

Occult Primary in the Head & Neck and its Diagnosis

ASGHAR ULLAH KHAN¹, NASEER AHMAD¹, ZAKIRULLAH¹, ISRAR U DIN¹, QAISAR KHAN², MUHAMMAD ASGHAR KHAN³, AKBAR SHAH⁴

ABSTRACT

Aim: To adopt a cost effective diagnostic protocol for occult primary.

Methods: A prospective case control study of 50 patients presented with metastatic neck masses with unknown primary at Deptt. ENT Khyber Teaching Hospital, Peshawar, during April 2008 to Dec. 2009.

Results: Male; female ratio was 18 versus 32, 1.78; 1. Male with advanced age (45-65 year) had major share 28(56%). Malignancy was confirmed in 66%, suspected in 24% and false negative in 10% nodes by FNAC & 100% on open biopsy. In 24 % cases the primary source was located by panendoscopy and blind biopsy. Nodal stage status was N1 (24%), N2 (48%), N3, (28%). Nodal levels involvement recorded was level 1(4%), level 2(32%), level 3(24%), level 4(12%), level 5(8%) level 6 (4%). Commonest site of origin was hypopharynx (12%) followed by nasopharynx 4%, supra glottic larynx (4%), Histology proved squamous cell carcinoma in 26(52%) cases, undifferentiated carcinoma 20(40%) cases, lymphoepithelioma 03(6%) cases and adenocarcinoma in 01(2%) case.

Conclusion: In cases of occult primary FNAC & panendoscopy are cost effective diagnostic tools. Open biopsy should be the last resort. CT & MRI imaging are helpful prior to panendoscopy.

Keywords: Head & neck cancer, Occult primary, FNAC, Panendoscopy

INTRODUCTION

Occult primary is a diagnostic dilemma, which can only be resolved by adopting a systemic approach. In the past, metastatic mass in neck with an unknown primary was labeled bronchiogenic carcinoma i.e. carcinoma arising from the bronchial remnant. Crile in his study of 28 cases reached a conclusion that treatment of such cases were difficult and the prognosis worse^{1,2}. It was a standard practice to exercise such mass. If on histology, squamous cell carcinoma was discovered, diagnosis of bronchial carcinoma was presumed and no farther efforts were made subsequently to search for a primary.

Martin and his contemporaries did not substantiate this idea; they were of the opinion that these metastatic masses are secondary to sub mucosal or microscopic nests of squamous cell carcinoma in the upper aero-digestive tract. They strongly urged that an external biopsy should be the last investigation and search for a primary must be made in head and neck region or some distant regions of body like stomach, testis and ovaries³

Plain X-ray has a very limited role. A shadow in the nasopharynx detectable on plain x-ray appears very late. Soft tissue shadow in post cricoid area appears only in larger lesion. Bronchial carcinoma

metastasizes less commonly in the cervical nodes. CT scan MRI from skull base to diaphragm should ideally be asked in every case of unknown primary. It can detect primary lesion(s), involvement of regional nodes, which helps to stage the disease. Flexible endoscopy and Hopkins endoscopic survey is also a useful modality in scanning occult primary. FDG PET scan and PET-CT reconstruction is the latest techniques with more precision of occult primary diagnosis available in advance setup only. This study was designed to determine the magnitude and type of occult primary and devise cost effective protocol for diagnosis of occult primary of head and neck.

MATERIAL AND METHODS

This prospective descriptive study was conducted at the department of ENT department of Khyber Teaching Hospital Peshawar in April 2008-Dec.2009. Most of the patient's belonged to Peshawar and the nearby districts. All 50 patients presenting with metastatic masses of neck with an occult primary were meticulously examined to locate their primary source in out door and finally the ward, where base line investigation i.e., CBC, X-ray, ECG and viralogy screening performed prior to endoscopy. Fine needle aspiration cytology (carried out before admission) and panendoscopy were the main tools of investigation carried out in all patients. CT/MRI was done in 32 cases. Patients with clinical suspicion and suspected or confirmed on FNAC as malignant mass in neck as a sole presenting symptom without any obvious primary lesion, were included in the study. All

¹Department of ENT, Khyber Teaching Hospital, Peshawar, ²Department of ENT Head & Neck surgery, KGMC/HMC Peshawar, ³Department of Surgery, Khyber Teaching Hospital, Peshawar, ⁴Department of Emergency, Khyber Teaching Hospital, Peshawar

For correspondence: Dr. Asghar Ullah Khan, Email: drasghar_1962@yahoo.com

patients with diagnosed non malignant, known primary and lymphoma were excluded from study.

