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Original Research Article

Clinical, radiological and morphological spectrum of squamous cell carcinoma

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ABSTRACT

Background: Squamous cell carcinoma is malignancy of the squamous epithelial lining. It has been a major cause of morbidity and mortality worldwide as well as in Indian population. This study was undertaken to analyse the spectrum of squamous cell carcinoma cases presenting at G.G.G. Hospital, Jamnagar to understand the clinical presentation, morphological patterns and anatomical site distribution pattern of squamous cell carcinoma lesions.

Materials and Methods: Over a 2-year period, 115 cases were retrieved from the files of cytopathology and histopathology laboratory, Department of Pathology and Radiology of M. P. Shah Government Medical College, Jamnagar.

Results: Out of total 115 cases, maximum cases- 103 (89.56 %) were of squamous cell carcinoma. The incidence was observed to be high in >40 years of age. In our institute, we studied total 115 cases of various sites which were diagnosed as squamous cell carcinoma. Of these 115 cases, 47 (40.86%) cases were of lung, 57 (49.46%) cases were of metastasis of Squamous cell carcinoma to lymphnode with maximum 31 (54.38%) cases presented to us as unknown primary. In our study 11 cases involving miscellaneous sites such as oral cavity, lip, cheek, midline neck, pre-auricular region, anterior chest wall and umbilical region, were presented as primary, metastasis and recurrence.

Conclusion: Correlation spectrum of morphology, clinical presentation and radiological examination of squamous cell carcinoma with its cytological and histopathological features are important tools to predict prognosis and to facilitate the diagnosis of squamous cell carcinoma and diagnostic dilemma can be prevented.

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1. Introduction

Squamous cell carcinoma (SCC), which is a malignant tumor of the squamous epithelium, has been a major cause of morbidity and mortality worldwide.

It has been a major health problem worldwide as well as in Indian population, recorded in the National Cancer Registry Program. Recently an increasing incidence of squamous cell carcinoma is observed among young persons in many regions of the world—a trend which is particularly concerning.¹

Squamous cell carcinomas are important from clinical point of view and have relevance to a wide variety of fields,

including Medicine, Pathology, Surgery and Radiotherapy.

The main purpose of this study is to present a detailed analysis of existing literature with emphasis on the clinico-pathological variables of squamous cell carcinoma and apply this information to the clinical setting, providing a reasonable approach when confronted with a patient with these disorders. The study has been inspired by the understanding that a good insight in establishing relationship between the clinical presentation, radiological, cytopathological and histopathological findings of the biopsy can contribute to early detection of the malignancy and reduce the incidence and prevalence of different squamous cell carcinoma after certain intervention of course.

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2. Aims and Objectives

1. To study the spectrum of squamous cell carcinoma cases presenting at G. G. G. Hospital, Jamnagar, during 2 years (i.e., 2019–2020).
2. To study the morphological patterns of squamous cell carcinoma lesions and its correlation with radiological findings.
3. To determine the incidence of squamous cell carcinoma at G G G Hospital, Jamnagar
4. To analyse the incidence of metastasis of squamous cell carcinoma in various anatomical site
5. To review the literature available on squamous cell carcinoma and compare it with our findings.

3. Materials and Methods

This study was carried out at the Department of Pathology, M. P. Shah Government Medical College, Jamnagar. It included cases of squamous cell carcinoma presenting at various departments- ENT, TBCD, Surgery and Radiotherapy of G. G. G. Hospital, during year 2019 and 2020. In all 115, such cases were reported to be squamous cell carcinoma during the period of 2 years. Clinical details were obtained from patient's record. H&E stained slides of the lesions were retrieved and then were reviewed. Further, following parameters were examined: Age, gender, clinical features, anatomical site of tumour with radiological and cytological findings.

4. Observation and Results

Total 115 cases of various presentations and of various sites, diagnosed as squamous cell carcinoma, of which 47 cases were of lung, 57 of lymph node and 11 of other miscellaneous sites were studied.

Table 1 Maximum incidence (45 cases: 95.74%) of lung carcinoma was observed in the age group of >40 years of age including male and female population, with a male preponderance (87.23%).

