

High-grade B-cell Non-Hodgkin's Lymphoma Masquerading as Thyroid Carcinoma; a Case Report

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Abstract

Introduction: High grade B-cell lymphoma and diffuse large B cell exhibiting myelocytoma (MYC) translocation with B-cell lymphoma 2 (BCL2) and/or B-cell lymphoma 6 (BCL6) re-arrangements, also known as double and triple hit lymphomas, are aggressive entities. World Health Organization update 2017 includes this cytogenetically defined category of "High grade B cell lymphoma with myelocytoma MYC and BCL2 and/or BCL6 rearrangements" as a distinct entity on their own. We present an interesting case of an obese patient presenting with a neck mass, suspected to be an aggressive thyroid carcinoma, which eventually turned out to be a high grade B-cell lymphoma. **Case Description:** A 64 years-old male presented with complaints of neck pain for 10 weeks and a huge swelling in front of neck for 4 weeks. Respiratory system evaluation revealed cough, pleuritic pain and expectoration. Rest of the systemic review was unremarkable. Baseline reports showed hypothyroid status. Ultrasonography (USG) thyroid showed right upper pole Thyroid Imaging Reporting and Data Systems - 4 (TIRADS-4) nodule with bilateral cervical lymphadenopathy for which correlation with fine needle aspiration cytology (FNAC) was advised. Magnetic resonance imaging (MRI) films were submitted for review which showed overall features of locally invasive primary thyroid malignancy. Case was discussed in a multi-disciplinary team (MDT) meeting and suspicion arose of non-thyroidal origin of tumor. Patient underwent Positron emission tomography/computed tomography (PET/CT) as per MDT recommendations. PET/CT findings were highly suggestive of lymphomatous disease as opposed to thyroidal malignancy suspicion early on, which was confirmed on histopathology of cervical nodes. **Practical Implications:** High grade B-cell lymphoma is an aggressive entity and can be very deceptive in its presentation, as evident from this case report. Functional imaging modalities such as Fluorodeoxyglucose (F-18 FDG) PET/CT can provide crucial assistance in unmasking a deceptive disease entity masquerading as some other, thus changing the management plan completely.

Key words: Case report, lymphadenopathy, lymphoma, myelocytoma translocation, thyroid carcinoma

Introduction

Lymphomas involving the B cells are known as B-cell lymphomas. Both Hodgkin's lymphomas and majority of the non-Hodgkin lymphomas (NHL) make up the B-cell lymphomas and are subdivided into low and high grade. Diffuse large B-cell lymphomas are known for their biological diversity, more so a subgroup having closeness to Burkitt's lymphoma and a poor prognosis is well known. It has been observed by cytogenetic evaluation that some patients with rearrangements of myelocytoma (MYC) and B-cell lymphoma 2 BCL2 and/or B-cell lymphoma 6 BCL6 (double/triple hit lymphomas [DHL] [THL]) increasingly require more intensive therapy.^[1]

High-grade B-cell lymphomas (HGBLs) and diffuse large B-cell lymphoma (DLBCL) demonstrating MYC translocation with simultaneous BCL2 (or BCL6) rearrangements are called DHL and THL.^[2] The World Health Organization (WHO) 2017 update also defines this category of 'HGBL with MYC and BCL2 and/or BCL6 rearrangements' (DHL/THL) as an entirely different entity.^[3]

MYC, BCL2 and/or BCL6 related groups are not clearly described in the recent genetic classifications, but they are present in two new WHO designations as high-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 translocation and high-grade B-cell lymphoma not otherwise specified.^[3] Optimum management plan approach to this group is difficult which is partly explained by the low frequency of groups such as DHL and the absence of a clear-cut biologic definition. This makes up a diverse category of related malignancies whose response and survival on standard therapeutic modalities varies quite a lot, with worse outcomes in some subtype cases.^[3]

Case Description

A 64-year-old male patient presented to the hospital with complaints of swelling and pain in neck. The swelling started 4 weeks ago, and pain presented nearly 6 weeks before the onset

of swelling. Furthermore, the patient reported difficulty in breathing, swallowing and changes in voice.

According to the patient, he was in the usual state of health approximately 10 weeks ago when he started experiencing pain in his neck. Subsequently, he developed swelling in the area of pain, which progressively increased in size. Swelling was associated with shortness of breath, which was worse on lying in a supine position. Around the same time, he developed hoarseness of voice and bilateral subcostal pain with productive whitish phlegm without any history of haemoptysis. There was no history of fever, nausea or vomiting. The patient had a history of 40 pack-year of smoking. However, he had quit smoking 2 months before his visit to the hospital.

