## **Original Research Article**

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# A case series of metastatic lateral cervical lymphadenopathy

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#### **ABSTRACT**

**Background:** Metastasis is a common cause of lymphadenopathy, seen mainly in patients above 40 years of age. Regional nodes entrap the tumor cells and setup complex immunological reactions within the nodes. The histological appearance of the nodes often suggests the primary tumor. The head and neck cancers spread to regional nodes via embolism and permeation. Primary site is evident most of times. The nodes are initially mobile but later may becomes fixed. The aim was to study the lateral cervical metastasis secondary to either lymphatic spread from distant primary or occult metastasis, their signs and symptoms, diagnostic procedure and treatment modalities.

**Methods:** The study was conducted from July 2012 to June 2015. All patients having cervical lymphadenopathy secondary to metastasis diagnosed by FNAC, are included in study. Patients are evaluated as a whole, starting with clinical history and examinations as per proforma. In cases of lympahdenopathy where the diagnosis was not established with FNAC, biopsy was performed and efficacy of FNAC has been calculated.

**Results:** Total 37 patients are studied. Most cases occurred in 5th decade of life, followed by 4th decade. More common in male 83.70% as compared to female 16.30% due to tobacco and smoking addiction more common in males. Change in voice is most common presentation in 46% of cases, followed by dysphagia in 35.13% of patients. Primary tumor was evident in 83.78% of cases and occult in 16.22%. Fixed nodes present in 54.05%, reduced mobility in 21.62% and mobile in 24.32%. FNAC was done in all the cases and positive results obtained in 91.8% with sensitivity of 90% and specificity of 98%. In patients treated by neoadjuvant chemotherapy followed by modified neck dissection, no recurrence occurred. Out of 10 patients treated by radical neck dissection only 2 patients had recurrence in follow up period and managed by radiotherapy. In 15 patients treated by radical radiotherapy, 5 patients had local recurrence and required selective neck dissection in follow up.

**Conclusions:** Cervical lymph node metastasis was major presentation of malignancies of head and neck region and also from distant site. Whenever presents, it should raise suspicion of metastatic origin. Early diagnosis of primary tumor followed by aggressive treatment via multimodal approach prolongs survival.

**Keywords:** Cervical lymph node, Metastasis

## INTRODUCTION

Metastasis is a common cause of lymphadenopathy, seen mainly in patients above 40 years of age. Regional nodes entrap the tumor cells and setup complex immunological reactions within the nodes. They first appear in the marginal sinus, from which they penetrate the medullary sinus, the medulla and then the cortex. Eventually there is

total parenchymal replacement by the tumor tissue. 1,2 The histological appearance of the nodes often suggests the primary tumor. Adenocarcinoma shows glandular pattern with signet ring appearance.

Squamous cell carcinoma shows keratin or epithelial cells. Anaplastic carcinoma cells are extremely pleomorphic with hyperchromatic nuclei.<sup>2,3</sup>

The head and neck cancers spread to regional nodes via embolism and permeation. Primary site is evident most of times. The nodes are initially mobile but later may becomes fixed. Lymph nodes may shows varying degree of replacement by tumor cells. The degree of differentiation depends upon the differentiation of primary tumor.<sup>3</sup>

The aim was to study the lateral cervical metastasis secondary to either lymphatic spread from distant primary or occult metastasis, their signs and symptoms, diagnostic procedure and treatment modalities.

#### **METHODS**

The study was conducted at Shri Vasantrao Naik Government Medical College, Yavatmal, Maharashtra, India from July 2012 to June 2015.

#### Inclusion criteria

All patients having cervical lymphadenopathy secondary to metastasis diagnosed by FNAC.

Patients are evaluated as a whole, starting with clinical history and examinations as per proforma. A provisional diagnosis is established and further investigations in the form of complete blood count, ESR, chest x- ray, FNAC, biopsy, computed tomography done. Patients are divided according to age and sex.

In cases of lympahdenopathy where the diagnosis was not established with FNAC, biopsy was performed and efficacy of FNAC has been calculated. After coming to final diagnosis, plan of treatment had been decided. Treatment modalities include neoadjuvant chemotherapy followed by radical neck dissection, radical neck dissection alone or radical radiotherapy alone.

#### **RESULTS**

Total 37 patients were studied.

Table 1: Prevalence of cases according to age group.

