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The Role of CD10 Expression in Basal Cell Carcinoma and its mimics: A Clinicopathological Study

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Abstract. **General Background:** Basal cell carcinoma (BCC) represents the most prevalent form of nonmelanoma skin cancer, predominantly affecting sun-exposed areas with increasing incidence among middle-aged and elderly populations. **Specific Background:** Accurate histopathological differentiation between BCC and its morphological mimics, particularly trichoepithelioma, remains clinically challenging due to overlapping features, potentially leading to inappropriate therapeutic decisions. CD10, a cell surface marker expressed in various neoplasms and normal skin structures, has emerged as a potential diagnostic tool for distinguishing BCC from histologically similar lesions. **Knowledge Gap:** The diagnostic utility and expression patterns of CD10 in differentiating BCC from its mimics within Middle Eastern populations remain inadequately characterized. **Aims:** This study investigated CD10 expression patterns in 50 BCC cases and one trichoepithelioma case, correlating findings with clinicopathological parameters including age, gender, anatomical distribution, and histological variants. **Results:** Analysis revealed 80% CD10 positivity in tumor cells (32% strongly positive, 48% positive), while 42% showed stromal positivity; nodular BCC comprised 70% of cases, with 84% located in head and neck regions, affecting predominantly middle-aged females. **Novelty:** This investigation provides novel evidence that CD10 positivity in tumor cells distinguishes BCC from trichoepithelioma, which demonstrates exclusive stromal positivity. **Implications:** These findings establish CD10 immunohistochemistry as a valuable adjunct marker for resolving diagnostically challenging basaloid proliferations in routine pathological practice..

Keywords: CD10 Immunohistochemistry, Basal Cell Carcinoma Diagnosis, Trichoepithelioma Differentiation, Nonmelanoma Skin Cancer, Histopathological Markers

Highlights:

1. Middle-aged adults showed highest lesion frequency, predominantly affecting sun-exposed head and neck regions.
2. Nodular histological pattern represented the most prevalent morphological presentation among examined biopsies.
3. Immunostaining positivity within neoplastic components supported differential diagnosis, while stromal reactivity characterized trichoepithelioma.

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Introduction

Basal cell carcinoma (BCC) is the most frequent skin cancer and is the major histological type of nonmelanoma skin cancer [1]. It was first described in 1824 by Jacob . It is constantly increasing incidence due to an aging population and widespread in sun exposed areas of the body, mostly on the head and neck (80%), trunk (15%), rarely on arms and legs . Also, very rarely, BCC affects the skin on axillary and perineal region, the hands and soles and genital region . BCC, although it is the most common skin cancer, accounts for less than 0.1% of patient deaths due to cancer and the cure rates for BCC exceed 90% with most treatment modalities [2].

BCC is a slow-growing and locally invasive skin tumor which rarely metastasizes, arising from nonkeratinizing cells that originate from the progenitor cells of the basal layer of the epidermis . Basal cell carcinoma is consisting of plugs and clusters of basal cells, with various clinical manifestations in accordance with the presence of various morphological features, which to a certain extent correspond with the histological . Although the mortality from this cancer is negligible, BCC can be associated with significant morbidity, especially if the tumor is untreated for a long period of time .

The pathogenesis is linked to the interplay between environmental and patient-derived characteristics . There are multiple therapeutic modalities, and appropriate selection requires knowledge of complications, cosmetic outcomes, and recurrence rates . Most BCC can be treated effectively and safely with standard surgery, or in selected cases with topical treatment.

BCC incidence was generally higher in men than in women probably due to increased recreational and occupational exposure to the sun, however, these differences are becoming less significant with changes in lifestyle, such as tanning bed use or smoking[3]. Gender substantially modifies the age-specific BCC risk [2]. BCC affects preferentially elderly males (>60 years old) and younger female (<40 years old) with (M:F = 1.5:1), and with the exception of genetic syndromes (i.e., basal cell nevus syndrome, xeroderma pigmentosum), it is rarely observed in patients younger than 40 years of age . So the number of cases is increasing every year worldwide, especially among young age group, with a predilection for women .