Table 2 Out of 47 cases of lung, maximum cases (30 cases: 63.82%) showed involvement of Middle lobe of lung and the commonest clinical presentation was observed to be cough with chest pain.

Table 3 In present study, 23 cases out of 47 of squamous cell carcinoma of lung Radiologically showed metastasis to various organs. Most common site for lung metastasis was observed to be mediastinal lymphnode (13/23 cases) followed by ipsilateral pulmonary region (4/23 cases). Least common incidence of metastasis from lung was seen in Adrenal gland.

Table 4 In present study, 10 cases were cytologically diagnosed as Non small cell carcinoma-Poorly differentiated carcinoma with diagnostic dilemma between squamous cell carcinoma and adenocarcinoma. These cases were confirmed with histopathological examination

and immunohistochemistry marker study. 36 (76.59%) cases had diagnostic concordance with histopathological diagnosis.

Table 5 Out of the total 115 cases, 57 were involving the lymph node. Maximum incidence (48/57 cases: 84.21%) of metastasis in lymphnode from squamous cell carcinoma was observed to in age group of > 40 years of age. Of these 48 cases, 43 were male and 05 cases were female, hence showing a male preponderance.

Table 6 In case of metastasis in lymphnode by squamous cell carcinoma, the most common clinical presentation of patient was observed to be cervical neck swelling. In radiological findings, 15 cases (26.31%) showed necrotic cervical lymphadenopathy most commonly at level II lymphnode. One case presented as inguinal swelling, highly suspicious for metastasis was confirmed as primary Lymphoepithelial cyst with Moderately differentiated keratinizing squamous cell carcinoma of the same site, hence being an exception to other cases in Lymph node.

Table 7 Maximum cases (31/57 cases) of lymphnode metastasis had an unknown primary. The primary site for metastasis to cervical lymphnode were as follows: Supraglottis (14.03%), Buccal mucosa (10.52%), Tongue (5.26%). Hardpalate, Hypopharynx and Lung showing same incidence (3.50%). Metastasis of SCC from esophageal carcinoma to lymph node showed least incidence.

Table 8 Out of the total 115 cases, 11 cases belonged to miscellaneous sites. Of these 11 cases, 06 were Primary SCC. Of these primary cases, involvement of Oral cavity, lip, cheeks and Anterior chest wall showed most common involvement, whereas Umbilical region showed least involvement. The remaining 3 out of 11 cases were secondaries, 2 of which involved anterior chest wall and remaining 1 involved umbilical region.

Table 9 Squamous cell carcinoma of various Head & Neck region had 100% concordance on both cytopathological and histopathological diagnosis.

5. Discussion

Lung cancer is now the leading cause of cancer mortality.² The mean age of carcinoma lung patients in the present study was 61.43 years. This showed that carcinoma lung is the disease of the older age. In the study of Wagner et al.³, the age ranged between 37 to 82 years which is comparable to the age group in the present study. The average age of the carcinoma lung patients in the present study is also comparable to some of the major Indian studies.⁴⁻⁶ The sex ratio reported in various Indian studies ranged from 4.5:1 to 8.2:1.⁶⁻⁹ The sex ratio in our study was 10.7:1 with a clear male preponderance. Cough was the most common symptom and was present in 87.23% patients in the present study. This is similar to other studies from India and abroad.⁶⁻¹⁰ Haemoptysis has been reported to be present in 11% to 24% carcinoma lung patients in various studies.^{5,9,10}

Table 1: Age and Gender Wise Distribution of Lung cases (n=47)

Age	Sex		Total
	Male	Female	
<40 Years	02(4.25%)	00(00 %)	02(4.25%)
>40 Years	41(87.23%)	04(8.51%)	45(95.74%)
Total	43(91.48%)	04(8.51%)	47(100 %)

Table 2: Distribution of cases according to clinical presentations and radiologically confirmed site of lung pathology (n=47)

Site of Pathology	Clinical Presentation				Total
	Cough with chest pain	Cough with dyspnea on exertion	Cough with hemoptysis	Dyspnea on exertion with chest pain	
Upper Lobe Mass	03	07	01	01	12
Middle Lobe Mass	12	10	04	04	30
Lower Lobe Mass	01	02	01	01	05
Total	16	19	06	06	47

