



Original Research Article

Clinicopathological study of secondaries in neck in relation to head & neck malignancies

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ABSTRACT

Cervical metastasis is the most critical prognostic factors in head and neck carcinoma. Accurate detection and measurement of metastases is important for precise staging of patients with head and neck cancers because it determines treatment strategy.

Materials and Methods: This cross-sectional study was carried out on 110 patients, presenting with neck secondaries with head and neck malignancy (primary and occult) in the Department of ENT, N.S.C.B.MCH, Jabalpur from March 2016 to August 2017.

Results: Head and neck carcinoma with neck secondaries is more common in males (M: F=6:1). Oral carcinoma was commonest followed by carcinoma larynx & majority with unilateral (left>right) neck node metastasis, Level II being the commonest. Most common Histopathology of primary was SCC and FNAC of neck node was metastatic deposits of SCC. Majority presented at stage IV.

Conclusions: It is concluded that patients usually present to a tertiary care centre at advanced stages, with locally as well as extensive metastatic spread.

This can be attributed to lack of awareness and unavailability of proper medical facilities in rural population. There should be health education in community about carcinogenic substances, to reduce the burden of carcinomas & proper medical facilities in low socioeconomic strata.

Pathological investigations are gold standard diagnostic modalities for head & neck carcinoma and neck node metastases, not only for confirmation but also for proper further management.

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1. Introduction

Cervical metastasis has been defined as one of the most critical prognostic factors in malignancies arising in head and neck. Accurate detection and measurement of clinical and sub-clinical metastases is important for precise staging of patients with head and neck cancers because it determines treatment strategy.

Most of the carcinomas of head and neck, sooner or later metastasize to cervical nodes which form a barrier that prevents further spread of disease for many months. Malignant tumors are extremely variable in their tendency to metastasize, some spread so viciously as to produce death in a few weeks or months, whereas others remain stationary

with or without metastasis for years.

The ability to spread both locally and to a distance is one of the most important characteristic of a malignant tumor, for it is the main stumbling block to the successful treatment of cancers. The onset and the method of spread constitute the main feature in the natural history of tumor. This may provide a valuable clue to correct diagnosis to the clinician and to the pathologist.

In this study, we have explain the clinico pathological features of secondaries in neck in relation to head & neck malignancies (including primary and occult). As otolaryngologist we have to deal with cervical metastases in ENT and head-neck malignancies. In view of wide variation in incidence, variability in natural history of cancer from person to person, the present study has been taken to evaluate patients presenting with metastatic neck nodes and

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their correlation with primary and occult disease in all age groups.

2. Materials and Methods

2.1. Type of study

This study was cross sectional study.

2.2. Selection criteria

All the patients presenting with malignant cervical lymphadenopathy associated with malignancy of head and neck region (primary and occult) were be constituted in this study.

2.3. Method of collection of data, study place, period and procedure

This study was carried out on 110 patients of all age groups with proven malignant cervical lymphadenopathy associated with malignancy of head and neck region came to the Department of ENT and head- neck surgery of N.S.C.B. Government Medical College, Jabalpur from March 2016 to August 2017.

The standard procedure of examination - a detailed clinical history, physical examination both local & general, biopsy & histopathological examination of primary site, Fine Needle Aspiration Cytology of cervical lymph node and radiological examination was done.

Prior informed consent was signed by all the participants enrolled as per guidelines and standards of research using human beings.

2.4. Ethical approval

The study was given approval by the institutional ethics committee (IEC), Jabalpur.

2.5. Statistical analysis

The variables used for comparison were treated using two sample test of probability and statistical significance was attributed when $p < 0.05$.

3. Results and Observation

Our study were conducted on 110 cases of head and neck carcinoma presenting with secondaries in neck & occult primary.

The mean age of presentation of head and neck carcinoma with neck secondaries, for males was 52.74 (± 13.06) years and for females 43.56 (± 16.30) years. Thus age of presentation for females was around one decade earlier than their male counterparts. Thus it is evident that head and neck cancer is more common in males but occurs earlier in females. The male and female ratio in studied

cases was 6: 1 with a significant male preponderance. 94(85.45%) were males and 16 (14.55%) were females.

Patients from rural locality reported more than urban locality which was 76.4%, and most were labourers (46.4%).