RESULTS

This study included 50 patients with occult primary in the head and neck region including 32 (64%) male and 18 (36%) women, male to female ratio was 1.77:1 (Fig; 1). The patient's age ranged between 8-68 years 3 (6%) patient aged below 20 years, while 7 (14%) cases belonged to 3rd & 4th decade, 18 (36%) and 14(28%) respectively presented in their forties and fifties while 8 (16%) patients belonged to elder group of 60 plus (Fig; 2). Regarding nodal status 12 (24%) patients were having N1 and 24 (48%) N2 while 14 (28%) had N3 nodal disease at the time of diagnosis (Table 1). Level 1 and 2 of neck were involved in 2 (4%) and 16 (32%) respectively. Twelve (24%) had level 3 disease and 6 (12%) patients presented with level 4 involvement while with level 5 and 6 disease only 4 (8%) and 2 (4%) patients were received (Table 2). The FNAC which was tested for its efficacy detected 33 (66%) cases correctly, 12 (24%) as suspected or doubtful for malignancy and 5 (10%) negative, while endoscopy revealed positive lesions only in 12 (24%) cases and negative in 38 (76%) cases (Tables 3-4). The histology revealed that 26 (52%) patients had metastatic squamous cell carcinoma, 20 (40%) anaplastic carcinoma, 03(6%) lymphoepithelioma and 01(2%) patient had adenocarcinoma (Table 5). Out of 12 (24%) positive cases on endoscopy half were found in different regions of hypopharynx, two(4%) in nasopharynx, 1(2%) on the tongue base and upper end of oesophagus, tracheobroncheal tree (Table 6).

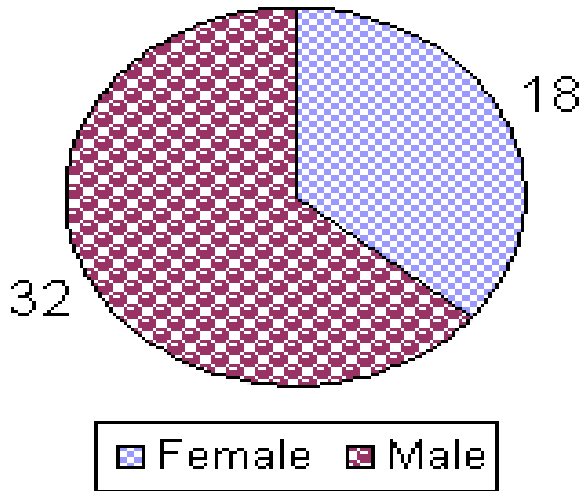


Fig. 1: Sex distribution of patients with occult primary in head & neck (n=50).

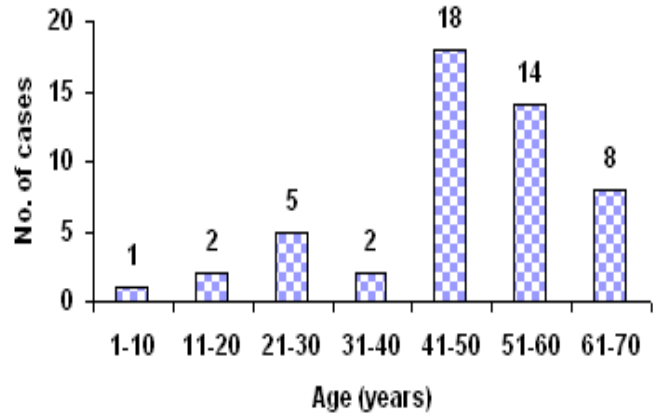


Fig. 2: Number of cases according to age

Table 1: Frequency of nodal status (n = 50)

Nodal status	n	%age
N1	12	24
N2	24	48
N3	14	28

Table 2: Neck node levels involved (n=50)

