Squamous Cell Carcinoma: Morphological & Topographical Spectrum: A Two Year Analysis

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Abstract Squamous cell carcinoma, which is a malignant tumor of the squamous epithelium, has been a major cause of morbidity and mortality worldwide. It is a major health problem across the world and among the most common cancers seen in both Indian men and women as can be gauged from the records of the National Cancer Registry Programme. This study was undertaken to analyze the spectrum of squamous cell carcinoma cases presenting at M.Y. Hospital, Indore, during 2 years between 2007 and 2008, to understand the morphological patterns of squamous cell carcinoma lesions and classify them into morphological categories given by International Classification of Diseases for Oncology (ICD-O, third edition), to analyze the anatomical site distribution pattern of squamous cell carcinoma lesions and categorize them in topographical classes given by ICD-O. Over a 2-year period, 959 cases were retrieved from the files of histopathology laboratory, department of pathology, M.G.M. Medical College, Indore. Out of total 959 cases, the maximum cases—290 (30.24 %)—of squamous cell carcinoma were found between the fourth and fifth decades of life. The frequency of squamous cell carcinoma in patients older than 30 years was 96.35 %, while in cases of less than 30 years, it was 03.65 %. Most of the reported cases of squamous cell carcinoma included invasive types (i.e., 94.3 %). Cases with distant metastasis constituted 4.7 %, while only 1 % were noninvasive or in situ. The frequency of squamous cell carcinoma presenting

at our institution was highest among those involving the lip, oral cavity, and pharynx (56.50 %), followed by those involving female genital organs (30.24 %). The respective involvement of skin, digestive organs, and respiratory systems was 4.70, 3.86, and 2.40 % in decreasing order of frequency. Frequency was least (1.05 %) among the cases reported to show metastatic deposits of squamous cell carcinoma in lymph nodes. Regarding the topographical spectrum, the maximum number of cases (26.07 %) of squamous cell carcinoma encountered belonged to ICD-O category C-53 (i.e., cervix). Among the morphological categories, the most frequently encountered was that of squamous cell carcinoma, keratinizing (35.2 %).

Keywords Squamous cell carcinoma · ICD-O · Squamous epithelium · Carcinoma in situ · Topographic spectrum · Morphologic categories

Introduction

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

It is a major health problem across the world and among the most common cancers seen in both Indian men and women as can be gauged from the records of the National Cancer Registry Programme. 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.

Squamous cell carcinomas are important from clinical point of view and have relevance to a wide variety of fields, including medicine, pathology, surgery, nuclear medicine, and radiation therapy.

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The main purpose of this study is to present a detailed analysis of existing literature with emphasis on the clinicopathologic 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 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.

This study aims to analyze the spectrum of squamous cell carcinoma cases, to study the morphologic pattern of squamous cell carcinoma and classify them into morphological categories given by ICD-O and to analyze the anatomical site distribution pattern of squamous cell carcinoma.

Aims and Objectives

This study was carried out at the Department of Pathology, M.G.M. Medical College and M.Y. Hospital, Indore (MP), with the following aims and objectives:

1. To study the spectrum of squamous cell carcinoma cases presenting at M.Y. Hospital, Indore, during 2 years (i.e., 2007–2008).
2. To study the morphological patterns of squamous cell carcinoma lesions and classify them into morphological categories given by ICD-O.
3. To analyze the anatomical site distribution pattern of squamous cell carcinoma lesions and categorize them in topographical classes given by ICD-O.
4. To determine the incidence of squamous cell carcinoma at M.Y. Hospital, Indore.
5. To review the literature available on squamous cell carcinoma and compare it with our findings.

Material and Methods

This study was carried out at the Department of Pathology, M.Y. Hospital, Indore. It included cases of squamous cell carcinoma presenting at various departments of M.Y. Hospital and Government Cancer Hospital, Indore (MP), during year 2007 and 2008. In all 959, such cases were reported to be squamous cell carcinoma during the period of 2 years. For this the H&E stained slides of the lesions were retrieved and then were reviewed. Further, the anatomical distribution of the lesions was analyzed, and they were then categorized into topographical classes given by ICD-O. The lesions were also classified into ICD-O morphological categories after careful evaluation.

Observations and Results

A total of 959 cases were included, out of which the maximum cases—290 (30.24 %) of squamous cell carcinoma—were found between the fourth and fifth decades of life. The frequency of squamous cell carcinoma in patients older than

Fig. 1 Incidence of squamous cell carcinoma. The maximum number of patients (30.24 %) belonged to age group of 41–50 years. The frequency of squamous cell carcinoma in patients older than 30 years was 96.35 %, while in cases of less than 30 years, it was 03.65 %. During the study, the maximum age encountered was 93 years, while the minimum was 19 years

30 years was 96.35 %, while in cases of less than 30 years, it was 03.65 %. During the study, the maximum age encountered was 93 years while the minimum was 19 years (Fig. 1).