Table 3: Distribution of cases according to Radiologically confirmed site of metastasis from primary lung mass (n=23)

Site of Metastasis	No of Cases
Adrenal Gland	02
Liver	03
Mediastinal Lymphnode	13
Pleural Effusion	02
Ipsilateral Pulmonary region	04
Total Cases	23

Table 4: Classification and comparison of cases of Lung according to Cytopathology, Histopathology and Immunohistochemistry (n=47)

IHC confirmed Diagnosis Of Lung	Cytopathology Diagnosis Of Lung	
	Non-small cell carcinoma-Poorly differentiated carcinoma	Non-small cell carcinoma-Squamous Cell Carcinoma
Primary Non small cell carcinoma-Squamous Cell Carcinoma	10 (21.27%)	36 (76.59%)
Metastasis in lung	00 (00%)	01 (2.12%)
Total Cases	10 (21.27%)	37 (78.72%)

Table 5: Age and gender wise distribution of lymphnode lesions (n=57)

Age	Sex		Total
	Male	Female	
<40 Years	06 (10.52%)	03 (5.26%)	09 (15.78%)
>40 Years	43 (75.43%)	05 (8.77%)	48 (84.21%)
Total	49 (85.96%)	08 (14.03%)	57 (100%)

Table 6: Distribution of cases of lymph node according to the clinically presenting site and their corresponding Radiological features (n=57)

Radiological Features of presenting lymph node	Site of clinically presenting Lymphnode					Total
	Cervical level I	Cervical level II	Cervical level III	Cervical level VI	Axillary Lymph node	
Necrotic	05	15	01	05	00	26
Conglomerated	01	10	01	02	00	14
Loss of Fatty Hilum	00	02	01	00	01	04
Calcification Foci	02	02	02	00	00	06
Neoplastic Mass	00	06	00	00	00	07
Total	08	35	05	07	01	57

Table 7: Distribution of cases of Lymphnode according to their primary site of malignancy (n=57)

Site Of Primary	Cervical Lymphnode	Inguinal Lymphnode	Axillary Lymphnode	Total
Buccal Mucosa	06	00	00	06
Supraglottis	08	00	00	08
Hard Palate	02	00	00	02
Tongue	03	00	00	03
Tonsillar Fossa	01	00	00	01
Lip	01	00	00	01
Lung	02	00	00	02
Hypopharynx	02	00	00	02
Esophagus	01	00	00	01
Unknown Primary	29	01	01	31
Total	55	01	01	57

Table 8: Distribution of cases of Squamous cell carcinoma according to miscellaneous (n=11)

Site of presentation	Total Cases	Primary	Metastatic	Recurrence
Oral cavity	02	02	00	00
Lip	02	02	00	00
Cheek	02	01	00	01
Midline Neck swelling (Larynx)	01	01	00	00
Preauricular region	01	00	00	01
Anterior Chest wall	02	00	02	00
Umbilical region	01	00	01	00
Total	11	06	03	02

Table 9: Correlation of Cytopathological and histopathological diagnosis of squamous cell carcinoma of miscellaneous sites (n=11)

S. No.	Site	Cytopathological Diagnosis	Histopathological Diagnosis	Total Cases
1	Oral cavity	Recurrence of squamous cell carcinoma Squamous cell carcinoma	Moderately differentiated keratinizing squamous cell carcinoma with therapy induced changes Moderately differentiated keratinizing squamous cell carcinoma OF HARD PALATE	02
2	Lip	Squamous cell carcinoma	Well differentiated keratinizing squamous cell carcinoma of lower lip	02
		Squamous cell carcinoma - Keratinizing type	Moderately differentiated keratinizing squamous cell carcinoma upper lip	
3	Cheek	Recurrence of Squamous cell carcinoma Squamous cell carcinoma	Moderately differentiated keratinizing squamous cell carcinoma with therapy induced changes Moderately differentiated keratinizing squamous cell carcinoma of Buccal mucosa	02
4	Midline Neck swelling(Larynx)	Squamous cell carcinoma	Well differentiated keratinizing squamous cell carcinoma of Larynx	01
5	Preauricular region	Recurrence of Squamous cell carcinoma	Moderately differentiated keratinizing squamous cell carcinoma with therapy induced changes	01
6	Anterior chest wall	Metastatic squamous cell carcinoma	Metastasis from Moderately differentiated keratinizing squamous cell carcinoma of Buccal mucosa	02
		Metastatic squamous cell carcinoma	Metastasis from non keratinizing squamous cell carcinoma of cervix	
7	Umbilical region	Metastatic squamous cell carcinoma	Metastasis from Moderately differentiated keratinizing squamous cell carcinoma of lung	01
	Total			11

