

CARCINOMA OF UNKNOWN PRIMARY WITH POSITIVE CERVICAL LYMPH NODE- A CASE REPORT

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ABSTRACT

The idiom CUP (carcinoma of unknown primary) is defined as the histological diagnosis of metastasis without the presence of a primary tumor. The prerequisites for the diagnosis of a CUP syndrome were defined as follows: biopsy and consecutive histological examination of a lymph node confirms malignant cell growth and makes a primary tumor at the location of the biopsy unlikely, while physical examinations and those carried out with technical equipment do not detect any primary tumor. There is an emergence of an occult primary in about 40% of CUP cases and about 70% of such lesions are detected in the head and neck region. In addition to thorough clinical examination of the head and neck mucosa (under general anesthesia), Positron emission tomography with fluoro-2-deoxy D- glucose is essential to identify or rule out the primary tumor, along with other modalities like CT/MRI, endoscopy and biopsy from all suspicious sites. Therapeutic approaches include neck dissection with or without post-operative radiotherapy, radiotherapy alone and radiotherapy followed by surgery.

Keywords: Carcinoma, unknown primary, lymph node, FDG-PET scan, neck dissection.

INTRODUCTION

Carcinomas with an unknown primary site represents a group of heterogeneous malignancies in which the diagnostic work-up fails to identify the site of origin but present with a positive regional lymph node or distant metastases. Such carcinomas account for about 5-10% of all tumours [1]. The most common histological sub type is squamous cell carcinoma, followed by adenocarcinoma, undifferentiated carcinoma and other malignancies. The most frequently involved nodal areas are level II followed by level III, levels I, IV and V involvement are less [2]. The median nodal size is reported to be 5cm (range 2-14cm) with increased prevalence of N₂ cases [2]. Diagnostic procedures should include a careful clinical evaluation and fiberoptic endoscopic examination of head and neck mucosa. Biopsy from all suspicious sites or blindly from sites of possible origin [3]. Imaging modalities like computerized tomography scan, magnetic resonance imaging aid in diagnosis. Positron emission tomography (PET) with fluoro-2-deoxy-D-glucose (FDG) is reported to

detect about 25% of cases. Therapeutic approaches include neck dissection with or without post-operative radiotherapy, radiotherapy alone and radiotherapy followed by surgery [4].

CASE PRESENTATION

65 years old female patient reported with a chief complaint of a painless swelling over the left side of her neck for the past 2 months. Patient had a history of similar swelling 3 years ago and was diagnosed as CUP and underwent radiation therapy to head and neck region along with chemotherapy. Clinical examination revealed a firm, non-tender swelling measuring 2cm*3cm in relation to the left level II lymph node region. Patient was subjected to nasal endoscopy, indirect laryngoscopy, gastro intestinal (GI) endoscopy and examination of oral cavity and oropharynx under general anaesthesia and no lesion was evident in the upper aero-digestive tract. Fine needle aspiration cytology was reported as metastatic squamous cell carcinoma. Positron Emission

Tomography and Computerized Tomography (PET CT) scan showed a hypermetabolic lesion in the left level II node region. Based on the clinical presentation and investigations, a diagnosis of recurrent CUP with a positive left level II cervical lymph node was made with a staging of T0 N2 M0. The treatment plan formulated was wide local excision with neck dissection, as the patient had history of chemoradiotherapy and recurrence at the same site indicates a radio-resistant tumour. Informed consent was obtained from the patient. Radical neck dissection was performed sacrificing the sternocleidomastoid muscle, spinal accessory nerve, internal jugular vein along with 1.5cm of margin of the skin and subcutaneous tissue of neck around the tumour. The defect was reconstructed with pectoralis major myocutaneous (PMMC) flap. The postoperative histopathological examination of the specimen revealed negative margins with extracapsular nodal spread. (Fig 1,2,3)

DISCUSSION

Volkman in 1882 was the first to describe three cases of latero-cervical lymph node metastasis in level II region while a primary malignant tumor could not be diagnosed. Since those malignant tumors were located in regions typical for lateral cysts of the neck, Volkman defined the disease as “deep branchiogenic carcinoma of the neck”.

Commes et al. described a cervical lymph node metastasis without diagnosis of a primary tumor and defined the malignant disease as “carcinoma of unknown primary” (CUP) [5].

