

Original Article

Role of panendoscopy and biopsy in cervical lymph node metastasis with unknown primary: a tertiary center experience

Azlan Iskandar Ishak,¹ Mohd Razif Mohd Yunus,¹ Mazita Ami,¹ Primuharsa Putra²

Department of Otorhinolaryngology Head and Neck surgery, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia

ABSTRACT

Objective

To evaluate the role of panendoscopy and biopsy in diagnosing occult primary site of cancer in the head and neck region.

Methods

A retrospective review of patient clinical notes, radiological, histological and intra-operative reports who underwent panendoscopy and biopsy of the upper aerodigestive tract.

Results

Out of 11 patients, six had undifferentiated carcinoma and five had squamous cell carcinoma (SCC) of the cervical lymph nodes. Nine underwent CT scan of the head and neck and one had a positron emission tomography scan. One patient had no radiological imaging. None of these studies were able to locate a primary tumor. Random biopsies from sites of possible origin of the primary tumor with

tonsillectomies confirmed the primary site in 10 patients; three had nasopharyngeal carcinoma, four had SCC of the tonsils with three patients with unilateral and one with bilateral involvement, one each with SCC of the base of tongue, SCC of both vocal cord and non Hodgkin's lymphoma of bilateral tonsils. In one patient, no site of origin of the primary tumor was identified in the head and neck region.

Conclusion

Panendoscopy and biopsies had significant role in arriving at a conclusive diagnosis as compared to imaging studies in cases of metastatic cervical lymph nodes with an occult primary. (Rawal Med J 2010;35:).

Keyword

Occult primary tumor, panendoscopy, head and neck cancer, aerodigestive tract

INTRODUCTION

Cervical lymph node metastasis from unknown primary is a relatively rare event constituting 3-9% of all head and neck cancers.¹ The most frequent histopathological diagnosis is squamous cell carcinoma (SCC) accounting for 65-76% of all cervical metastases from unknown primary, followed by undifferentiated carcinoma (14%), adenocarcinoma (13%) and nasopharyngeal-type undifferentiated carcinoma (8%).² The occult primary tumor is eventually found in approximately 10-40% of patients during the follow-up and the

upper aerodigestive tract is the most common site. Proper and directed treatment strategies can then be carried out, limiting the extent of the treatment and thus reduce the unwanted side-effects. The purpose of this study was to compare the diagnostic management in our institution with those previously published.

PATIENTS AND METHODS

We retrospectively reviewed the clinical records of patient with cervical lymph nodes metastasis with an unknown primary, who underwent panendoscopy and biopsy of the upper aerodigestive tract over 3 years from March 2005 to July 2008 at Universiti Kebangsaan Malaysia medical center. Patients' demographics data, clinical presentation, examination findings of the neck and initial neck biopsy result were collected. We also reviewed the radiological findings, final histology and the modality of treatment conducted on each patient.

RESULTS

A total of 11 patients who had cervical metastasis with unknown primary tumor were seen in our center during the study period. There were nine male and two female patients with ages ranging from 31 to 70 years (mean 55.3 years). The racial distribution consisted of seven Malays (63%) and four Chinese (37%). The main presenting symptom was the presence of a neck mass which was either painless (72 per cent) or painful (28 per cent). The duration of neck mass ranged from one to eight months. Other symptoms included hoarseness of voice, chronic cough, nasal obstruction, loss of weight and loss of appetite. The size of the neck mass ranged from 3x3 to 15x20 centimetres. Lymph node level from level one to level five was involved. None had a level six node. Eight patients (73%)

had unilateral neck mass while three (27%) had bilateral neck involvement. Based on TNM staging system, the N- staging for these patients were N1 in two patients, N2 in four patients while the remaining five patients had N3 stage. Of these, eight patients had a fixed immobile neck mass (72%) while three patients had mobile neck mass (28%). Particular attention was paid to the possible primary site in the upper airway namely the nasal cavity, nasopharynx, base of tongue, vallecula, vocal cords, pyriform sinus, post cricoid region and posterior pharyngeal wall.