The mean average for males came out to be 48.1 years, while that for females, it was 47.8 years. A male-to-female ratio of 1.01:1 (nearly equal) was yielded (Fig. 2).

Most of the reported cases of squamous cell carcinoma included invasive types (i.e., 94.3 %). Cases with distant metastasis constituted 4.7 %, while only 1 % were noninvasive or in situ. The frequency of squamous cell carcinoma presenting at our institution was highest among those involving the lip, oral cavity, and pharynx (56.50 %), followed by those involving female genital organs (30.24 %). On the other hand, only 1.25 % cases involved the male genital organs. The respective involvement of skin, digestive organs, and respiratory systems was 4.70, 3.86, and 2.40 % in decreasing order of frequency. Of all the oral squamous cell carcinoma cases, majority (38 %) involved the unspecified parts of mouth which included floor of mouth, cheek, buccal mucosa, retromolar trigone, and parts of jaw. Next in frequency, there were the cases involving gum (including alveolus, gingival, and gingivobuccal sulcus) together constituting 27 %. Total cases involving the tongue were 91 (17.9 %), out of which 16 originated from the base of tongue while the rest involved other unspecified parts of tongue. The frequency of involvement of palate and tonsils was almost equal (about 5 %). Oropharynx and lip were affected in 4 and 3.1 %, cases respectively. Larynx was involved in 20 cases of squamous cell carcinoma. The highest numbers of cases were those involving the epiglottis (30 %), closely followed by unspecified parts of larynx (25 %). About 15 % cases showed involvement of supraglottis. About 10 % cases, each of squamous cell carcinoma of ventricular bands, arytenoids, and subglottis, were found

in our study. In the category of cutaneous squamous cell carcinomas, the highest percentage (70 %) of cases was constituted by the head and neck together including cases from scalp, face, ears, and neck. Among them the facial area predominated (34 %), and majority included cases from cheek, chin, and eyes. We came across squamous cell carcinoma affecting the skin of lower limbs (13 %) more frequently as compared to the upper limbs (4 %). The respective frequency of squamous cell carcinoma involving skin of axilla, trunk, and inguinal region was 7, 4, and 2 % (Fig. 3).

Among the morphological categories, the most frequently encountered was that of squamous cell carcinoma, keratinizing (35.2 %). This was followed in decreasing order of frequency by squamous cell carcinoma, with horn formation (20.8 %) and squamous cell carcinoma, clear cells (13.5 %). The rest of categories individually constituted less than 10 % cases. Out of 959, only 10 cases (1.0 %) could be categorized into squamous cell carcinoma, metastatic (Fig. 4).

Regarding the topographical spectrum, the maximum number of cases (26.07 %) of squamous cell carcinoma encountered belonged to ICD-O category C-53 (i.e., cervix). The next was category C-06 (i.e., parts of mouth), unspecified with its frequency being 19.08 %. Squamous cell carcinoma of anal canal (C-21), pyriform sinus (C-12), bronchus and lung (C-34), and vulva (C-51) individually constituted less than 1 % cases, with least number of cases (0.1 %) being that of vulva (Figs. 5, 6, 7, 8, 9, 10 and 11).

Discussion and Review of Literature

This study was conducted at the Department of Pathology, M.G.M. Medical College and M.Y. Hospital, Indore (MP).

Fig. 2 Sex incidence of reported cases of squamous cell carcinoma with relation to age. The highest frequency of squamous cell carcinoma was observed among the age group of 41–50 years, affecting more number of females (166) as compared to males (124). Females were also involved predominantly in the age group of 51–60 years. In the rest of the age groups, male predominance was evident. Overall frequency for females was 49.85 %, while for males, it was 50.15 %. Thus, overall incidence is almost equal in both sexes

Fig. 3 Site distribution of reported cases of squamous cell carcinoma. Out of 959 cases, 542 cases (56.5 %) were from lip, oral cavity, and pharynx, followed by those involving the female genital tract (290 cases, 30.24 %)