In the patients with neck secondaries, most common primary site of carcinoma observed was carcinoma oral cavity (36.36%) followed by carcinoma larynx (21.8%) & carcinoma oropharynx (13.64%). (Table 1)

But if specific site wise observed, then most common diagnosis was c arcinoma larynx (21.8%) followed by c arcinoma buccal mucosa (16.3 %), carcinoma oropharynx (13.64 %), & carcinoma tongue (11.8%).

12.7% cases were of occult primary.

9.1% cases of head and neck carcinoma with neck secondaries had distant metastases at the time of presentation.

Out of 110 case of neck secondaries in head and neck carcinoma 73.6% cases presented with neck swelling, 41% cases presented with oral ulcer, dysphagia was seen in 37.3% of cases, hoarseness in 23.6%, dyspnoea in 14.5%, reduced mouth opening in 11.8% and cough in 9.1% of cases. Thus it is seen that in neck secondaries of head and neck carcinoma, neck swelling was the most common presenting complaint followed by oral ulceration. (Figure 1)

Among the other symptoms dysphagia was the common presenting complaint followed by hoarseness, dyspnoea, reduced mouth opening and then cough.

Most common type of addiction was smoking alone (29.1%) followed by tobacco chewing alone (24.5%) and tobacco chewing + smoking both (24.5%). 10% were non-addicts.

Mean duration of addiction was 24.94(± 10.96) years. This finding strongly suggests that smoking for a longer duration is a primary cause for carcinoma.

In this study, most common side of neck node metastases is left side 49(44.5%) followed by right side 37(33.6%) & then bilateral 24(21.8%). It is observed that out of 27 case of carcinoma larynx, right & left side equally involved 13(48%) each cases & bilateral is very rare only 4%. In carcinoma base of tongue, neck node enlargement is almost equally distributed to right, left & bilateral side. In carcinoma oral cavity, out of 40 cases most common side of neck node metastases is left side 18(45%) cases followed by right side 14(35%) & then bilateral 8(20%) cases. In occult primary most common side is left 60% followed by right & bilateral equally distributed 20% each. (P- Value = 0.038). (Table 2)

In 53% cases of head and neck carcinoma, duration of onset of node before presentation was within 2 month followed by 2-5 months (38%). (P- Value = 0.122)

In head and neck carcinoma most common neck node level involved were level II (52%) of 110 cases, (of these 23% right side, 22% left side & 7% Bilateral) followed by

level I (50%) of 110 cases (of these 17% right side, 20% left side & 13% bilateral). (Table 3)

The most common neck node level involved in carcinoma larynx is level II – 50%, followed by level III – 22.5%, level I – 15%. In carcinoma base of tongue most common is level II – 39% followed by level I & II are equally distributed – 19.5%, then level IV- 16.6%. But in carcinoma oral cavity most commonly level I – 52%, followed by level II – 27% then level III – 16%. In carcinoma nasopharynx & carcinoma maxilla most commonly level I involved. In occult primary in head and neck carcinoma & 1 lymphoma level I to level V are almost equally distributed. (P- Value = 0.014). (Table 4)

Majority of cases of our study, Histopathological grading of primary head & neck carcinoma is grade II – 69% followed by grade I – 11%, then grade III – 4.5%.

In Histopathological report of primary from head and neck carcinoma, majority shows squamous cell carcinoma which was 91.5%.

It is observed that majority of cases of entire diagnosis, FNAC of node shows metastatic deposit of SCC (84%), followed by metastatic deposit of a denocarcinoma & metastatic SCC with granulomatous reaction equally distributed 2% each, then Non-Hodgkin's Lymphoma & Hodgkin's Lymphoma equally distributed 0.9% each. But carcinoma nasopharynx 100% metastatic deposit of adenocarcinoma. 11% of node FNAC reported as metastatic carcinoma (5.5% each of metastatic carcinoma & metastatic poorly diff carcinoma). (P- Value = 0.20). (Table 5)

Majority of the cases of head and neck carcinoma with neck secondaries presented at stage IVa – 55.5% followed by III – 27% then IVb & IVc 9 & 8% respectively. But carcinoma larynx most commonly present at stage III (48%), followed by stage IVa (37%) then stage IVc & IVb – 11% & 4% respectively. No case presented in early stage I & II. (P- Value = 0.00028). (Table 6)

For nodal staging, most of cases had N2 stage (55.5%) followed by N1 stage (34.3%) & for tumour size T2, T3 & T4 was almost equally involved – 24%, 25% & 26% respectively. Oral cavity carcinoma most commonly had T4 stage (62.5%) and N2 stage (55%). Carcinoma larynx most commonly had, T3 stage (48%) followed by T2 stage (37%) and of nodal size, N1 stage (52%) followed by N2 stage (37%). In carcinoma base of tongue, most common was T2 stage (45%) & N2 stage (75%).