Age	No .of cases	Percentage
21-30	2	5.40%
31-40	5	13.51%
41-50	10	27.00%
>50	20	54.00%
Total	37	100%

In our study most cases occurred in 5th decade of life, followed by 4th decade.

The malignancies after 5th decade are mainly oropharyngeal found in our country mainly due to addictions.

Table 2: Prevalence according to sex.

Sex	No of cases	Percentage
Male	31	83.70%
Female	06	16.30%
Total	37	100%

Malignancies are more common in male 83.70% as compared to female 16.30% due to tobacco and smoking addiction more common in males.

Table 3: Symptomatology of cervical lymphadenopathy.

Symptoms	No. of patients	Percentage
Loss of appetite	8	21.62%
Pain	5	13.5%
Dysphagia	13	35.13%
Dyspnoea	7	18.91%
Change of voice	18	46%
Cough	3	8.1%
Swelling only	7	18.91%
Pus discharge	0	0%

Change in voice is most common presentation of cervical metastasis and present in about 46% of cases, followed by dysphagia in 35.13% of patients. Loss of appetite is present in 21.62%, pain in 13.5%, dyspnoea in 18.91% and only swelling in 8.1% of patients. The symptoms are produced mainly due to infiltration of tumor rather than constitutional due to prolonged disease.

**Table 4: Clinical findings.** 

Clinical findings	No. of patients	Percentage
Sinus/ Pus discharge	0	0%
Fungation	3	8.1%
Platysma sign	19	51.35%
s/o medical complication	3	8.1%
Evident primary	31	83.78%

Primary tumor was evident in 83.78% of cases and occult in 16.22%. Platysma sign was present in 51.35% of cases and correlates with the incidence of fixed nodes. Fungation was present in 8.1% due to late presentation and neglected health care attitude.

Table 5: Nodal status in malignant secondary lymphadenopathy.

Status	No. of cases	Percentage
Fixed	20	54.05%
Reduced mobility	8	21.62%
Mobile	9	24.32%

Maximum number of patients had fixed nodes due to late presentation in the course of disease. Fixed nodes present in 54.05%, reduced mobility in 21.62% and mobile in 24.32%.

Table 6: Nodal occurrence.

Nodal status	No. of patients	Percentage
N1	04	10.8%
N2	25	67.5%
N3	08	21.6%

The maximum number of patients had N2 nodes in 67.5% of cases of malignant secondary lymphadenopathy followed by N3 nodes in 21.6%.

Table 7: Association of addiction in secondary metastatic lymphadenopathy.

Addiction	No. of cases	Percentage
Smoking	18	48.64%
Tobacco chewing	10	27.02%
Both	05	13.5%
None	04	10.8%

Smoking was found commonly associated with carcinoma of oropharynx and pyriform fossa. Tobacco chewing was found to be associated with carcinoma of oral cavity. Patients who did not have any addiction were of secondary from testis, stomach, esophagus etc.

Table 8: Efficacy of FNAC in diagnosis.

Disease	Positive results	Negative results
Malignant secondary LN (37)	34	3
Percentage	91.8%	8.2%

FNAC was done in all the cases and positive results obtained in 91.8% with sensitivity of 90% and specificity of 98%.

Table 9: Patients requiring biopsy for diagnosis.

Disease	Biopsy	Repeat biopsy
Malignant secondary LN	3	1
Percentage	100%	33.34%

Only 3 patients required biopsy suspected lesions and diagnosis is confirmed after biopsy in all patients. So biopsy has highest sensitivity and specificity of nearly 100%.

Table 10: Occult primary on follow up.

Diagnosis	No. of cases	Percentage
Remained occult	06	60%
Diagnosed	04	40%
Total	10	100%

Table 11: Incidence of different primary in metastatic lymphadenopathy.

Disease	No. of cases	Percentage
Ca. tongue	10	27%
Ca. alveolus	03	8.1%
Ca. tonsil	02	5.4%
Ca. pyriform fossa	04	11.76%
Ca. cricopharynx	02	5.4%
Ca. oropharynx	01	2.7%
Ca. larynx	04	11.76%
Ca. nasopharynx	01	2.7%
Ca. oesophagus	01	2.7%
Ca. stomach	02	5.4%
Ca. testis	01	2.7%
Occult primary	06	18.9%
Total	37	100%

Table 12: Treatment modalities.

