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Case Report

Can FDG PET/CT Replace Bone Scan in Detection of Bone Metastasis in Patients of Nasopharyngeal Carcinoma?

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Abstract

Nasopharyngeal cancer (NPC) is quite a rare malignancy worldwide. Literature has shown that there is a marked variation in the prevalence of nasopharyngeal carcinoma (NPC) in different regions of the world. It has an incidence of 0.5 - 2 per 100,000 in Europe and the United States [1]. However, it is much more common in certain parts of Southeast Asia, North Africa, Middle East and particularly in southern China [2].

Majority of the nasopharyngeal carcinomas (NPC) are epithelial in origin and have a strong association with Epstein-Barr virus (EBV). Due to the rich submucosal lymphatic system of nasopharynx, more than 70% of patients have clinically involved lymph nodes at initial diagnosis.

Keywords: *Nasopharyngeal Cancer (NPC); Epstein-Barr Virus (EBV); Lymph Nodes*

Introduction

Nasopharyngeal cancer (NPC) is quite a rare malignancy worldwide. Literature has revealed there is a much larger variation in the prevalence of nasopharyngeal carcinoma (NPC) in different parts of the world. It shows an incidence of 0.5 - 2 per 100,000 in Europe and the United States [1]. However, it is much more prevalent in certain regions of Southeast Asia, North Africa, Middle East and particularly in southern China [2].

Majority of the nasopharyngeal carcinomas (NPC) are epithelial in origin and have a strong association with Epstein-Barr virus (EBV). It has been observed that more than 70% of patients demonstrate clinically suspicious lymph nodes at initial diagnosis due to the rich submucosal lymphatic system of nasopharynx. The increased risk of distant metastasis is directly dependent on clinical lymph-nodal staging. Skeletal metastasis from nasopharyngeal carcinoma represents the most common type of distant metastasis, followed by pulmonary and hepatic metastases [3]. The bone metastatic sites are usually multifocal and commonly present as pain, resulting in immobility, anxiety and depression, therefore severely compromising patient's quality of life [3].

In this case report, we will discuss a case of a 17-year-old young man who developed solitary metastasis to the spine.

Case Report

We present a case of a 17-year-old young caucasian man who had presented with neck pain and swelling for the last 7 - 8 months and nasal bleeding for 5 days. He underwent CT head and neck as a primary investigation for the evaluation of his symptoms. His CT scan showed an enhancing soft tissue density nasopharyngeal mass (Figure 1) with numerous cervical and parapharyngeal lymph nodes (Figure 2). He then underwent a nasopharyngeal biopsy was performed. The histopathological report showed an undifferentiated non-keratinizing carcinoma of the nasopharynx (WHO type III) in May 2015. This diagnosis was followed by metastatic workup which included

MRI head and neck and bone scan. His MRI demonstrated an abnormal signal intensity lesion in the left half of nasopharynx with parapharyngeal extension. The bone scan showed increased focal radiotracer uptake in the nasal and maxillary region without evidence of bone metastasis (Figure 3). The initial staging CT scan had no metastatic disease in lung, liver or bones.