Respiratory system evaluation revealed cough with expectoration and pleuritic chest pain. Rest of the systemic review was unremarkable. Neck pain intensity was given a score of 2 out of possible 10, on an 11-point numeric verbal pain rating scale, where 0 was indicative of 'no pain' and 10 was suggestive of 'worst pain ever,' by the patient. There were no known drug or food allergies. The patient was on tablet prednisolone 5 mg 2 times a day, for the management of compromised airway.

During the general physical examination, the patient was fully conscious, well oriented in time, place and person. He had a bilateral neck swelling which was stony hard in consistency. The left side cervical lymph nodes were palpable. The examination of respiratory, cardiovascular, abdominal and central nervous systems was unremarkable. Likewise, the motor and sensory system evaluation of the upper and lower extremities was normal, and all reflexes were present and symmetric.

Diagnosis and management

Baseline blood reports of the patient revealed that the levels of the thyroid-stimulating hormone and the total thyroxine (T4) were low (44.8 milli-international units/litre [mIU/L] and

2.4 picomole/litre, respectively). These were suggestive of hypothyroidism, and the patient was started with 50 µg tablet thyroxine, on a daily dose of 100 µg, in the morning, 20 min before the breakfast.

Before the hospital visit, the patient had a magnetic resonance imaging (MRI) scan of the neck. The MRI films showed large locally advanced unresectable tumour of the left lobe of thyroid gland with local extension along with enlarged cervical nodal disease. The large lobulated locally advanced tumour was involving the left thyroid lobe and extended into the left carotid sheath. It completely encased the common carotid artery and extended to the suprasternal notch. It was inseparable from the brachiocephalic vessels. Tumour had a significant mass effect on trachea and displaced it to the right side of the midline. Tumour was also inseparable from proximal cervical oesophagus and infiltrated into tracheo-oesophageal recess. No extension into the spinal canal was seen. Tumour was deemed inseparable from the prevertebral muscles. Enlarged cervical nodes were seen in bilateral Level II and III, and a lobulated mass was observed at the right Level IIa, which measured 3 cm in maximum dimensions.

In the hospital, as part of initial workup, the patient underwent ultrasonography (USG) of thyroid gland and a repeat MRI of the neck. The USG showed heterogeneous thyroid gland with a right upper pole solid hypoechoic thyroid imaging reporting and data systems-4 nodule with irregular margins^[4] [Figure 1]. The gland was associated with extensive bilateral cervical lymphadenopathy. The MRI neck suggested presence of a locally unresectable soft-tissue abnormality in the anterior neck, which was involving the left thyroid lobe with retrosternal and superior mediastinal extension and cervical adenopathy. Overall these features were suggestive of locally invasive primary thyroid malignancy [Figure 2].

The case was discussed in a multidisciplinary team meeting and suspicion arose of non-thyroidal origin of tumour. The patient was advised

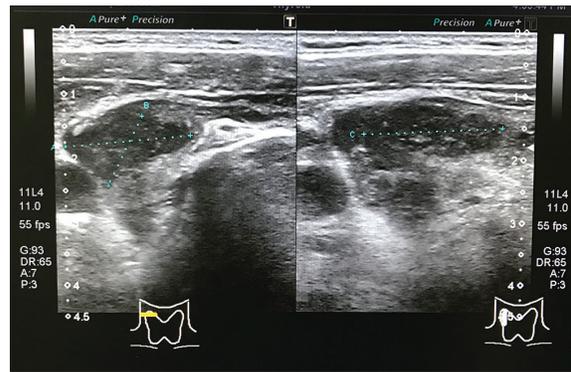


Figure 1: Ultrasound thyroid axial and sagittal images showing right upper pole solid irregular hypoechoic thyroid imaging reporting and data systems-4 nodule



Figure 2: Magnetic resonance imaging neck without contrast showing a neck mass, supposedly thyroidal in origin

computed tomography (CT) and positron emission tomography/CT study (PET/CT) of neck, chest, abdomen and pelvis region and fine-needle aspiration (FNA)/tru-cut biopsy of cervical node and thyroidal mass. CT of neck, chest, abdomen and pelvis region demonstrated neck mass as before and right lower segmental pulmonary embolism for which enoxaparin was administered.

The PET/CT showed hypermetabolic bulky confluent nodal disease above the diaphragm with tonsillar, thyroid, oesophageal, anterior chest wall and skeletal involvement. There was no evidence of nodal disease below the level of diaphragm.

PET/CT findings were highly suggestive of lymphomatous disease as opposed to thyroid malignancy suspicion early on [Figure 3].