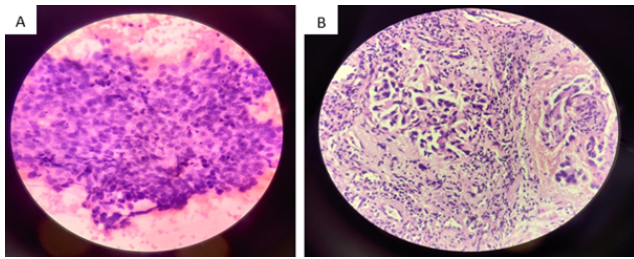


Fig. 1: **A:** H & E stained FNAC smear (40 x) from lung mass show cluster of pleomorphic epithelial cells showing high N : C ratio and moderate amount of eosinophilic cytoplasm suggestive of Non small cell carcinoma-Poorly differentiated carcinoma. **B:** H & E stained section (40 x) from lung mass show small cluster of malignant epithelial cells showing nuclear pleomorphism, individual cell keratinization and hyperchromatic nucleus suggestive of Non-small cell carcinoma-Squamous cell carcinoma.

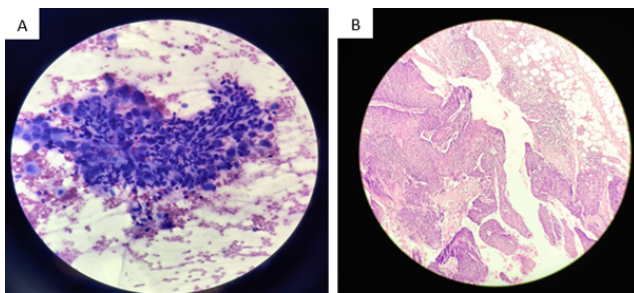


Fig. 2: **A:** H & E stained FNAC smear (40 x) from Cervical lymphnode show cluster of hyperchromatic nucleus, nuclear pleomorphism and eosinophilic cytoplasm against lymphoid background suggestive of metastatic lymphadenopathy from Squamous cell carcinoma. **B:** H & E stained section (10 x) from cervical lymphnode show sheets of Squamous cells with lymphoid cells suggestive of metastasis from Squamous cell carcinoma.

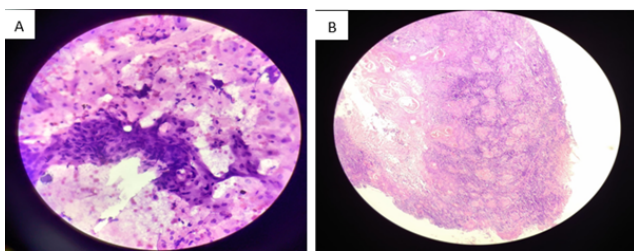


Fig. 3: **A:** H & E stained FNAC smear (40 x) from lip swelling show sheets of cells showing hyperchromatic nuclei, individual cell keratinization with background shows mature squamous cell suggestive of Squamous cell carcinoma. **B:** H & E stained section (10 x) from lip swelling show squamous epithelial cells with mild dysplasia, individual cell keratinization and well-formed keratin pearls suggestive of Well differentiated keratinizing squamous cell carcinoma.

Pandhi et al.⁵ and Jindal and Behera.⁶ have reported a higher percentage of haemoptysis in their studies (50% and 69.2% respectively). In the present study haemoptysis was present in 12.76% patients.

It is well known that squamous cell carcinoma presents mostly as a central tumour. In this study 63.82% of squamous cell carcinoma patients had central lesion. In Gupta R et al study about 75% of the patients with squamous cell carcinoma had central tumours.¹¹ This again is in concordance with most reports published from elsewhere.