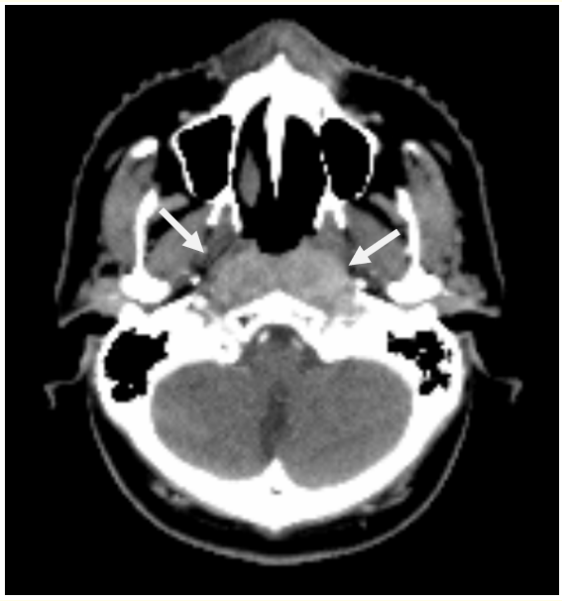

Figure 1: *CT neck demonstrates an enhancing nasopharyngeal mass.*

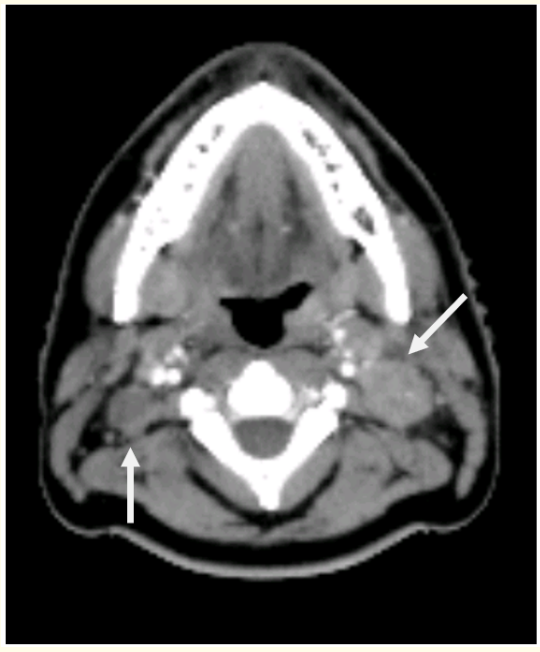

Figure 2: *CT neck showing cervical lymphadenopathy bilaterally.*

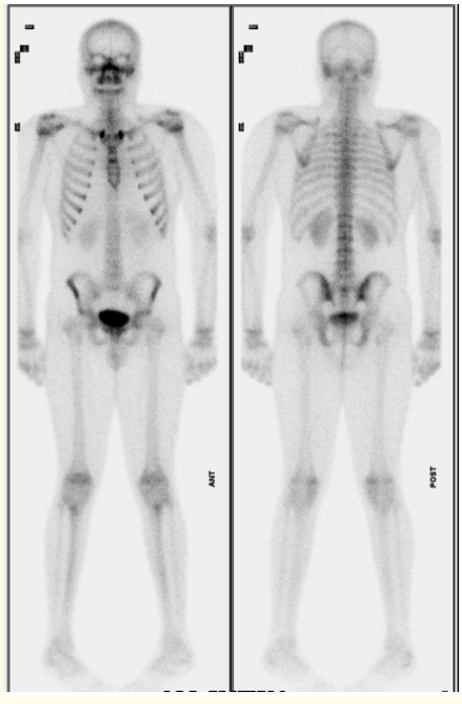

Figure 3: *Whole body scintigraphy showing no evidence of distant bone metastases.*

His treatment included 6 cisplatin-based chemotherapy sessions followed by 35 sessions of radiotherapy in November 2015.

During his chemotherapy treatment, he had presented in the emergency department twice due to excessive sweating, fever, sore throat and nausea. This was managed conservatively, and he was discharged from the hospital in stable condition.

A follow up CT scan of the head and neck was performed to evaluate the response of chemoradiation. It revealed a very good response to disease evident by resolution of nasopharyngeal soft tissue mass (Figure 4) with significant interval decrease in the size of cervical lymph nodes in keeping with marked disease improvement.

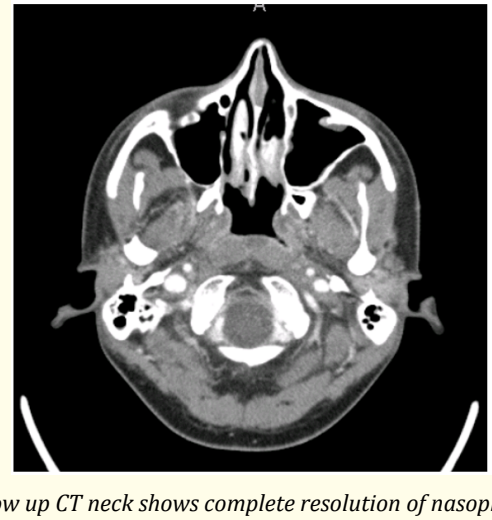

Figure 4: *Follow up CT neck shows complete resolution of nasopharyngeal mass.*

By the end of chemoradiation, the patient was clinically labelled as a complete responder. He then underwent a FDG PET/CT in January 2016 which revealed a focal sclerotic lesion giving FDG uptake with SUV max of 5.03 in the vertebral body of L4 (Figure 5a-5c) compatible with bony metastasis.

