The underlying etiology is not known, autoantibodies, mainly IgG class, deposited intercellularly antibodies, Pemphigus vulgaris as well as damage to desmosomes by antibodies directed against the desmosomal cadherins, desmoglein 1 and 3. Biopsy of perilesional tissue, with histological and immunostaining examinations, is essential to the diagnosis. C-erb B2 is an oncogene that encodes for transmembrane glycoprotein receptor involved in cell growth and differentiation. It has been shown over expressed in aggressive breast cancer, salivary gland adenocarcinoma and oral carcinoma. The present investigation aimed firstly at studying and comparing the expression of c-erb B2 oncogen in pemphigus and atypical pemphigus vulgaris cases, and secondly at adding to the literature 2 reports of cases of atypical pemphigus vulgaris.

Methods: Five cases of PV were examined clinically and histopathologically, among which 2 cases interestingly revealed histopathologically moderate epithelial dysplasia. This study is done using the labeled Strepavidin Biotin (LSAB + Dako) immunohistochemical method utilizing monoclonal antibodies for anti-Cerb-B2 proto-oncogene (HER-2 or neu).

Results: In the present study c-erb B2 interestingly was markedly observed as intense staining of the cytoplasmic membranes, the basal cell layer and parabasal cell layers in atypical pemphigus vulgaris. In comparison to the usual PV which showed mild expression or no changes.

Conclusion: According to the present findings c-erb B2 might constitute useful prognostic marker for the evaluation of potentially malignant transformation. The reasons for malignant transforming cells could be due to chronicity and smoking since all the examined five cases were males (chronic autoimmune diseases are associated with the development of localized neoplastic transformation).
accumulation and vesiculobullous lesions (8). Biopsy, with histological and immunostaining examination, is essential to diagnosis. Oral lesions of pemphigus vulgaris may respond to topical or systemic corticosteroids or other immunosuppressants.

C-erb B2 belongs to the human epidermal growth factor receptor family that plays an important role in the regulation of fundamental processes such as cell growth, survival and differentiation. C-erb B2, or human epidermal growth factor receptor-2 (HER2) gene, is a proto-oncogene mapped to chromosome 17q21 and encodes a 185-kD transmembrane glycoprotein, designated as p185HER2, which is often simply called the HER2 protein or receptor. C-erb B2 is known to be overexpressed, amplified or both in several human malignancies, including breast cancer, salivary glands and oral squamous cell carcinoma (9, 10).

C-erb B2 overexpression can be detected by immunohistochemical staining of formalin-fixed-paraffin-embedded sections of tumor tissue. Membrane staining of the cells is the only reaction considered positive (11). It was reported that there is a correlation between c-erb B2 gene amplification and bad prognosis in breast and bladder carcinoma (12).

Amplification of c-erb B2 can be determined by a copy number or by immunochemical staining of the gene product (13).

Materials and methods

Five biopsies specimens of PV were taken from the Department of oral pathology at Benghazi University (Libya). All specimens were fixed in 10% neutralized formaldehyde solution and embedded in paraffin wax. Serial sections 3 mm thick were prepared for histological and immunohistochemical studies. One section from each specimen was stained with hematoxylin and eosin for histological evaluation; other sections were processed for subsequent immunohistochemical study of c-erb B2.

Immunohistochemical analysis

Tissue sections were deparaffinized and immersed in methanol with 3% hydrogen peroxide to eliminate endogenous peroxidase activity.

Sections were boiled for antigen retrieval by microwave heating in 0.01 M citrate buffer (pH 6.0) for 9 minutes (120 C°, 2 atm). After treatment with normal rabbit serum for 20 minutes to block non-specific binding, the sections were incubated with primary monoclonal c-erb B2 antibody.

The standard streptavidin–biotin-peroxidase complex method was performed to bind the primary antibodies with the use of Histofine SAB-PO kits (Nichirei, Tokyo, Japan).

Briefly, biotin-labeled antiimmunoglobulin-antibodies and peroxidase-conjugated streptavidin were reacted, and then the reaction product was visualized by immersing the sections for 3-5 minutes in 0.03% 3,3 diaminobezidine (DAB) solution containing 2 Mm hydrogen peroxide.

Results

Histopathological findings

All the included cases revealed suprabasilar clefting, forming intra-epithelial vesicle or bullae. Connective tissue showed dense chronic inflammatory cells infiltration.

Out of five cases, two showed mild to moderate epithelial dysplasia.