Age and Sex Incidence

Adigun et al. [1] retrospectively reviewed 443 patients managed for squamous cell carcinoma (cutaneous and non-cutaneous) from January 1979 to December 2002. The age distribution showed peak incidence between the fourth and sixth decades of life, which was consistent with the findings of our study. We also found the maximum cases—534 (55.68 %)—of squamous cell carcinoma between the fourth and sixth decades of life. According to study of 385 cases of oral malignancies by Lawoyin et al. [2], 102 were squamous cell carcinoma. The age of patients at the first presentation ranged from 19 to 80 years, with a mean average of 48.0 years for females and 50.6 years for males. Fifty-five patients were males while 35 patients were females, a ratio of 1.6:1. In this study, the age of patients at the first presentation ranged from 19 to 93 years. The mean average for males came out to be 48.1 years, while that for females, it

was 47.8 years. These findings of our study were quite similar to the study by Lawoyin et al. [2]. A study carried out by Iype et al. [3] at Regional Cancer Centre, Trivandrum, Kerala (India), in young patients with squamous cell carcinoma of the tongue showed the mean age at presentation was 30.5 years with a 1.7:1 male-to-female ratio. As compared to this data, the mean age in our study was quite higher (47.95 years). In most of the studies, the male-to-female ratio ranged approximately from 1.5 to 1.7:1. While in our study, 481 patients were males and 478 were females, with a male-to-female ratio of 1.01:1 (i.e., nearly equal).

Site Distribution

During the study, we did not come across any other records quoting the generalized distribution pattern of squamous cell carcinoma in the body. The frequency of squamous cell carcinoma presenting at our institution was highest among

Fig. 4 Morphological distribution of reported cases of squamous cell carcinoma in ICD-O categories. Most frequently encountered category was that of squamous cell carcinoma, keratinizing (338 cases, 35.2 %). This was followed in decreasing order of frequency by squamous cell carcinoma, with horn formation (199 cases, 20.8 %) and squamous cell carcinoma, clear cells (129 cases, 13.5 %). The rest of the categories constituted less than 10 %

TOPOGRAPHICAL DISTRIBUTION IN ICD-O CATEGORIES

Fig. 5 Distribution of squamous cell carcinoma in ICD-O category. In our study, we encountered the maximum number of cases (250 cases, 26.07 %) of squamous cell carcinoma belonging to ICD-O category C-

53 (i.e., cervix). The next was category C-06 (i.e., parts of mouth, unspecified)

those involving the lip, oral cavity, and pharynx (56.50 %), followed by those involving female genital organs (30.24 %). On the other hand, only 1.25 % cases involved the male genital organs. The respective involvement of skin, digestive organs, and respiratory systems was 4.70, 3.86, and 2.40 % in decreasing order of frequency. Frequency was least (1.05 %) among the cases reported to show metastatic deposits of squamous cell carcinoma in lymph nodes. However, in some studies the distribution pattern of squamous cell carcinoma at some particular sites was found.

Distribution Patterns of Oral Squamous Cell Carcinoma

According to Smith et al. [4], of all the oral squamous cell carcinomas, 40 % begin on floor of mouth or on lateral or ventral surface of tongue. About 38 % of all oral squamous cell carcinomas occur on lower lip, about 11 % in palate and tonsillar area. During a study of 14,253 cases of soft tissue squamous cell carcinoma of the oral cavity in the files of

Armed Forces Institute of Pathology, Krolls and Hoffman [5] found most common locations to be the lower lip (38 %) and tongue (21 %). A study by Lawoyin et al. [2] showed the distribution of oral squamous cell carcinoma as follows: palate (42.3 %), tongue (24.5 %), lip (16.7 %), gingiva (6.6 %), cheek (7.7 %), and floor of mouth (2.2 %). A large study by MacComb et al. [6] from the M.D. Anderson Hospital in Houston, Texas, revealed the location of tumors within the oral cavity as follows: lips (45 %), tongue (16 %), floor of mouth (12 %), buccal mucosa (10 %), lower gingiva (12 %), and upper gingiva and hard palate (5 %). In our study of oral squamous cell carcinoma cases, majority (38 %) involved the unspecified parts of mouth which included floor of mouth, cheek, buccal mucosa, retromolar trigone, and parts of jaw. This was consistent with the study by Smith et al. [4] in which the prominent site of oral squamous cell carcinoma was floor of mouth. The lips constituted a significant proportion (ranging from 16.7 to 45 %) in all the studies, but in our study their involvement was not much (3.1 %). According to our study,

Fig. 6 Squamous cell carcinoma, keratinizing, NOS (H&E 40×)

Fig. 7 Squamous cell carcinoma, with horn formation (H&E 10×)

Fig. 8 Squamous cell carcinoma, non-keratinizing, small cell types (H&E 40×)

total cases involving the tongue were 91 (17.9 %), out of which 2.9 % originated from the base of tongue while the rest involved other unspecified parts of tongue. Other studies also showed involvement of tongue in about 16–25 % cases. In this study, the frequency of involvement of palate and tonsils together was 10 %. This was in concordance with involvement of palate and tonsillar area (11 %) as given by Smith et al. [4]. Gum malignancy, including alveolus, gingival, and gingivobuccal sulcus, constituted 27 % cases in our study. The frequency was relatively less in other studies (<15 %).