Level	n	%
1	2	4
2	16	32
3	12	24
4	6	12%
5	4	8
6	2	4

Table 3: Efficacy of FNAC (n = 50)

Efficacy	n	%age
Positive	33	66
Negative	5	10
Suspicious	12	24

Table 4: Efficacy of Pan Endoscopy in detection of primary malignancy (n = 50)

Efficacy	n	%age
Positive	12	24
Negative	38	76

Table 5: Histologic types of positive biopsies (n =50)

Histology	n	%age
Squamous carcinoma	26	52
Undifferentiated carcinoma	20	40
Lymphoepithelioma	3	6
Adenocarcinoma	1	2

Table 6: Sites of primary lesion (n=50)

Sites of primary lesion	n	%age
Nasopharynx	02	4
Base of tongue	01	2
Larynx (Supraglottic)	02	4
Hypopharynx		
• Pyriform fossa	02	4
• Post cricoid+oesophageal	03	6
• Post pharyngeal wall	01	2
Broncheal tree	01	2
Undetected Primary	38	76

DISCUSSION

The head & neck has rich lymphatic supply and is the sixth commonest site for cancer⁴. The incidence of metastasis with an occult primary lesion varies between 5-10%^{3,4,5}. This figure is in close range to a regional study by Abbas et al⁶ showing approximately 5% lumps in neck with malignant changes without an obvious primary sources. In our study, the incidence of occult primary in a cross section of population falls below 10%. Males dominate females by a ratio of 2:1.⁷ In the current study, 32 patients were male while 18 were female forming a ratio of 1.77:1. Most of the patient's belonged to the 4th, 5th and 6th decade of life which is similar to the published material. Male predilection can be explained in our region as they are more habituated to smoking, tobacco chewing and liquors. Most of the patients presented with one or more constitutional symptoms such as malaise, fatigue, weight loss, dyspepsia. These symptoms are more appropriately termed as paraneoplastic symptoms⁹. In this series, approximately 30 of our patients reported these trivial symptoms, i.e., malaise, weight loss etc. Symptoms indicative of primary tumours such as dysphagia, hoarseness, epistaxis etc. were registered by a few of our patients at the time of their first presentation. However, in patients, whom primary became overt lately the discovery of second primaries were greatly guided by specific symptoms of head and neck region. Lymph nodes form an ecological barrier to the spread of cancer. Disruption of this barrier increases the morbidity of patient by promoting furthers spread of the disease¹⁰.

There is a great deal of inter observer variability on clinical examination. The UICC/AJCC classification are based on clinical examinations Sako have reported a 30% observer error at different centers. Imaging techniques have increased accuracy over 90%^{11,12}. Therefore, CT scan rapidly became a very popular tool in devising the type of modality of definitive treatment.

In our study, unfortunately we could not carry out imaging techniques in every case, due to the economical constrains and only 32 patients under went CT or MRI scan. As expected in 20 (40%) cases, the nodal status increased from N 1/2 to N3. In a small study of 10 patients, conducted between 1978-1987 by Croce (70%) cases were N 1(10%) was N2 and 2(20%) were N3¹³. The prognosis and selection of modality of treatment of metastatic disease depends upon the anatomical level of neck¹⁴. If metastatic mass is in the supraclavicular regions the prognosis is good and selection of treatment is easear.¹⁵ In Croce's study of 10 patients cervical metastasis were found to be as follows: 3(30) at