CD 10 was originally found to be expressed on the cell surface of most cases of acute lymphoblastic leukemia, and was soon found in many other types of neoplasms [4]. CD10 expression has been shown in tumors of follicular differentiation, including trichoepithelioma, pilomatrixoma, basaloid follicular, hamartoma and BCC [5]. CD10 has been reported in both epithelial (bladder, hepatocellular, renal cell) carcinomas and mesynchymal neoplasms (endometrial stromal sarcoma of the uterus) [6] .

In normal skin, CD10 immunostainting is present in sebaceous glands, periadnexal dermis, and inner root sheath cells of vellus hair follicles and occasional endothelial cells [7]. It has been claimed that CD10 can be useful as a specific marker to distinguish BCC from its mimics because the distinction between BCC and its mimics may be very difficult in some cases because of the close similarities of these lesions clinically and histopathologically, and therefore misdiagnosis can lead to either unnecessary excision or delayed treatment of metastatic disease and an accurate diagnosis of these lesions is essential for effective, timely treatment and appropriate therapeutic decisions [8]–[9].

- To determine the frequency of CD 10 expression in basal cell carcinoma and its mimics.

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- To assess the correlation of basal cell carcinoma occurrence and its variants with age, sex and different sites of the body.

Materials and Methods

Study Design and Setting: A retrospective and prospective case series study done at period from (October 2021- October 2022), which included a total of 51 formalin –fixed paraffin embedded block of skin biopsies who clinically presented with symptoms suspicious for BCC or one of its mimics, the cases were received from Al-Jamhori Teaching hospital and private laboratories in Mosul city /Iraq through one year. The study was undertaken in the department of pathology, college of medicine/ University of Mosul, a clinico- pathological data including (age, gender, site) were obtained from patients' files.

Processing and collection of specimen: The skin biopsies (either punch biopsy or complete excision biopsy) were embedded, blocks were sectioned using microtome for H&E and CD 10 immunohistochemical staining, the slides were examined for the presence of neoplastic cells (basaloid cells). CD 10 immunoreactivity and pattern of staining for neoplastic and stromal cells were evaluated in IHC stained slides.

Hematoxylin & Eosin staining procedure and interpretation: Following standard fixation in formalin and embedding in paraffin wax, tissue samples were sectioned at a thickness of 3 microns onto slides. These slides then underwent a meticulous staining procedure to prepare them for microscopic examination. First, the paraffin was removed and the tissue was rehydrated through a series of xylene and ethanol baths. The core staining process involved immersing the slides in hematoxylin to color cell nuclei, followed by differentiation and "bluing" steps to enhance contrast, and then in eosin to stain cytoplasmic components. Finally, the slides were dehydrated, cleared in xylene, and permanently mounted with cover slips. A specialized pathologist then carefully assessed all prepared slides under a light microscope. A positive diagnosis for basal cell carcinoma (BCC) or one of its histological mimics was made based on the identification of characteristic features, including nests of basaloid cells with peripheral palisading set within a fibromyxoid stroma.

CD 10 immunostain procedure and interpretation: For immunohistochemical analysis, tissue sections four microns thick were prepared from the formalin-fixed, paraffin-embedded blocks and mounted on charged slides. Following baking and a thorough deparaffinization and rehydration series, the slides underwent antigen retrieval using a heated Tris-EDTA buffer. The staining procedure utilized a labelled polymer system (PathnSitu) for CD10 antibody. This involved sequentially applying a peroxidase block, the primary CD10 antibody, a target binder, and a polyHRP enzyme, with buffer washes between each step. The bound complex was then visualized by applying a DAB chromogen, which produces a brown precipitate. Finally, the slides were counterstained with hematoxylin, dehydrated, cleared, and permanently mounted. All corresponding sections were evaluated for CD10 immunoreactivity, with positive staining—identified as brown cytoplasmic or membrane coloration—quantified in tumor cells and peritumoral stromal cells. Expression levels were categorized based on the percentage of positive cells and were interpreted in comparison to established internal and external controls.