Treatment modality	No. of patients	Percentage
Neoadjuvant chemotherapy f/b neck dissection	12	32.43%
Radical neck dissection	10	27.02%
Radical radiotherapy	15	40.54%

In patients treated by neoadjuvant chemotherapy followed by modified neck dissection, no recurrence occurred. Out of 10 patients treated by radical neck dissection only 2 patients had recurrence in follow up period and managed by radiotherapy. In 15 patients treated by radical radiotherapy, 5 patients had local recurrence and required selective neck dissection in follow up.

#### **DISCUSSION**

The study was conducted at Shri Vasantrao Naik Govt Medical College, Yavatmal from July 2012 to June 2015. Age plays the major role in occurrence and prevalence of malignant disease, in particular age. In our study most cases occurred in 5<sup>th</sup> decade of life, followed by 4th decade. The malignancies after 5th decade are mainly oropharyngeal found in our country mainly due to addictions. Malignancies are more common in male 83.70% as compared to female 16.30% due to tobacco and smoking addiction more common in males. Glesson M et al in a meta-analysis of 8500 patients found secondary to be present in more than 75% in age group above 40 years. Shah J, Phillip M et al also observed the same findings. 5.6

Change in voice is most common presentation of cervical metastasis and present in about 46% of cases, followed by dysphagia in 35.13% of patients. Loss of appetite is present in 21.62%, pain in 13.5%, dyspnoea in 18.91% and only swelling in 8.1% of patients. The symptoms are

produced mainly due to infiltration of tumor rather than constitutional due to prolonged disease. Glesson M et al proposed, the clinical features and examination alone in 50% of cases could do the early diagnosis of head and neck cancers.<sup>4</sup> Symptoms of hearing loss, earache, hoarseness, dysphagia, dyspnoea should be sorted out. Symptoms thus give clue to the diagnosis as well as rough idea about the stage of disease. Dolan RW et al stated the same thing but considered it as an inadequate indicator, which can give clue to diagnosis.<sup>7</sup> The constitutional symptoms of weight loss and appetite loss were either related directly to the mechanical obstruction or due to interleukins and tumor necrosis factors.

Primary tumor was evident in 83.78% of cases and occult in 16.22%. Platysma sign was present in 51.35% of cases and correlates with the incidence of fixed nodes. Fungation was present in 8.1% due to late presentation and neglected health care attitude. Phillip M et al in a study of 594 patients found incidence of large and fixed nodes in 20% of cases, this is contrast to our study. The reason for it was that, most patients were from rural background and presented usually late due to lack of facilities. In same study, he demonstrated significance of fixed nodes, where radiotherapy and salvage surgery did not prolong the survival in fixed nodes. Morris J et al in his study of 126 patients found 40% had fixed nodes, 29% had reduced mobility, while 31% had mobile nodes. The property of the survival in fixed nodes and preduced mobility, while 31% had mobile nodes.

In nodal status, 67.5% had N2 status, 21.6% had N3 status and only 10.8% had N1 status. Morris J et al in his study of 126 head and neck malignancies, 31% had N1 status, 29% had N2 status and 40% had N3 status. Shah J et al, in 149 patients of laryngopharyngeal cancers found, 70% were having N1 status and 30% had N2 status and no N3 nodes which is contrast to our study. This is because of late presentation of people in rural Indian setup.<sup>8,9</sup>

Smoking was found commonly associated with carcinoma of oropharynx and pyriform fossa in 48.64% of patients. Tobacco chewing was found to be associated with carcinoma of oral cavity in 27.02% of patients. Patients who did not have any addiction were of secondaries from testis, stomach, esophagus etc. Jayant K et al in a study of 2005 patients showed the common association of the oral cavity cancers with tobacco chewing and carcinoma base of tongue and larynx with smoking. <sup>10</sup>

In secondary malignant lymphadenopathy FNAC was done in all the cases and positive results obtained in 91.8% with sensitivity of 90% and specificity of 98%. Similar findings obtained in studies of Nada A et al and Podar AK et al showing sensitivity of 90% and specificity of 98%. Only 3 patients required biopsy suspected lesions and diagnosis is confirmed after biopsy in all patients. So biopsy has highest sensitivity and

specificity of nearly 100%. Complications of biopsy were studied; no major complications was encountered.

