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Original Research Article

To Determine Clinical and Histopathological Correlation of Oral Ulcers in Common Oral Mucocutaneous Disorders

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ABSTRACT

Background: Oral ulcers are difficult to diagnose because of the anatomical and functional peculiarities of oral cavity. Oral ulcers are usually the result of local diseases, but they may be the early signs of systemic diseases which include mucocutaneous disorders and in some instances, may cause the main symptoms. For early and correct diagnosis of any oral mucocutaneous disorders, complete history, clinical examination & histopathological examination are required.

Aims: To determine clinical and histopathological correlation of oral ulcers in common oral mucocutaneous disorders.

Methods and Material: Total 125 patients who had oral ulcers were included in the study. Complete history, clinical examination and routine investigations were done. All the patients were informed about the mucosal biopsy and their consent was recorded. A punch biopsy was taken under local anaesthesia and sample was sent for histo-pathology.

Results: Out of these 125 cases, 68 were male & 57 were female with peak incidence observed in the age group of 31-50 years. There were 51 (42.73%) recurrent aphthous ulcer, 27 (21.6%) Pemphigus vulgaris, 12 (9.6%) Lichen planus, 10 (8%) drug reactions, 9 (7.2%) lupus erythematosus, 11 (8.8%) herpes viral infections and 5 (4%) traumatic ulcers. Buccal mucosa (64.8%), lip (54.4%) and tongue (44%) were the most common sites involved. 36% cases were associated with cutaneous lesions.

Conclusion: The diagnosis of oral ulcers may be difficult due to its diverse clinical presentation observed. Our study revealed the importance of establishing oral ulcer diagnosis in dermatology practice by its clinico-histopathological correlation in various oral mucocuataneous disorders.

Key Words: Oral ulcer, Punch biopsy, Histopathological examination.

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INTRODUCTION

Oral mucocutaneous disorders involve both skin and mucosa. These groups of disorders that are frequently observed in dermatology practice & frequently present as oral ulcer. Oral ulcer is a localized defect of the mucosal surface in which the covering epithelium is destroyed leaving an inflamed area of exposed connective tissue. The oral cavity is a site of various mucosal ulcers. Oral ulcers are usually the result of local diseases, but may be the early signs of systemic diseases which include dermatological disorders and in some instances may cause the main symptoms[1]. Clinical examination of oral mucosa is difficult because of the anatomical and functional peculiarities. The physical examination is completed by doing a histopathological examination in order to establish a final diagnosis[2]. The mucosa of oral cavity is very important from the dermatologist's point of view as it originates from the ectoderm[3]. Oral mucosa involvement may be a part of the systemic disease, a component of cutaneous disease or it may be limited to the oral cavity itself. A biopsy of the suspicious areas of the oral cavity often requires the cooperative effort of the dermatologist and the pathologists[4]. To confirm diagnosis of oral mucocutaneous disorders, correlation between clinical diagnosis & histo-pathological diagnosis is essential so that the final diagnosis can be established.

Only a few studies related to oral ulcers have been done. Therefore, we reported this randomized case control study of clinico-histopathological correlation of oral ulcer in various oral mucocutaneous disorders.

MATERIALS AND METHODS

Total 125 patients with oral lesions were selected from outpatient department of Skin, VD and Leprosy, Dr. S.N. Medical College and associated group of hospitals, Jodhpur, irrespective of age sex and duration of the disease, from 2011 to 2012 to study the clinico-histopathological correlation of oral ulcers in various oral mucocutaneous disorders. A detailed history, clinical examination

and relevant investigations were recorded. Diagnosis was made clinically & baseline workup including complete blood count, Tzanck smear, ESR and punch biopsy of mucosa were done after taking consent and sample sent for hispathological examination. The clinical diagnosis was correlated with the pathological findings and any dissociation between the two was recorded.