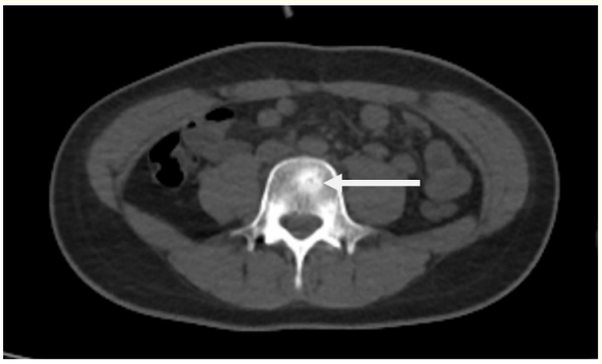

Figure 5a: *CT abdomen bone window demonstrating a solitary sclerotic deposit in L4 vertebral body.*

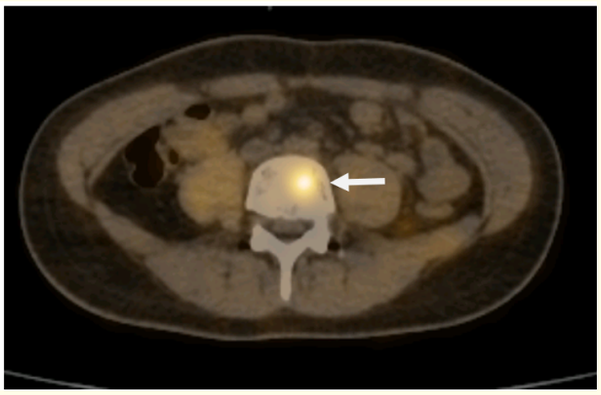

Figure 5b: *PET/CT abdomen is showing corresponding FDG avid lesion in L4 vertebral body consistent with metastasis.*

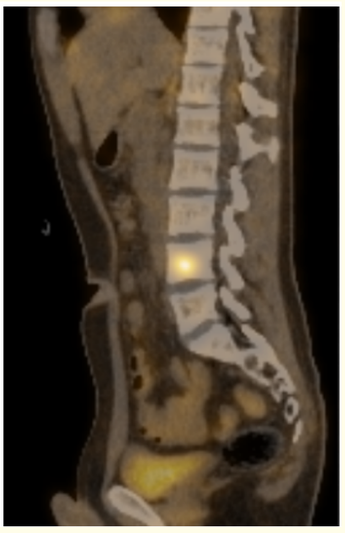

Figure 5b: *PET/CT abdomen is showing corresponding FDG avid lesion in L4 vertebral body consistent with metastasis.*

Discussion and Conclusion

In recent times, NPC has gained world-wide attention because of multiple complex interactions involving viral, genetic, dietary and environmental risk factors [2].

It is a unique malignancy with a carcinogenesis involving a virus (EBV), environmental carcinogens, and an NPC susceptibility gene [2].

Excessive intake of preserved foods at an early age has also been linked to the risk of developing NPC in all population group. Other established risk factors include smoking, and occupational exposure to cotton dust, caustic acids and formaldehyde [4].

According to the World Health Organization, the NPC has been categorised into the following types: type 1, squamous cell carcinoma; type 2a, keratinizing undifferentiated carcinoma; and type 2b, non-keratinizing undifferentiated carcinoma.

Type 1 is less common and has the worst prognosis, however types 2a and 2b are more common and tend to have a better prognosis. In endemic regions, undifferentiated carcinomas usually dominate, accounting for as many as 93% of NPC cases. In contrast, differentiated carcinomas account for 50% of the cases in non-endemic areas. Undifferentiated NPC is associated with Epstein-Barr virus (EBV) infection, whereas differentiated NPC is associated with smoking and alcohol intake [5].

The symptoms of NPC may sometimes be obscured due to its anatomical location. These comprise of nasal, aural, and neurologic symptoms like sore throat, blocked nose, nosebleed, double vision or blurring of vision, headache, earache, which becomes a diagnostic challenge [6].

Cervical lymphadenopathy is commonly found in physical examination as the majority of newly diagnosed NPC patients have locoregional advanced disease. The cervical nodes are usually involved in more than 13% of the patients presenting with occult primary tumors [6].

Treatment is usually involving a nonsurgical approach as the anatomic location is difficult to manage and in majority of the cases, there is a locoregional disease; therefore, currently the standard of care for these patients includes concurrent chemotherapy and radiation with cisplatin-based regimens, generally followed by adjuvant chemotherapy. This therapy regime results in cure for a majority of patients, with 3-year disease-free and overall survival rates of approximately 70% and 80%, respectively. Surgery is usually performed in cases of residual or recurrent disease [6].

Conventional imaging is quite helpful in the management of patients with NPC. MRI has become a fundamental tool in the management of NPC due to its exceptional spatial and soft tissue contrast resolution. The role of CT is restricted to staging workup and radiotherapy planning. MRI serves as a useful aid in diagnosis, staging, treatment planning, and prognosis of the disease. MRI has shown to have a high sensitivity, specificity, and accuracy of 100%, 93%, and 95%, respectively, in establishing a diagnosis of NPC [7].

MRI is vital in the accuracy of local and regional staging of NPC by recognizing local primary tumor spread; orbital, parapharyngeal and paranasal involvement; and lymph nodal spread, especially the retropharyngeal nodes [8].