In our study 10 cases were cytologically diagnosed as Non small cell carcinoma-Poorly differentiated carcinoma with diagnostic dilemma between squamous cell carcinoma and adenocarcinoma. These cases were confirmed with histopathological examination and immunohistochemistry marker study as Non small cell carcinoma- Squamous cell carcinoma. 36 cases had diagnostic concordance with histopathological diagnosis of Non small cell carcinoma-Squamous cell carcinoma. Study show 1 case which is diagnosed as Non small cell carcinoma- Squamous cell carcinoma in cytology. Further radiological evaluation, histopathological examination and immunohistochemistry marker study proved the case as metastasis in lung from mediastinal mass as a primary lesion.

Computed tomography of the chest and upper abdomen has already been shown to be an important tool in the diagnosis and staging of lung cancer.^{12,13} In our study the computed tomography of chest and upper abdomen (including adrenals) was done in all 47 patients. The reported incidence of adrenal metastasis diagnosed by computed tomography is 10-15 percent.¹⁴ In our study computed tomography diagnosed adrenal metastasis in 4.25% patients. Moreover computed tomography of chest diagnosed significant mediastinal lymphadenopathy in 13 patients in our study which was most common site of metastatic involvement. In our study 3 patient presented with liver metastasis. In Gupta R et al.¹¹ reported mediastinal lymphadenopathy in about 121 patients and liver metastasis in 38 cases.

Enlarged lymph nodes are accessible for FNAC and are of importance specially to diagnose secondary or primary malignancies. It plays a significant role in developing countries like India, as it is a relatively cheap procedure, simple to perform and has minimal or no complications.¹⁵⁻¹⁷ The diagnosis given on the cytological material is often the only diagnosis accepted and sometimes there is no further correlation with histopathology, especially in cases of advanced malignancies. It also provides clues for occult primaries and sometimes also surprises the clinician who does not suspect a malignancy. The primary sites identified in each lymph node group in our study correlated with other similar studies.^{16,18,19} A full history, radiological investigations and immunohistochemistry in difficult cases may help to arrive

at a definitive diagnosis.¹⁹ Specialized investigations such as ultrasonography-guided FNAC's of sentinel lymph nodes in the head and neck area have been found to be good in picking up metastases in clinically undetectable lymph nodes.²⁰

In present study, 57 cases presented with lymphnode swelling suggesting primary or metastatic lymphadenopathy of squamous cell carcinoma based on their clinical presentation and radiological features. These 57 cases belonged to age group 30 to 90 years with sex ratio of male to female- 6.15:1, showing a clear male preponderance. Maximum incidence (84.21%) was observed in age group of >40 years of age. Cervical group of lymphnode (Cervical level II) was found to be the most common group of lymph nodes to be involved by metastasis of squamous cell carcinoma. 54.38% cases had an unknown primary or lesion.

In present study we found one rare case of Carcinoma of Unknown Primary Site (CUPS) at inguinal region. Fine needle aspiration of the inguinal region swelling was suggestive of high grade metastasis from epithelial malignancy from poorly differentiated squamous cell carcinoma. On further histopathological investigation, it was confirmed as Moderately differentiated keratinizing squamous cell carcinoma in lymphoepithelial cyst of inguinal lymphnode. Incidence of known primary lesion was commonly seen in oral cavity like Supraglottis (14.03%), Buccal mucosa (10.52%), Tongue (5.26%), Hard palate, Hypopharynx (3.50%) and tonsillar fossa.

Various site of presentation of head and neck and other region as squamous cell carcinoma occur as primary (54.54%), metastatic (27.27%) and recurrence (18.18%). Squamous cell carcinoma of various Head & Neck region had 100% concordance both cytopathological and histopathological diagnosis.

6. Conclusion

The spectrum of morphology, clinical presentation and radiological examination of squamous cell carcinoma with its cytological and histopathological features was studied. Correlation of these findings are important tools to predict prognosis and to facilitate the diagnosis of squamous cell carcinoma and diagnostic dilemma can be prevented.

7. Source of Funding

No financial support was received for the work within this manuscript.

8. Conflict of Interest

The authors declare they have no conflict of interest.

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