Table 1: Age and Sex distribution of study group

Age groups (in years)	Sex				Total	
	M	%	F	%	No	%
0-10	2	1.6%	3	2.4%	5	4.0%
11-20	14	11.2%	6	4.8%	20	16%
21-30	17	14.4%	12	9.6%	29	24%
31-40	12	9.6%	16	12.8%	28	22.4%
41-50	11	8.8%	10	8%	21	16.8%
51-60	7	5.6%	4	3.2%	11	8.8%
60-70	5	4.0%	6	4.8%	11	8.8%
Total	68	54.4%	57	45.6%	125	

Table 2: Number of Cases of Disease

Diseases	Male	Female	Total no. of cases	%
Erosive Lichen planus	5	7	12	9.6%
Pemphigus vulgaris	12	15	27	21.6%
Recurrent Aphthous ulcer	35	16	51	40.8%
Lupus erythematosus	3	6	9	7.2%
Herpes zoster	2	3	5	4%
Herpes simplex stomatitis	4	2	6	4.8%
Drug reaction	5	5	10	8%
Traumatic ulcer	2	3	5	4%
Total	68	57	125	

Table 3: correlation between oral ulcers and cutaneous lesions

Diseases	Oral lesions	Cutaneous lesions	% of Cutaneous lesions
Erosive Lichen planus	12	2	16.66%
Pemphigus vulgaris	27	22	81.48%
Recurrent Aphthous ulcer	51	0	0
Lupus erythematosus	9	9	100%
Herpes zoster	5	5	100%
Herpes simplex stomatitis	6	0	0
Drug reaction	10	7	70.00%
Traumatic ulcer	5	0	0
Total	125	45	36%

Table 4: Site of Oral Ulcer

Diseases ► / Site ▼	Erosive Lichen planus	Pemphigus vulgaris	Recurrent Aphthous ulcer	Lupus erythematosus	Herpes zoster	Herpes simplex stomatitis	Drug reactions	Traumatic ulcer	Total
Buccal mucosa	10	24	19	8	5	4	10	1	81
Tongue	6	12	23	1	0	4	7	1	55
Hard plate	1	5	2	8	3	5	4	0	28
Lip	4	17	26	7	1	1	7	3	68
Gingiva	2	6	2	0	1	2	0	0	13
Other site	0	1	5	0	2	2	2	0	12

RESULTS

In our study showed the male to female ratio was 1.19:1 and peak incidence was observed in the age group of 31-50 years (Table1). Duration of the oral ulcers ranged between 2 days to 4.5 years, with maximum number of cases 55 (44%) having less than 1 month's duration. Out of these 125 cases; 51(42.73%) were diagnosed clinically maximum as recurrent aphthous ulcer and minimum traumatic were 5(4%) (Table 2). In present study observed maximum oral lesions was recurrent aphthous ulcer and cutaneous lesions was pemphigus vulgaris (table 3).

In our study showed the multiple sites were involved in 82 (65.6%) of the patients and the buccal mucosa, lips were affected most commonly (Table 5) and morphology of oral ulcer were variable. There were 54 (43.2%) cases of erythematous ulcer, 40 (32%) cases of ulcerative type, 23 (18.4) cases of erosive type and 8 (6.4%) cases were grouped ulcer (table5). In histological mostly were polymorphonuclear infiltrate in connective tissue (70.4%) (Table 6). In 113(90.4%) cases, a clinico-histopathological correlation was present, as shown in (Table 7).

Table 5: Morphological pattern of Oral Ulcer

Diseases ► / Morphological pattern ▼	Erosive Lichen planus	Pemphigus vulgaris	Recurrent Aphthous ulcer	Lupus erythematosus	Herpes zoster	Herpes simplex stomatitis	Drug reaction	Traumatic ulcer	Total	%
Grouped ulcer	0	0	0	0	5	3	0	0	8	6.4%
Erythematous ulcer	0	0	51	0	0	3	0	0	54	43.2%
Ulcerative type	3	22	0	6	0	0	4	5	40	32%
Erosive	9	5	0	3	0	0	6	0	23	18.4%