4. Discussion

In our study, head and neck cancers were observed to be more common in males (85.5%) with a male to female ratio of 6:1. According to the age groups head and neck cancers were more common in 5th to 6th decade. It was also observed that the presentation of cancer in males, majority seen in 5th to 6th decade but in females, majority seen in 3th to 4th decade.

Jesse Neff et al, Wizenberg et al, Teshima T. et al, Issing et al, Kim KM et al and Ologe et al. found almost similar i.e. higher incidence in age group of 5th to 6th decade and male to female ratio around 4:1.^{1,2}

Majority of cases were from rural areas (76.4%) and most were labourers (46.4%). This was comparable with the study of Heeranandani.³ The higher incidence in lower income group seems to be due to larger population of the group in the catchment area, malnutrition leading to lowered resistance, lack of health education, ignorance regarding the lump in neck which is not considered seriously. Poor diagnostic facilities in rural area also play some role in the higher incidence in this group.

Most common primary site observed was carcinoma oral cavity (36.36%) followed by carcinoma larynx (21.8%) & carcinoma oropharynx (13.64 %). This study compared with study of Remmert et al. which shows the same i.e. most common was carcinoma oral cavity (52%) followed by carcinoma larynx (26%).⁴

If seen specific site wise, most common diagnosis was carcinoma larynx (23%) followed by carcinoma buccal mucosa (16.3 %), carcinoma oropharynx (13.64 %), carcinoma tongue (11.8%), 2.7% each of carcinoma lip & carcinoma maxilla, and 0.9% each of carcinoma floor of mouth, carcinoma nasopharynx, Non-Hodgkin's lymphoma & classical Hodgkin's lymphoma. This correlated well with the study of Wizenberg J et al⁵ & Kim et al who found almost similar order of diagnosis.

In our study 12.7% cases of neck secondaries with occult primary were reported. This finding was in accordance with the observations of Issing et al.⁶ and Ologe et al.¹ However Vaamonde P et al, reported only 3.4% cases of occult primary.⁷

We observed neck swelling was most common presenting complaint (73.6%) followed by oral ulcer (41%) followed by dysphagia by 37.3%, hoarseness (23.6%) & dyspnoea (14.5%).

Issing et al.⁶ worked on diagnosis and management of squamous cell carcinoma of the head and neck region with unknown primary in 167 patients. Cervical swelling was the first noted symptoms in all cases. Other symptoms were pain and dysphagia.

Nearly four fifth of the addiction i.e. 85.9% had duration of addiction > 10 year with a mean duration of 24.94 (±10.96) years. This finding strongly recommends that higher duration of smoking/ addiction is a primary cause of carcinoma.

85% of cases of head and neck carcinoma with neck secondaries presented with unilateral neck nodes (54% left side & 31% right side) and 15% cases were bilateral. (P- Value = 0.038, which shows significant relationship). Heeranandani observed almost similar incidence of bilateral neck node by 18% & rest was unilateral.³

It was also observed that frequency of metastatic lymph node on left side was 42%, right side 37% & bilateral side was 21%. (i.e. right & left almost equal which was in accordance with the findings of Berg T. et al).

In the present study it was observed that in head and neck carcinoma the most common neck node level involved were level II followed by level I. These finding strongly correlated with study of Lindberg⁸ and Trivic et al.

In occult primary & lymphoma, level I to level V are almost equally involved. But Remmert et al.⁴ described that in occult primary most common neck node level was level II.

In most cases of head and neck carcinoma with neck secondaries, the duration of onset of neck swelling was <2 months i.e. Out of 110 cases 58(53%) followed by 2-5 months 42(38%) & rest > 5 months. (P- Value = 0.122 because in almost every site of head and neck carcinoma shows similar duration of onset). This was in accordance with the study of Fried et al.

In most cases of head and neck carcinoma with neck secondaries, Histopathological grading of primary head & neck carcinoma is grade II – 69% followed by grade I – 11%, then grade III – 4.5%. But for carcinoma maxilla most common is grade I followed by grade II. These incidence correlated with study of Metka et al.

It was observed that, over 91.5% of primary site of head & neck carcinoma were squamous cell carcinoma. Second common is epidermoid carcinoma which is 4.2%. This finding strongly correlated with study of R J Sanderson, who also found, more than 90% of tumours in head and neck are squamous cell carcinoma.