The dosage of radiotherapy and the decision to add concurrent chemotherapy to the treatment plan depends on the clinical and imaging stage of the tumour. The gross tumor volume (GTV) can be outlined using MRI and CT and the planned treatment volume to be irradiated is decided. The volume of the primary tumor detected by MRI and CT is an independent prognostic indicator [8].

The American Joint Committee on Cancer (AJCC) TNM staging manual aids in establishing the stage of NPC [9].

Chen., *et al*. [10] assessed overall TNM staging in 70 cases of NPC (20 newly diagnosed cases and 50 cases in patients who had undergone treatment) and compared the efficacy of fused FDG PET/CT and CT alone. The sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of FDG PET/CT (96%, 94%, 95%, 96%, and 94%, respectively) were significantly better than those of CT (71%, 76%, 73%, 80%, and 67%; $p < 0.05$ [5].

The metabolic information about the tumor derived from FDG PET scans has been found to be extremely valuable in predicting prognosis in patients. SUV max, TLG, and MTV are some of the parameters that have been shown to correlate with survival. SUV max is a parameter that has been researched extensively in prognosis of NPC cases. The product of mean SUV and MTV determines the TLG. Thus, TLG, as a single value, incorporates both the SUV and MTV of the tumor and is potentially a better prognostic marker [5].

As describes earlier, the risk of distant metastasis is not directly related to tumor stage, however it has been observed that it correlates strongly with clinical lymph-nodal status. Skeletal metastasis from nasopharyngeal carcinoma represents the most commonly presented distant metastasis, followed by pulmonary and hepatic metastases. Bone metastatic sites are usually multiple and commonly present with pain, causing immobility, anxiety and depression and hence severely affecting patient's quality of life [11].

Despite the improvement in treatment optimization, the incidence of distant metastasis from nasopharyngeal carcinoma remains high. It is ranging from 15% to 57% in N3 disease at initial diagnosis [5-9,11].

It is well established in literature that axial skeleton is the most common site of distant bone metastasis, with most frequently involved region being the spine and pelvis. The first site of metastatic involvement was found to be lumbar spine (28.4%), followed by dorsal spine (27.7%), sacrum and pelvis (16.3%), femur (9.9%), and rib and sternum (7.8%) [12-14]. Even though the sites of distant metastases to the bone are clearly described, it is very rare to see solitary bone metastases in nasopharyngeal carcinoma [15].

Taira., *et al*. states that bone lesions identified as abnormal at both the PET and CT portions of the FDG PET/CT examination were very likely to be malignant, with a PPV of 98% PET/CT has a very high PPV for bone metastases (98%) when the findings at PET and CT are concordant [16].

The conventional method for bone scintigraphy has been Technetium (Tc) methylene diphosphonate (MDP) for the last three decades. (18)F sodium fluoride ((18)F NaF) positron emission tomography (PET)/computed tomography (CT) has better resolution and is considered a superior modality. The role of 2-deoxy-2- [(18)F] fluoro-D-glucose ((18)F FDG) PET/CT is proven in a variety of cancers, for which it has changed the practice of oncology [17].

F-18 FDG PET/CT and bone scans, both are widely utilized in the detection of suspected skeletal metastatic disease and in assessment of treatment response in patients with known skeletal metastatic disease. Overall, PET/CT is shown to be more specific for metastatic disease than bone scan. In a study, Ohta [19] and his colleagues determined the role of PET and bone scan in the evaluation of skeletal metastases in 51 patients with breast cancer and found that the sensitivity, specificity and accuracy of the bone scan were 77.7%, 80.9% and 80.3%, respectively. Corresponding values of PET for the detection of bone metastases were 77.7%, 97.6% and 94.1%, respectively. The difference in specificity was statistically significant, with the *P* value of 0.0392. FDG-PET had a higher specificity and can be used to monitor response to therapy [18].

In another study, Damle., *et al*. compared the role of (18)F-fluoride PET/CT, FDG PET/CT and (99m) Tc-MDP bone scans in the detection of bone metastases in patients with lung, breast and prostate carcinoma. They concluded that in cases of high clinical suspicion, (18) F-fluoride PET/CT is the most authentic investigation and (18)F-fluoride PET/CT has the potential to replace the (99m) Tc-MDP bone scan in detection of skeletal metastases [18].

Therefore, we can infer from this case that 18F-FDG-PET/CT is perhaps more sensitive than bone scan in the detection of bone metastasis in oncology patients. It is cardinal in detecting unknown primary cancers and visceral metastases besides bone metastases as well [19].

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