Table 6: Histopathological findings

Epidermis	N=125	%
Hyperkeratosis	15	12%
Parakeratosis	14	11.2%
Acanthosis	17	13.6%
Hypergranulosis	8	6.4%
Acantholysis	25	20%
Cleft formation	25	20%
Spongiosis	53	42.4%
Elongation of rete ridges	5	4%
Ballooning degeneration	10	8%
Basal cell degeneration	26	20.8%
Follicular plugging	7	5.6%
Inclusion bodies	10	8%
Colloid bodies (necrotic keratinocytes)	20	17.6%
Basement membrane thickening	5	4%
Dermal	0	0
Subepidermal bullae	3	2.4%
Colloid bodies (necrotic keratinocytes)	6	4.8%
Pigmentary incontinence	7	5.6%
Oedema	10	8%
Collagen degeneration	5	4%
Lymphocytic infiltrations	82	65.6%
Polymorphonuclear	88	70.4%
Eosinophils	18	14.4%
Perivascular	15	12%
Plasma cells	29	23.2%
Granulation tissue	2	1.6%

Table 7: Clinical and Histopathological Correlation

Diseases	Clinical diagnosis	Confirmed on histopathology		Discordance	
Erosive Lichen planus	12	11	91.66%	1	8.34%
Pemphigus vulgaris	27	25	92.59%	2	7.41%
Recurrent Aphthous ulcer	51	43	84.31%	8	15.69%
Lupus erythematosus	9	9	100%	0	0%
Herpes zoster	5	5	100%	0	%
Herpes simplex stomatitis	6	5	83.33%	1	16.67%
Drug reaction	10	10	100%	0	0%
Traumatic ulcer	5	5	100%	0	0%
Total	125	113	90.4%	12	9.6%

DISCUSSION

The diagnosis of ulcers in the mouth can be extremely difficult because a variety of conditions can appear clinically as ulcerations. So the study of oral ulcers has importance in diagnosis of various oral mucocutaneous disorders. The correct diagnosis of oral ulcers is a challenging task for the dermatologist. It requires complete history, clinical examination, laboratory investigations and histopathological examination. Oral ulcers may be part of any mucocutaneous disorders, a manifestation of systemic disturbance or related to treatment.

The non-malignant, ulcerous diseases of the oral cavity often require repeated histological and clinical observations to establish a diagnosis[2]. It was observed that punch biopsy of the oral cavity was a safe and useful technique that could be easily employed by dermatologists[5]. The accurate diagnosis of chronic oral ulcers requires a peri-lesional biopsy[6]. The biopsy is required to establish the diagnosis and the histo-pathological examination must be coordinated with the clinical findings[7]. The histological examination confirms the diagnosis and it helps to formulate a prognosis and to allow the commencement of the treatment[8].

In present study, the male to female ratio was 1.19:1. The age varied from 05 years to 70 years and the mean age of male & female was 34 years & 36.95 years respectively. These data were comparable with the study of Vippan et al.[8] which showed male to female ratio was 1:1.5 and age varied from 13 years to 72 years and mean the mean age of male & female was 38.95 years & 41.03 years respectively. In another study frequent oral conditions in dermatology clinic showed male to female ratio of 1:4 and the median age of the patients 51 years (range 18-81 years).

In present study recurrent aphthous ulcers were more frequent than other oral ulcers studied and the age of patients with aphthous ulcers ranged between 9 to 70 years. Velia et al.[9] reported age range between 28- 72 years. RAUs involved most commonly the labial mucosa, the tongue and buccal mucosa. In our study histological finding in RAUs were spongiogis & inflammatory cells infiltrates in dermis. Similar finding were observed by Vippan et al.[8]

In the present study, oral pemphigus vulgaris was second most frequently observed oral condition as oral ulcers. It occurres most frequently in the fourth decade. It was interesting to note most of PV had only oral manifestations in 18.52% & involvement of skin and the oral mucosa 81.48%. In 10 cases oral lesions preceded the skin lesions. A majority of the cases had oral mucosal involvement in addition to skin lesions (66%). This observation was noticed in the study by Fernandez et al.[10]

As the oral cavity is always subjected to minimal trauma and the roof is very thin it ruptures and forms an extreme area of erosion or ulcer. In our case series, some cases presented as ulcers and some as erosions. Since the clinical features of oral pemphigus vulgaris are similar to benign mucous membrane pemphigoid and lichen planus, the diagnosis of pemphigus vulgaris should be confirmed with conventional histology and tzanck smear. Histologically, there is an intraepidermal blister associated with acantholytic cells.