In majority of the cases, FNAC of node shows metastatic deposit of squamous cell carcinoma (84%), followed by metastatic deposits of adenocarcinoma (2%), then Non-Hodgkin’s lymphoma & Hodgkin’s lymphoma equally distributed as 0.9% each. Carcinoma nasopharynx shows 100% metastatic deposit of adenocarcinoma. (P- Value = 0.20). This correlated well with study of Lindberg,⁸ Ghazala Mehadi et al, Sucheta Devi Khurajam et al.

Most of the cases presented at stage IVa – 55.5% followed by III – 27% then IVb & IVc 9 & 8% respectively. But carcinoma larynx most commonly presented in stage III (48%), followed by stage IVa (37%) then stage IVc & IVb – 11% & 4% respectively. But no case presented in early stage like I & II. (P- Value = 0.00028 which shows significant relationship).G.A Vernham et al.⁹ also found similar incidence of presentation i.e. 61% of patients were presenting with advanced disease (stage III and IV).

In the present study of tumour size & node metastases in head & neck cancer it is observed that N2 stage is most common i.e. 55.5% followed by N1 (34.3%) & then N3 (8.3%). And for tumour size T2, T3 & T4 stage are almost equally distributed which is 24%, 25% & 26% respectively, followed by Tx (14%) & then T1 (10%).

Krishna Koirala et al found in their study that T3 was majority in carcinoma larynx & carcinoma oral cavity and T2 stage was commonest in oropharyngeal carcinoma. Akmansu et al and Pinnilla et al also reported similar findings.

Krishna Koirala et al found that N2 stage was the most common followed by N1 and N3 as seen in this study.

In present study it was noted that out of 110 cases of head and neck carcinoma with neck secondary, 10(9.1%) cases had distant metastases to lung, liver, kidney etc. at the time of presentation and this is observed mostly in those patients who presented with longer duration (more than 5 months) of neck swelling. This correlated with study of Black RJ, et al in which they observed out of 121 patients with advanced head and neck carcinoma 15(12.4%) patients had distant metastasis.

Table 1: Diagnosis of primary site

Diagnosis	No. of Cases	Percent
Ca Larynx with neck secondary	24	21.82
Ca Oropharynx with neck secondary	15	13.64
Ca Oral cavity with neck secondary	40	36.36
Ca Maxilla with neck secondary	3	2.73
Ca Nasopharynx with neck secondary	1	0.9
Ca Ear with neck secondary	2	1.8
Neck secondary with occult primary	14	12.73
Lymphoma	2	1.8
Head & Neck Ca with neck secondary with Mets	9	8.2
Total	110	100

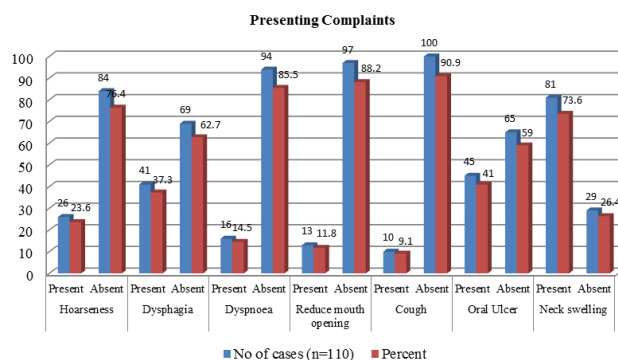


Fig. 1:

Table 2: Correlation B/W Diagnosis and Side of Node Enlargement (Clinically & Radiologically)

Side of Node Enlarged	Ca larynx (%)	Ca BOT (%)	Ca Oral cavity (%)	Ca Maxilla (%)	Ca Nasopharynx (%)	Ca Ear (%)	Occult Primary (%)	Lymphoma (%)	Total (%)
Right	13(48.15)	5(25)	14 (35)	1(33.33)	0	1(50)	3(20)	0	37(33.64)
Left	13(48.15)	7(35)	18 (45)	0	1(100)	1(50)	9(60)	0	49(44.55)
Bilateral	1(3.70)	8(40)	8 (20)	2(66.67)	0	0	3(20)	2(100)	24(21.82)
Total	27	20	40	3	1	2	15	2	110