level-1, 1(10%) at level-IV, 1(10%) at level-V, 2(20%) at level-II and in one case unilateral and multiple nodes presented as simultaneous involvement of level-III and IV¹³. In our series, almost equal number of metastatic nodes were at level-I 2(4%). Level-II 16 (32%) cases, level-III 12(24%) cases. interestingly four cases (8%) were found at level-IV and six cases (12%) at the level-V. FNAC helped in acquiring an early knowledge about the histology of such masses. FNAC has made it possible to start definitive treatment on time for the malignant tumours.^{16,17} In cases of adenocarcinoma and squamous cell, the sensitivity of FNAC is 90-97%¹⁸. In our study, 33 (66%) cases were true positive right from onset by FNAC. This is in full conformity with the previous reports. The remaining 10% (false negative) indicated the absence of malignancy along with 12(24%) suspected cases, which proved malignant later on by open biopsy. Open biopsy should be kept as the last resort to diagnose the nature of suspects-malignant lumps in neck. After the needle cytology technique, flexible endoscopy is yet another effective tool. Any abnormal finding visualized during this procedure immensely guided us in envisaging where to attempt a punch biopsy in subsequent quadruple endoscopy. Also it is very useful in continuously assessing the patient without general anesthesia, in which primary did not become obvious in first presentation. The idea of palpating the accessible suspected lesion before a biopsy carries substantial logic because inconspicuous small tumours particularly involving base of tongue or tonsil are better palpated than seen.¹⁹ Pan endoscopy in our 50 cases yielded 12 conclusive primaries (24%), while 38(76%) remained inconclusive. Blind biopsies as recommended in the literature, were not of much help in our series in picking up the tissue for diagnosis. Contrary to our experience, Lee claimed results in 3 of 18 cases with random biopsies (17%)²⁰. In all of 12 (24%) conclusive primaries, 6(12%) of them had visible exophytic lesions. In remaining 5(10%) cases, the mucosa was unhealthy and in 1(2%) case ulceration was present.

It will be more rational to carry out CT scan/MRI before endoscopy and in lieu of that, the crude term "blind" be replaced by more logic term 'guided or directed' in the diagnostic sequence.¹⁹ Plain radiology does not have any real place in detecting the elusive primary. However, in cases of supraclavicular masses involving level-V and VI of neck, X-ray chest is of paramount importance because in such presentation 20% of primaries are likely to be found in the aerodigestive tract^{21,22}. In our series, the most ordered plain x-ray of skull, paranasal sinuses were not found to be helpful to suggest possible primary. However, in one case, which presented with lower

cervical lymph adenopathy, X-ray chest did show a shadow in the left hilar region. Bronchoscopic biopsy subsequently revealed a poorly differentiated squamous cell carcinoma. All patients with metastatic lesion at lower neck, barium studies were carried out in 16 cases in the hope to find a primary in the digestive tract. Glynoe in his study proved adenocarcinoma discovered primaries in 2 cases below clavicles²³. Despite an extensive diagnostic working, the percentage of discovery of primary sources remains very variable. 05-55% discovery of primaries were reported by Lee, Croce, and Shenoy showed a success rate of 20% and 30% respectively^{20,24}. In our series, we managed to unearth 12(24%) of primaries which otherwise could not be discovered. A non-supraclavicular cervical nodes metastasis from an unknown primary is considered to have greater than 80% chances of having originated in the head and neck region while in remaining 20% primary is found below clavicle.²⁵ In our series, in 6 patients, the primaries were discovered from hypopharynx e.g., in 3 cases, from pyriform fossa 2 post cricoid and one post pharyngeal wall region respectively. Two cases each from supraglottic larynx and in nasopharynx were seen while one case later on was diagnosed as malignancy of the tracheo-broncheal tree almost the same results are reported by Crose et al¹³ and Luqman¹⁷.

In metastatic mass of an occult primary, squamous cell carcinoma, (52%) was the commonest histological type followed by undifferentiated carcinoma (40%) and lymphoepithelioma 3(6%) and adenocarcinoma 2%. Almost the same results are reported by Hussain et al and Luqman. Hussain et al. series revealed squamous cell carcinoma in 50% of cases while undifferentiated carcinoma was present in 45% of cases and lymphoepithelioma is 4.5% very close to our findings^{1,17}.

CONCLUSION

To detect source of an occult primary of a metastatic lesion in head and neck, remains a formidable task. It needs to employ prompt, accurate and cost effective scientific approach. The open biopsy should be kept as last resort, FNAC and Panendoscopy and imaging should be carried out before open biopsy. The definite treatment must not be unduly delayed in the exercise to find out elusive primary lesion.

REFERENCES

- Hussain SI, Shaikh GA, Yousfani A. Diagnosis of occult primary in the head & neck cancer. *Pak J Otolaryngol* 2005; 21:53-5.
- Crile G. Excision of carcinoma of head & neck with special reference to plan of dissection based on 132 patients. *J Am Med Assoc* 1906; 47: 1780-6.