Tzanck smear was done in all cases in the present study, 25 cases showed the presence of acantholytic cells, while others showed degenerative changes and mixed inflammatory cells which were composed of eosinophils and lymphocytes. Fernandez et al.[10] observed suprabasal bulla with neutrophils, eosinophils and acantholytic cells which were similar to our findings in most of the cases. In our study 10 cases of drug reactions were reported.5 cases were Stevenson Johnson syndrome (SJS), 2 were Erythema multiforme (EM) 1 was Toxic epidermal necrolysis (TEN) and 2 were adverse drug reactions. Out of 5 patients of SJS 3 patient gave history of analgesic and 2 of anticonvulsants.

In present study, 11 patients of herpetic muco-cutaneous infection were included. Out of 11 patients, 5 cases were of herpes zoster & 6 cases were of herpes simplex stomatitis. The median age of patients with herpetic ulcers was 40.6 years (range 19-70 years). Velia et al.[9] observed 4 cases (6.7%) and median age of patients with herpetic ulcers was 27 years (range 18-59 years).

Total 125 cases with oral ulcers were examined and clinical diagnosis was made. Then oral biopsy was taken and sent for histo-pathological examination. Out of 125 cases only 113 (90.4%) cases were confirmed by histo-pathological examination. Rest of 12 cases showed other diagnosis, these were 1 case of oral lichen planus, 2 cases of pemphigus vulgaris, 8 cases of recurrent aphthous ulcers and 1 case of herpes simplex stomatitis. Biopsy reports of clinically diagnosed 2 cases of pemphigus vulgaris, 1 case of oral lichen planus and 2 cases of recurrent aphthous ulcers showed histological features suggestive of ulcerative stomatitis. Other 7 cases were herpes simplex stomatitis (1 case) and recurrent aphthous ulcers (6 cases). These cases biopsy reports did not reveal any suggestive histopathological finding due to inadequate sample size or due to inappropriate processing of the sample.

This discordance in clinical diagnosis & histo-pathological diagnosis suggest that we cannot rely on clinical examination or histopathological examination alone to confirm our diagnosis. To

approach a correct diagnosis of oral ulcers both are required. This discordance may be due to the fact that oral mucosal biosy is challenging and a difficult task. Biopsy specimens of predominantly erythematous and ulcerated mucosal lesions should be taken a few millimeters away from the ulcers, so that the specimen's epithelium and connective tissue remain intact[11]. It has been suggested that punch biopsies provide greater inter-observer reliability than wedge biopsies in the histopathological diagnosis[12].

The discordance between clinical diagnosis & histo-pathological diagnosis may be due to wrong clinical diagnosis, inadequate biopsy sample, error in sample processing or due to wrong histopathological interpretation by pathologist.

In 110 cases of oral lesions study by Vippal et al.[8] observed 92.73% cases showed concordant clinical & histopathological diagnosis. In the clinico-pathological discordance for lesions of the oral mucosa, it was observed that the statistical analysis demonstrated 17 cases of agreement (81%) and 4 cases of discordance (19%) between the clinical diagnosis and the pathological diagnosis[13]. In the 51 cases of subepidermal bullous disease which were correlated clinicopathologically, it was observed that there was a good clinicopathologic correlation, with 46 out of 51 cases showing concordant clinical and histological diagnoses[14]. In 213 cases of oral lichen planus which were correlated clinico-pathologically, in spite of considerable variabilities in both the aspects; it was observed that there was a clinical and histopathological agreement in 96% cases[15].

CONCLUSION

In conclusion, our study suggests us to confirm the diagnosis of any mucocutaneous condition by both clinical as well as histopathological examination of oral ulcers, as diagnosis of oral ulcers may be difficult due to its diverse clinical presentation observed. Our study revealed the importance of establishing an oral ulcer diagnosis in dermatology practice by its clinico-histopathological correlation in various oral mucocuataneous disorders.

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