may further result in fungal infection.[5] Besides that, those who are immunocompromised due to lymphoproliferative

disorders, diabetic, post-transplant and patients on immunosuppressive therapy showed tendency in developing this dualpathologies.[5] There are no pathognomonic radiological features of PPS lymphoma. However, CECT is useful in clinical staging, assessment of prognosis as well as treatment planning of head and neck lymphomas. Choi *et al*. (2006) suggested that the common criteria in CECT neck findings of head and neck carcinoma, lymphoma and granulomatous diseases are an ill-defined margin with heterogeneous enhancement of the lymph node with central nodal necrosis.[9] However, discriminating these diseases exclusively based on imaging findings of the involved lymph node are inconclusive. Thorough evaluation involving a patient's history and histologic findings are needed to an accurate diagnosis.

Gold standard for diagnosing TB is via culture, however, it is a very laborious and time-consuming procedure. The result may take approximately 4 to 6 weeks, hence significantly affecting patient care. The advance technique of PCR has a greater advantage, with 90.3% and 98.6% sensitivity and specificity respectively in the diagnosis of TB.[10] The concentration of M. tuberculosis mRNA declines after initiation of therapy with 90% of patient becoming negative within 2 months of treatment.[11]

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma representing approximately 30% of newly diagnosed NHL cases worldwide.[12] This lymphoma can be diagnosed based on histological findings, cytogenetic and immunophenotyping. Morphologically, the neoplastic cells and their nuclei are relatively larger than reactive lymphocytes. Based on immunophenotyping, the neoplastic cells of DLBCL express Pan-B antigens such as CD19, CD20, CD22, CD75 and CD79a.[13] These markers will determine the subtypes for appropriate therapy. With the presence of CD-20 antigen, the patient was given rituximab (anti-CD20 antibody) in addition to the chemotherapy regime.

One of the alarming symptoms presented by this patient was the recurrent episodes of syncopal attacks associated with hypotension and bradycardia. In view of the PPS consists of many vital structures namely, carotid artery and its branches, lower four cranial nerves (glossopharyngeal, vagus, accessory and hypoglossal nerves), sympathetic trunk, and internal jugular vein (IJV). Due to its vital contents and a complex anatomy, any pressure from masses within the space can lead to significant morbiditysuch as carotid sinus syncope (CSS). Syncope is a transient global cerebral hypoperfusion characterised by its rapid onset, short duration and spontaneous complete recovery. The aetiologies range from benign disorders to severe life-threatening diseases. However, it was estimated that the incidence of syncope caused by head and neck neoplasms was less than one in 250.[14]The occurrence of syncope could be an indication of malignancies in the head and neck. Other conditions include carotid body tumours and vagal schwannoma. Of the reported cases of neck lymphoma, only a few presented with CSS.[15-16] In this patient, we postulate that the direct stimulation to the carotid body leads to carotid sinus hypersensitivity (CSH) syndrome; hence an exaggerated vasodepressor response resulting in syncope during each dressing procedure. Furthermore, the infiltration in the carotid sinus area continuously stimulates carotid nerve depolarisation, thus lowering its threshold and increases the activity of parasympathetic reflex arc.[17] There are no specific treatment guidelines for syncope in this patient. Cardiac pacing via pacemaker may be part of the options, however, tumour debulking or tumour shrinkage following specific treatment of the lesion can be the best option here.

CONCLUSION

The diagnosis of lymphoma of the parapharyngeal space can be misleading, especially with the coexistence of TB and fungal infections. Clinically, the perplexity of the manifestations was made worst by the occurrence of recurrent syncopal attacks. An adequate tissue biopsy is imperative to prevent serious clinical errors. Hence, we should be aware of the possibility of an underlying malignant lesion masked by coexisting infections in patients who do not respond well to the initial treatment.

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