- Jungi WF, Osterwelder B. Approach in metastasis with an unknown primary tumour. *Sdhweii-med-Wochenschr*, 1990; 120(35): 1273-9.
- Khan AU, Hamza A, Khan IU, Clinical presentation of 56 cases of Ca Larynx admitted at services hospital Lahore. *Pak J Med Health Sci* 2012;6(1):59-62.
- Yabuki K, Tsukuda M, Horiuchi C, Taguchi T, Nishimura G. Role of 18-F-FDG PET in detecting primary site in the patient with primary unknown carcinoma. *Eur Arch Otorhinolaryngol* 2010; 267(11): 1785-92.
- Abbas S, Zaidi SH: Evolution of neck masses (82 cases). Thesis for M.S. University of Karachi. 1993-1994.
- De Brand F, Heilbunn LK, Ahmed K: Ahmed K. Metastatic squamous cell carcinoma of unknown primary localized to the neck. Advantages of an aggressive treatment. *Cancer* 1989; 64: 510-5
- Maran AGD. Neck masses, Logan Turner's disease of ear, nose and throat. 10th Ed. London: Maran Wright 1983: 202-4.
- Pagenster A, Faraz M, Volk BA Case of paraneoplastic limbic encephalitis in occult primary. *Nervenarzt* 1994.
- Fisher ER, Fisher B. Role of regional lymph nodes. In: Stoll BA, ed. Secondary breast cancer. Chicago: Heinemann, 1977.
- Winegar LK, Griffin W; The occult primary tumour. *Arch Otolaryngol* 1973; 98: 159-93.
- Ghulam Saqlain, Khalid Iqbal. Iqbal H, Jalisi ML. Distant metastasis in Head and Neck cancers. *CPSP* 1994; 4(10): 19-23.
- Croce A, De Vincentia M, Cakagno P; Later O; Cervical adenopathies due to occult tumours. *Acta Otorhinolaryngol Ital* 1989; 9(1): 115-24.
- Spiro R, Alfonso AE, Far HW, Strong EW: Cervical node metastasis from epidermoid carcinoma of oral cavity and or pharynx. *Am J Surg* 1974; 128: 562-7.
- Still PM: Cervical node metastasis in the neck: Recent advances in Otolaryngology. 1978: pp 125-41.
- Ackerman I. Del Regato JA. Cancer, diagnosis, treatment and prognosis. Mosby St. Louis, 1970
- Luqman M: FNAC of lymph node. Thesis for M. Phil, JPMC Karachi. 1990; 85.
- Oyafuso MS, Loogatta FUho A, Ikeda MK: the role of fine needle aspiration cytology in the diagnosis of head and neck excluding thyroid and salivary glands. *Tumour* 1992; 78(2): 134-6.
- Gruefolman JL, Bobbins KT, Fried MP. Cervical metastasis squamous carcinoma of unknown primary source. *Head & Neck* 1990;12 951: 440-3.
- Lee DJ, Restock RA, Harris A, Kashima H, Johns M. Clinical evaluation of patients with metastatic; squamous carcinoma of the neck with occult primary tumour. *Br Med J* 1986; 79:979-83.
- Steiner W. Early detection of cancer in the upper aerodigestive tract. *Head Neck Oncol* 1993; 41(7): 360-7.
- Wang RC, Geopert AE. Unknown primary squamous cell carcinoma metastasis to the neck. *Arch Otolaryngol Head Neck Surg* 1990; 116:1388-93.
- Glynoe-Jones RG, Auand AK, Young TE: Metastatic adenocarcinoma in cervical lymph nodes from an occult primary. *Clin Oncol R Coll Radiol* 1989; 10: 19-21.
- Shenoy Ashok MN, Anath A. Sohail Haasan BKM, Redd Road Naiundappa V, Kannan MK, Bharga V. Treatment strategy for neck metastasis from an occult head and neck primary. *Pak J Otolaryngol* 1991; 7:8-12.
- Michael D: Determination of non-endemic basipharyngeal carcinoma by in situ hybridization. *Laryngoscope* 1995; 105: 407-11.