Later in 1992, the prerequisites for the diagnosis of a CUP syndrome were defined as follows: biopsy and consecutive histopathological confirmation malignant lymph node and no evidence of primary tumor on physical examinations and those carried out with technical equipment [6].

Diagnostic work up should include systematic clinical examination of nasal cavity, oral cavity and oropharynx (under general anaesthesia) and imaging by Computed Tomography/ Magnetic Resonance Imaging is recommended for identifying the primary tumours and for guiding biopsy during panendoscopy [7].

Nieder et al systematically reviewed PET scan and

other diagnostic modalities and reported that PET scan detects primaries with a wide range from 5-25% with an overall staging accuracy of 69-78%, positive prediction of 56-83%, negative prediction of 75-86%, sensitivity of 63-100% and specificity of 90-94% [8]. PET scan results should be considered as ultimate when conventional diagnostic modalities have failed [4].

Loco-regional recurrence of the tumor is reported to be about 26.4% [5]. CUP patients where a primary tumor was secondarily diagnosed, have a tumor-specific survival rate of 41.12% and 31.43% after 3 and 5 years, respectively. In patients where a primary tumor was not detected, the survival for the same time was 46.7% and 37.9% and significantly higher [8].

Till date the therapeutic intervention in cervical CUP is of debate. Mackenzie et al [9] outlined a treatment protocol,

T0N1-No Extracapsular Spread (ECS)-modified radical neck dissection (MRND) type III or selective neck dissection (SND).

T0N1-with ECS- MRND/SND and ipsilateral neck irradiation.

T0N2a, T0N2b and T0N2c- ipsilateral MRND/SND and contralateral SND, bilateral radiotherapy with or without concomitant chemotherapy.

T0N3- RND or type I MRND and chemoradiotherapy. A more aggressive treatment including surgery and irradiation of both sides of the neck, laryngopharyngeal mucosa extending from the nasopharynx to the upper oesophagus is proposed by some authors [2,10]. According to Grau et al. the incidence of emerging primary in the head and neck was significantly higher in patients treated with surgery alone than those treated with radiotherapy. They also reported lesser loco-regional recurrence in patients treated with surgery and extensive irradiation of both sides of neck and pharyngeal mucosa [10].

CONCLUSION

In CUP patients with positive cervical lymph nodes, FDG-PET scan plays a major diagnostic role in the detection of primary tumor, disease dissemination and may be used for the planning of treatment. The choice of treatment should be neck dissection (RND/ MRND/SND) followed by radiotherapy or adjuvant

chemoradiotherapy depending on the staging of the disease. Combined treatment modalities, neck dissection and radiotherapy, adds the positive therapeutic effects of the both. A multidisciplinary follow up care with periodic tomographies and FDG-PET scans are necessary to monitor the emergence of primary tumor, local recurrence or secondary tumors.

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LEGENDS OF FIGURES

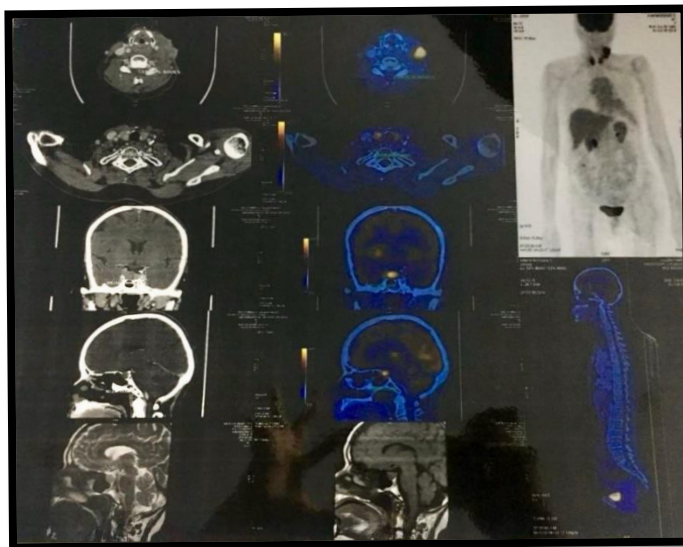


Figure 1- FDG-PET scan Figure 2- Marking of lesion



Fig II MARKING OF LESION



Figure 3- Clearance



Figure 4- Reconstruction with PMMC Flap