The cells of basal and parabasal layers demonstrated hyperkeratosis, pleomorfism and prominent nuclei (Figure 1, 2). Loss of epithelial adhesion (acantholysis), increasing of mitotic figures also noticed and proliferation of basal and...
equally (1), while other studies have reported females predominated over males (14). All of our cases were males and no female. This discordance may be due to different and ethnic nature of the patients studied.

Oral lesions usually begins as vesicles, bullae or shallow ill defined irregular ulcers. The buccal mucosa is most commonly affected (14). Floor of the mouth and soft palate are also involved. Gingival lesions are less common and usually comprise severe desquamative or erosive gingivitis; they may appear with other mucosal lesions or as an isolated blister or erosion mainly on the free and attached gingiva (14).

C-erb B2 is an oncogen that encodes for transmembrane glycoprotein receptor involved in cell growth and differentiation. It has been shown to over express in aggressive breast cancer, rhabdomyosarcoma, salivary gland adenocarcinoma, oral carcinoma and oral lichen planus (15, 16, 17).

The perception that the excessive expression of c-erb B2 antigen exists in malignantly transformed cells revealed the necessity to identify this antigen as a status indicator of malignantly changed lesions. Strong expression of c-erb B2 oncogene was observed in many neoplasms where its expression was positively correlated with their invasiveness and ability to metastasize in other tissues (18). In the present study c-erb B2 expression was assessed with five cases of PV. Interestingly, c-erb B2 showed markedly staining of cytoplasmic membrane and layer of basal cells in atypical pemphigus vulgaris, compared to normal pemphigus vulgaris which showed mild or no changes.

Discussion

Pemphix in greek means bubbles or blisters and vulgaris in latin means common. Though pemphigus is a rare disease, PV is the commonest of all, comprising of the disease entity.

It is defined as an autoimmune disorder that manifests with damage to the desmosomes of epithelial cells induced by the activity of antibodies against transmembrane desmosomal glycoproteins belonging to the cadherin supergene family of desmogleins (Dsg), resulting in intraepithelial immuno-deposits and breaking of intercellular bridges (3).

It always affects the mouth and it can be the initial site of presentation in most of cases before skin and other mucosal sites. The most common sites of oral involvement include the buccal mucosa, soft palate, labial mucosa, and gingiva, although any oral site may be affected (4). In the present study most of our patients developed PV during their fifth to sixth decade of life, these results are consistent with previous reports (1). PV affects men and women equally (1), while other studies have reported females predominated over males (14). All of our cases were males and no female. This discordance may be due to different and ethnic nature of the patients studied.

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The findings of this study are in agreement with previous studies, where pre-malignant and malignant oral lesions showed progressive increase of c-erb B2 expression as the cells acquired amore malignant phenotype (19). Thus, the expression of c-erb B2 in the studied cases was considered to be a useful
Finding indicating immunohistochemical expression of the cerb-B2-

Conclusion

The reason for dysplastic changes of our two cases of atypical PV, may be due to local environmental factors such as smoking, with candida infection, chronicity or drug intake such as corticosteroids (chronic autoimmune diseases are with the development localized neoplastic transformation).

According to the present findings, c-erb B2 might constitute a useful prognostic marker for the evaluation of potentially malignant proliferation. This investigation has been done for the first time, to the best of our knowledge to add to the literature.

Conflict of interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

Table 1 Clinical characteristics features of each patient

<table>
<thead>
<tr>
<th>Case</th>
<th>age</th>
<th>sex</th>
<th>Duration</th>
<th>medications</th>
<th>Systemic disease</th>
<th>Skin manifestation</th>
<th>location</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>63</td>
<td>male</td>
<td>6 months</td>
<td>Local corticosteroids</td>
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<td>B.m.,floor of mouth</td>
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<tr>
<td>2</td>
<td>58</td>
<td>male</td>
<td>3 months</td>
<td>Oral Hypoglycemic</td>
<td>D:M</td>
<td>no</td>
<td>B.m,soft palat</td>
</tr>
<tr>
<td>3</td>
<td>60</td>
<td>male</td>
<td>7 months</td>
<td>Oral Hypoglycemic</td>
<td>D:M</td>
<td>no</td>
<td>B.m.,L.m.&amp; gingiva</td>
</tr>
<tr>
<td>4</td>
<td>57</td>
<td>male</td>
<td>2 months</td>
<td>no</td>
<td>yes</td>
<td>B.m.</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>62</td>
<td>male</td>
<td>5 months</td>
<td>Systemic corticosteroids</td>
<td>yes</td>
<td>Lm.&amp;floor of mouth</td>
<td></td>
</tr>
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B.m (Buccal mucosa), L.m. (Labial mucosa)

References