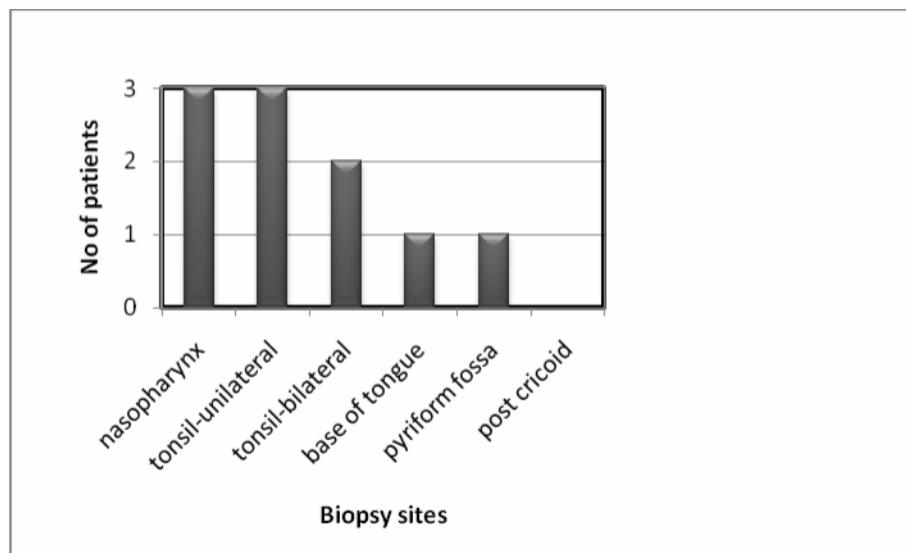


Fig. 1. Location of primary tumor after pan endoscopy with random biopsy and tonsillectomies.

Pre operative evaluation included fine needle aspiration cytology (FNAC) or an excisional biopsy. All patients had an FNAC as a primary line of tissue investigation. From this, eight patients (72%) yielded result while the other three patients' sample was

inadequate for cytological evaluation. These three patients (28%) then underwent an excisional biopsy in which the smallest and most palpable cervical nodes were chosen. The pre operative cytological and histological diagnosis from these neck masses were metastatic undifferentiated carcinoma (55%) and metastatic SCC (45%).

Nine patients underwent CT of the head and neck including the thorax and abdomen. In each patient, the report stated the presence of cervical neck nodes at different levels in the neck but was not able to locate the presence of any possible location of a primary tumor in the upper aero digestive tract as well as in the thorax and abdomen. One patient had a PET scan at another center prior to our clinic follow up. The report stated that no primary tumor site was found. None of these patients had MRI. One patient did not undergo any imaging studies due to financial constraints.

All these patients underwent evaluation under anaesthesia (EUA) with panendoscopy. This included direct laryngoscopy, bronchoscopy and esophagoscopy with biopsy of the possible sub clinical tumor site and bilateral tonsillectomy. Blind tissue biopsies were taken from the post cricoid and pyriform sinus in the hypopharynx, base of tongue and nasopharynx. These random biopsies with tonsillectomies confirmed the primary site in 10 patients (Fig 1). In one patient, no site of origin of the primary tumor was identified.

Table 1. Demographics and management of study population.

No	Age/ Sex	Duration of neck mass (month)	Neck involvemen t	Lymph node level	Pre-op pathology investigat ion	Imaging done	Positive biopsy site	Final HPE	Treatment
1	63/F	6	Unilateral	2,3,4,5	FNAC	CT	Base of tongue	SCC	defaulted
2	34/F		Bilateral	2	FNAC	CT	Nasopharynx	NPC	Chemo RT
3	69/M	2	Bilateral	2,3	FNAC	CT	Tonsil (both)	NHL	chemo
4	49/M	1	Unilateral	1	Excisional biopsy	Nil	Nasopharynx	NPC; undifferentiated	defaulted
5	51/M	2	Unilateral	2	FNAC	CT	Right tonsil	SCC; moderately differentiated	RND, RT
6	70/M	6	Unilateral	4	Excisional biopsy	CT	Right tonsil	CIS	RND, RT
7	65/M	3	Unilateral	4,5	FNAC	CT	Nil	?origin	Palliative RT
8	31/M	8	Bilateral	2	FNAC	PET scan	Pyriform fossa, both tonsils	SCC; poorly differentiated	Lost follow up
9	57/M	3	Unilateral	2	FNAC	CT	Right tonsil	SCC; poorly differentiated	Chemo RT
10	50/M	6	Unilateral	5	Excisional biopsy	CT	Nasopharynx	NPC	Chemo
11	70/M	1	Unilateral	2,3	FNAC	CT	Vocal cord	SCC; moderately differentiated	Chemo RT

FNAC, fine needle aspiration cytology; CT, computed tomography; PET, positron emission tomography; SCC, squamous cell carcinoma; NPC, nasopharyngeal carcinoma; NHL, non Hodgkin's lymphoma; RT, radiotherapy; RND, radical neck dissection

A summary of the clinical findings, investigation and treatment given for each patient are shown in Table 1.