Enlarged hypermetabolic palatine tonsils had standardised uptake value (SUV) 18.4. Fluorodeoxyglucose (FDG) avid cervical and supraclavicular adenopathy was noted involving all nodal stations with contiguous extension into anterior mediastinum to the level of carina. This was more on the left side, and it was encasing the trachea, neck vessels and the oesophagus, which was thickened and avid up to the level of carina. Conglomerate dimensions were 19.7 cm craniocaudally (CC) with SUV 28 on the left side and 16.5 cm CC having SUV 24.1 on the right side. Thyroid gland was involved as well. The mass was extending anteriorly into anterior chest wall with oedema and stranding. Multiple hypermetabolic mediastinal nodes were noted in right paratracheal, aortopulmonary window and subcarinal regions. Hypermetabolic right axillary nodes were seen, the largest node measured 3 cm with SUV 27.3 along with tiny left retropectoral nodes. FDG avid foci of marrow uptake were noted in sternum (SUV 7.5) and left 6th costochondral junction (SUV 6) [Figure 4].

An USG-guided core biopsy of the right cervical lymph node and FNA of thyroid mass was planned. However, only cervical node biopsy was completed. The thyroid biopsy was aborted due to the possibility of high vascularity of the neck mass. The right cervical node histopathology report revealed a high-grade B-cell non-Hodgkin's lymphoma with extensive necrosis and crush artefact.

Immunohistochemical stains showed positive leukocyte common antigen and B lymphocyte cluster differentiation (CD20). Proliferation marker protein (Ki67) showed a high proliferative index of 90%. Cellular myelocytomatosis oncogene (C-MYC) was positive in 60% lymphoma cells while Bc12 was weakly positive in tumour. Mouse monoclonal antibody (Cam 5.2), synaptophysin, cluster differentiation (CD3), cluster differentiation (CD10), cluster differentiation (CD 5), terminal

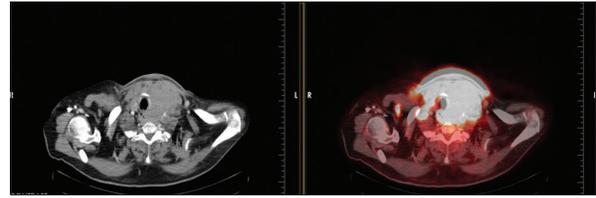


Figure 3: Axial images of F-18 fluorodeoxyglucose positron emission tomography/computed tomography, unmasked the high-grade B-cell lymphoma masquerading as thyroid carcinoma



Figure 4: Maximal intensity projection image F-18 fluorodeoxyglucose positron emission tomography/computed tomography, unmasked the high-grade B-cell lymphoma masquerading as thyroid carcinoma

deoxynucleotidyl transferase (TdT) and cluster differentiation (CD34) were negative. Fluorescent *in situ* hybridisation (FISH) for C-MYC and B-cell lymphoma 2 BCL 2 was also suggested to evaluate for double hit type of high-grade B-cell lymphoma, but the test could not be performed.

Discussion

Among NHL, DLBCL is the most common and the most aggressive type of tumour. DLBCL is an inhomogeneous disease at the genetic and molecular levels. Gene expression profiling studies divide the DLBCL on the basis of cell of origin into two major groups; germinal centre B-cell and activated B-cell subtypes. However, 15%–20% of these approximately do not fit into the above

two mentioned categories and therefore are unclassifiable on a molecular basis.^[5]

For the classification of DLBCL based on cells of origin, various immunohistochemistry methods have been used. Moreover, additionally to the cells of origin, prognostic role for MYC and BCL2 genetic translocations and coexpression of proteins have been identified by proteomics and genetic studies tests.^[3] Studies using FISH have reported that 7%-10% of DLBCL have MYC, BCL2 and/or BCL6 translocations. These have previously been called DHL or THL.^[3] The WHO in its recent revision of lymphoma classification has recognised high-grade B-cell lymphoma with rearrangements of MYC and BCL2 and/or BCL6, separately.^[3]

Repair of genetic/DNA damage, protein synthesis, metabolism and reactions to stressors are all closely related to MYC, a transcription factor which regulates the expression of several target genes involved in the cell cycle.^[6] Mutations involving promoter/regulatory regions, chromosomal translocation and increase in copy number can lead to activation of MYC on chromosome 8 (8q24). MYC activates the tumour protein 53 (TP53) pathways in normal functioning cells which results in cell apoptosis. However, it has been noted that cells having MYC translocations can have TP53 inactivating mutations, which prevent the process of cell apoptosis.

DLBCL with MYC translocations can be accompanied by BCL2 and/or BCL6 translocations and has conferring aggressive clinical behaviour secondary to central nervous system involvement. Due to these reasons, additional central nervous system prophylaxes with aggressive induction regimens are recommended.^[7]

With this report, we hope to illuminate that FDG PET not only compliments other anatomical imaging

modalities but also further provides invaluable information and has the capability of redirecting the entire treatment protocol in confusing cases as evident in this case.

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Authorship Contributions

Conceived and designed the analysis; RB. Collected the data; N/A. Contributed data or analysis tools; IKN and HB. Performed the analysis; IKN and HB. Wrote the paper; AJ and RB. Other contributions; N/A.