Distribution Patterns of Squamous Cell Carcinoma of Larynx A retrospective analysis of 690 cases of carcinoma larynx presenting to Nehru Hospital, Postgraduate Institute of Medical Education and Research, Chandigarh, between 1988 and 1997, was conducted by Bakshi et al. [7]. The majority of tumors were squamous cell carcinoma of which maximum involved supraglottis (55.94 %), followed in decreasing order of frequency by glottis (17.3 %), transglottis (13.04 %), and subglottis (03.62 %). However, our study

Fig. 9 Squamous cell carcinoma, non-keratinizing, large cell types (H&E 40×)

Fig. 10 Squamous cell carcinoma, clear cell types (H&E 40×)

constituted a relatively small proportion of squamous cell carcinoma of larynx, just 20 out of 959 with cases involving the supraglottis constituting 15 %. The highest numbers of cases in our study were those involving the epiglottis (30 %), closely followed by unspecified parts of larynx (25 %). Subglottis was involved in 10 % cases in our study, with involvement of ventricular bands and arytenoids in the same proportion.

Distribution Patterns of Squamous Cell Carcinoma of Skin In a study on skin cancer incidences over a 15-year period (1987–2001) by Noorbala and Kafaie in Yazd (Iran) [8], the frequency distribution of squamous cell carcinoma in the facial area alone comprised 71.7 % of all cases. Overall, 92 % of all skin cancers occurred in the face, head, and neck regions. In our study also, the highest percentage (70 %) of cases were constituted by the head and neck, out of which 34 % were from facial area. Another retrospective population-based Swedish cohort study was carried out by Lindelof et al.

Fig. 11 Squamous cell carcinoma and adenocarcinoma, mixed (adenosquamous carcinoma) (H&E 40×)

[9] to establish the anatomical site distribution of cutaneous squamous cell carcinoma in organ transplant recipients with regard to age and sex. The head and the neck were the predominant sites in male patients, and the trunk was the predominant site in female patients. The most common site in younger patients was the chest, while in older patients, the face. The ear was a common site in male patients, but in contrast, no tumors were located there in female patients. In this study, overall incidence of squamous cell carcinoma was higher in males. Our study showed male predominance at the head and neck region as well trunk. Similarly, involvement of ear was in males only, while no such case was reported in females. During the study we encountered squamous cell carcinoma affecting the skin of lower limbs (13 %) more frequently as compared to upper limbs (4 %). The respective frequency of squamous cell carcinoma involving skin of axilla, trunk, and inguinal region was 7, 4, and 2 %.

ICD-O—Morphological and Topographical Categories During this study, we did not come across any other such study classifying squamous cell carcinoma into ICD-O categories according to the morphology and topography.

- (A) *Topographical distribution:* In our study, we encountered the maximum number of cases (26.07 %) of squamous cell carcinoma belonging to ICD-O category C-53 (i.e., cervix). The next was category C-06 (i.e., parts of mouth), unspecified with its frequency being 19.08 %. Squamous cell carcinoma of anal canal (C-21), pyriform sinus (C-12), bronchus and lung (C-34), and vulva (C-51) individually constituted less than 1 % cases, with least number of cases (0.1 %) being that of vulva.
- (B) *Morphological distribution:* Most frequently encountered category among the studied cases was that of squamous cell carcinoma, keratinizing (35.2 %). This was followed in decreasing order of frequency by squamous cell carcinoma, with horn formation (20.8 %) and squamous cell carcinoma, clear cells (13.5 %). The rest of the categories individually constituted less than 10 % cases. Out of 959, only 10 cases (1.0 %) could be categorized into squamous cell carcinoma, metastatic.

Summary and Conclusion

Thus, in this study we came across the topographical and morphological spectrum of squamous cell carcinoma

presenting at our institution. The maximum number of cases encountered involved the oral cavity, with predominant involvement of males, emphasizing the role of tobacco chewing (a prevalent practice in this particular geographical area) as an important predisposing factor. The maximum number of cases of squamous cell carcinoma of skin involved the sun-exposed areas (i.e., head and neck) including the face. This implicated the role of UV light exposure and tropical climate in the pathogenesis. The predominant ICD-O topographical category was that of squamous cell carcinoma of cervix. The majority of females affected were more than 45 years of age. Morphologically, the spectrum at our institution showed maximum cases belonging to ICD-O category, squamous cell carcinoma, keratinizing. This morphological type is usually considered to be well differentiated and has a good prognosis. As far as the behavioral pattern of the squamous cell carcinoma was concerned, most of cases in our study were invasive types. Only 10 cases out of 959 were in situ. This may demand better clinical vigilance of the premalignant lesions in early stages.

So, through this study, we were able to study the present spectrum of squamous cell carcinoma at our institution. With this study, the relevant data of squamous cell carcinoma for years 2007 and 2008, as per the requirements of Cancer Registry Programme and ICD-O, have been compiled and analyzed.

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