DISCUSSION

The definition of metastatic cancer of unknown primary is a biopsy-confirmed malignancy for which the site of origin is not identified by routine workup.³ The diagnosis of metastases of unknown primary site makes up 5% to 10% of all cancer patients, making it the seventh most common malignancy.⁴ The primary lesion, which has escaped detection by a staging workup, can be identified in only 30% to 82% of cases at autopsy.⁵ This inability to detect the primary tumor has two possible explanations. The first is that the primary has involuted and is not detectable when the metastasis becomes evident, as spontaneous tumor regression has been described.⁶ The second explanation is that the primary tumor's malignant phenotype and genotype favour metastatic ability over local tumor growth.⁷ In this scenario, a slow-growing primary tumor might produce early metastatic lesions whose growth outstrips that of the parent tumor. In two to eight per cent of such cases, no primary malignancy is ever identified despite a diligent search.⁸⁻¹⁰ Mostly it occurs in adult in the middle age group as, more than 50 per cent of our patients were of the middle age to elderly group (above 40 years old). Our series recorded a higher preponderance for male gender (81%) as compared to female. Similar demographic data was also seen in other studies.⁵

The gold standard for tumor verification is tissue biopsy. Search for the primary usually involves triple endoscopy (rigid laryngoscopy, bronchoscopy and esophagoscopy), and most series have emphasized the significance of directed or 'blind' biopsies.⁸⁻¹⁰ Panendoscopic biopsy is generally performed superficially with cup- or biting-type forceps, which is appropriate for most mucosal sites but inadequate for tonsil biopsy. Most published reports in which a primary site was

ultimately diagnosed support the fact that traditionally described locations such as the nasopharynx, tonsil, tongue base, and hypopharynx remained the likely sites.^{8,9} From the previously published studies, the yield of these biopsies appeared to be low.^{8,9} This is in contrast to our series where the biopsies yielded positive result in about 90% of the cases. It is also our center's policy to perform bilateral tonsillectomy as opposed to unilateral tonsillectomy though tonsillectomy ipsilateral to the cervical metastasis has been recommended.^{9,11,12} The tonsil deserves special attention as a potential source of hidden malignancy because small tumors can originate in the depths of tonsil crypts without being detected at the surface.¹³ Also, the rich lymphatic drainage of the tonsil facilitates early spread to regional nodes despite a low tumor volume of the primary site. We successfully detected a case who had bilateral SCC of the pharyngeal tonsils (Table 1, case no 8). This showed that we can increase the detection rate of these occult primary tumors. By doing so, we also think that it could decrease the morbidity of these patients by not subjecting them to multiple general anesthesia, should another tonsillectomy is required. Therefore, we strongly advocate the use of these combinations of diagnostic procedures since it takes up little time, effort and minimal risk while a more conclusive diagnosis can be made from the biopsies. In our study, we were successfully able to detect the primary tumor in more than 90% of the patients.

In our series, imaging studies were not able to identify the primary tumor site, although CT or MRI and PET scanning have been useful.¹⁴ In a study by Kresnik et al, imaging studies with fluoro-deoxyglucose (FDG) PET showed that the detection rate reached 73.3%.¹⁵ The ability of FDG PET to detect disease consistently and reliably at the primary site in head and neck cancer patients has encouraged its use for the assessment of the occult primary cancer.^{14,16} Several

studies suggest that biopsies carried out after FDG PET can improve the number of occult primaries detected compared with endoscopic examination with speculative biopsies.^{17,18}

CONCLUSION

Our results showed that by performing a combination of random biopsies with bilateral tonsillectomy, the detection rate of an occult primary in the head and neck region was higher. Imaging studies are a worthwhile adjunct tool in diagnostic process for this group of patients.

¹ Department of Otorhinolaryngology Head and Neck surgery, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia.

² Department of Otorhinolaryngology Head and Neck surgery , Seremban Specialist Centre.

Correspondence: Azlan Iskandar Ishak,
Department of Otorhinolaryngology Head and Neck Surgery,
Medical Faculty, University Kebangsaan Malaysia Medical Centre,
Jalan Yaacob Latif, 56000 Cheras, Kuala Lumpur. Tel: 0060391456046
email : drazlan76@gmail.com

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