Computed tomography scanning gives complete threedimensional anatomical details of swelling, but is not needed in all patients in whom other clinical findings and other investigations are diagnostic. In malignant secondary lymphadenopathy, computed tomography has been done in cases of patient had occult primary and found to have multiple brain metastasis, carcinoma of stomach, carcinoma esophagus and nasopharyngeal carcinoma.

Differential occurrence of primaries in our study found to be 27% for carcinoma of tongue, followed by 18.9% for occult primary. More than 90% secondaries were from head and neck primaries. Oral malignancies found to be commonest followed by laryngopharyngeal malignancies. Joseph R et al in a study of 38 patients, 14% patients were found to be of carcinoma tongue and carcinoma of larynx was commonest in about 23% of patients. 13 Phillip M et al in a study of 1683 patients found, 21% were from oral cavity, 24% from hypopharynx and 17% from larynx.<sup>6</sup> Glesson M et al in a study of 267 patients, 89% were secondary from head and neck malignancy and only 11% were from the distant sites.<sup>4</sup> This correlates with our study. In Vasalius storyboards an interesting rule was mentioned, called as rule of 80%. 14 Given as, 80% lateral neck masses in adult are malignant, 80% are metastatic, 80% from above clavicle and 80% of squamous cell origin. It correlates with our study.

Occult primary is an interesting and always a challenging entity. In our study, total 10 cases of occult primary are found. Out of which 4 patients (40%), were diagnosed of primary on further investigations while 6 patients (60%) remained occult constituting 18.9% of total malignant secondary lymphadenopathy. Two of the patients had distant metastasis, one had liver metastasis and other had brain metastasis. In a study of 475 patients with isolated neck masses by Jean L et al, 40% found to be unknown primary and 27% of them had another metastatic lesion. Joseph R and Richard H found similar results in their studies. <sup>13,15,16</sup>

Treatment modalities differ from case to case according to primary malignancy, nodal status and stage of disease. In our study we offered neoadjuvant chemotherapy followed by modified neck dissection in 32.43% of patients, radical neck dissection in 27.02% of patients and radical radiotherapy in 40.54% of patients. Endicott JN et al in a study of 197 patients, where induction chemotherapy was used, 15% achieved complete response, 3.4% partial response while rest had stable disease. Radiotherapy was not used in this study, although overall response rate was good. Keith et al in study conducted on 158 patients, where adjuvant chemotherapy was used in head and neck malignancies, observed 50% response rate. Phillip M et al, in a study conducted on 594 patients found, 56.4% patients

considered untreatable and given palliation, which was slightly more than our study.<sup>6</sup> Two year survival with radiotherapy or salvage surgery found to be same.

Surgical treatment when possible is always a better option. Yves et al in a study of carcinoma of tongue, of 291 node positive patients, 101 received preoperative radiotherapy and 37% of them after surgery had pathologically negative nodes.<sup>19</sup> Recurrence rate was only 8% at five year follow up, signifying the usefulness of preoperative radiotherapy. During the same study, postoperative radiotherapy was considered mandatory for major nodal involvement. Morris J et al, in a study of 109 patients treated with irradiation alone, most were stage III and IV, 44% had control of both primary and secondary.8 This supports our study, where maximum patients were from stage III and IV, and treated with radiation alone or with adjuvant chemotherapy. John V on his report of 519 patients of radical neck dissection, which constituted 85% squamous cell carcinoma and 15% adenocarcinoma, 5 year survival rate was found to be 35%.<sup>20</sup> Operative mortality was 5.2% which is in contrast to our study. This was because the bulk of cases were low in our study and almost all patients had mobile nodes reducing the risk of surgery. Laurence W et al, in a collective review on radical neck dissections, proposed it for palpable significant nodes that are not fixed.<sup>21</sup>

Elliot et al in his study of 344 cases, proved low dose irradiation followed by radical neck dissection, to be useful, which produced subsequent reduction in recurrence. Louis J et al, Shah J in their study of unknown primary, better survival was proved with radical neck dissections provided no metastasis at other sites and nodes are mobile. Up to 30% survival at 3 years was observed. Metastatic lesions were treated palliatively. The common complications noted in radical neck dissection by Laurence W et al were cosmetic loss, shoulder syndrome and mortality. Apart from the cosmetic loss, no major complication found in our study. Thus these observations and references suggest and justify the modes of treatment used according to stage of disease. Lagrangian states are references of the stage of disease.

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