Table 3: Lymphadenopathy on Clinical Examination

Side of Lymphadenopathy	Level of Cervical LN (No. of cases & %age)				
	L1	L2	L3	L4	L5
Right	19(17.3)	25(22.7)	10(9.1)	5(4.5)	3(2.7)
Left	22(20.0)	24(21.8)	17(15.5)	7(6.4)	6(5.5)
Bilateral	14(12.7)	8(7.3)	4(3.6)	5(4.5)	4(3.6)
No Lymphadenopathy	55(50.0)	53(48.2)	79(71.4)	93(84.5)	97(88.2)
Total	110(100)	110(100)	110(100)	110(100)	110(100)

Table 4: Correlation B/W Diagnosis and Level of Lymph Node enlarged (By Clinically & Radiologically)

Level of LYMPH NODE	Ca larynx (%)	Ca BOT (%)	Ca Oral cavity (%)	Ca Maxilla (%)	Ca Nasopharynx (%)	Ca Ear (%)	Occult Primary (%)	Lymphoma (%)	Total (%)
L1	6(15)	7(19.45)	29(51.79)	3(75)	1(100)	1(25)	5(18.52)	2(33.33)	54
L2	20(50)	14(38.89)	15(26.79)	1(25)	0	2(50)	6 (22.22)	1(16.67)	59
L3	9(22.5)	7(19.45)	9(16.07)	0	0	0	5(18.52)	1(16.67)	31
L4	2(5)	6(16.67)	2(3.57)	0	0	0	6(22.22)	1(16.67)	17
L5	3(7.5)	2(5.56)	1(1.79)	0	0	1(25)	5(18.52)	1(16.67)	13
Total	40	36	56	4	1	4	27	6	110

Table 5: Correlation B/W Diagnosis and FNAC of Node

FNAC of NODE	Ca larynx (%)	Ca BOT (%)	Ca Oral cavity (%)	Ca Maxilla (%)	Ca Nasopharynx (%)	Ca Ear (%)	Occult Primary (%)	Lymphoma (%)	Total (%)
Mets deposit of SCC	22 (81.48)	19(95)	34(85)	2 (66.67)	0	2 (100)	13 (86.67)	0	92
Metastatic Carcinoma	1(3.70)	0	4(10)	0	0	0	1 (6.67)	0	6(5.45)
Mets deposit of Adenocarcinoma	1(3.70)	0	0	0	1(100)	0	0	0	2(1.82)
NHL	0	0	0	0	0	0	0	1 (50)	1(0.9)
Hodgkin's Lymphoma	0	0	0	0	0	0	0	1 (50)	1 (0.90)
Metastatic SCC with granulomatous Reaction	1(3.70)	1(5)	0	0	0	0	0	0	2(1.82)
Metastatic Poorly Diff. Carcinoma	2(7.41)	0	2(5)	1(33.33)	0	0	1(6.67)	0	6(5.45)
Total	27	20	40	3	1	2	15	2	110

Table 6: Correlation B/W Diagnosis and Stage at Presentation

Stages	Ca larynx (%)	Ca BOT (%)	Ca Oral cavity (%)	Ca Maxilla (%)	Ca Nasopharynx (%)	Ca Ear (%)	Occult Primary (%)	Lymphoma (%)	Total (%)
I	0	0	0	0	0	0	0	0	0
II	0	0	0	0	0	0	0	0	0
III	13(48.15)	4(20)	8(20)	0	1(100)	0	3(20)	1(50)	30(27.27)
IVa	10(37.04)	10(50)	30(75)	3 (100)	0	0	8(53.34)	0	61(55.45)
IVb	1(3.70)	2(10)	1(2.5)	0	0	2 (100)	3(20)	1(50)	10(9)
IVc	3(11.11)	4(20)	1(2.5)	0	0	0	1(6.67)	0	9(8.2)
Total	27	20	40	3	1	2	15	2	110

5. Conclusion

It is concluded that patients usually present to a tertiary care centre at advanced stages, with locally as well as extensive metastatic spread.

This can be attributed to lack of awareness and unavailability of proper medical facilities in rural population. There should be health education in community about carcinogenic substances like tobacco, smoking, alcohol etc., to reduce the burden of carcinomas & proper medical facilities in low socioeconomic strata.

Pathological investigations (Histopathology and Fine Needle Aspiration Cytology) are gold standard diagnostic modalities for head & neck carcinoma and neck node metastases, not only for confirmation but also for proper further management.

Knowledge of the preferred area of spread of cervical node metastasis and those that are almost never involved allows the design of more adequate plans to manage the individual lesions.

6. Source of Funding

None.

7. Conflict of Interest

None.

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