Data processing and Statistical analysis: The data were collected, tabulated, and statistically analyzed, using Statistical Package for Society Study (SPSS) statistical software version 26.0. Qualitative data were presented using the frequency and related percentage, by using of Chi-square and Fisher exact test for comparison of qualitative variables between groups. A "P" value of ≤ 0.05 was considered statistically significant

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with confidence interval of 95%.

Result

Clinicopathological data of BCC cases: The patient' age ranged from 41 years to 87 years, the mean ± SD 63 ± 5.3 years. Of the 50 of BCC cases, 8 (16%) were between (41-50) years of age, 16 (32%) patients between (51-60) years of age and 15 (30%) patients between(61-70) years of age, 7 (14%) from (71-80) year and 4 (8%) between (81-90) years of age, P value <0.05 which is statically significant [10], [11]. Descriptive analysis for gender demonstrated 22 (44%) male and 28(56%) female, Male to Female ratio was 1:1.27 P value >0.05 i.e. not statically significant. So there is no association between gender type and BCC incidence [12]. Most of the collected BCC biopsies were located in the nose (20 biopsies) (40%), 10 biopsies in the eyelid (20%), 6 biopsies in the cheek (12%), 5 biopsies in the forehead (10%), 1 biopsy in the lip (2%), and 8 biopsies in other sites (neck, axilla, ear) (16%). 88% of the biopsies located in head and neck, while 12% of them located in other sites of the body. The P value is < 0.05 which is statically significant (Figure 1).

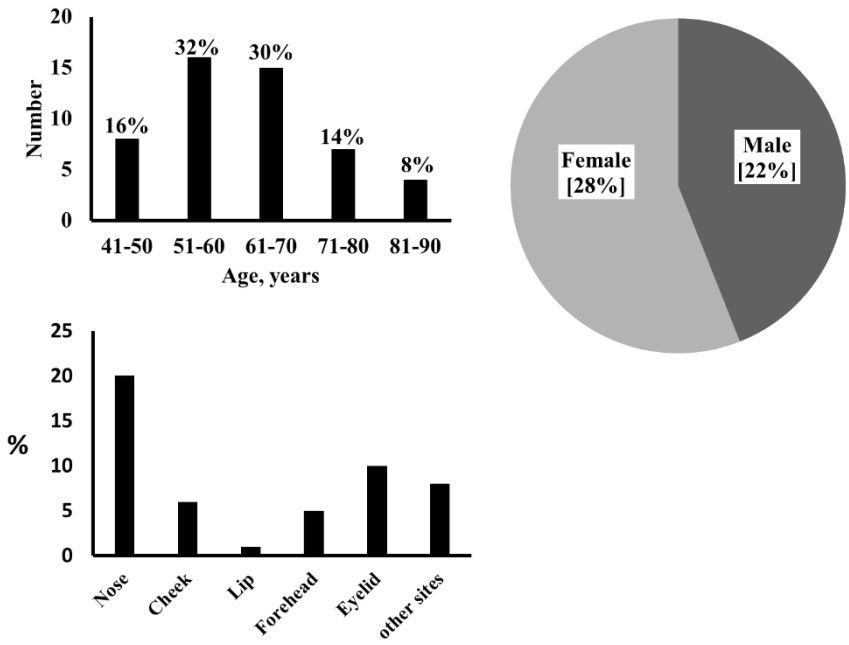

Figure 1. Distribution of BCC according to the (A) age, (B) Gender, (C) site.

Most of the collected biopsies were of Nodular variant of BCC with 35 cases out of 50 and 5 of them were pigmented (70%), 8 biopsies were of adenoid variant (16%), 3 of the biopsies were Infiltrative variant (6%), 3 biopsies were of morpheaform (6%) and 1 biopsy was of superficial variant of BCC (1%), The P value >0.05 (Table 3.1).

Table 1. Distribution of BCC cases according to its variants. P-value >0.05

Type of BCC variant	Number	Percentage
Nodular	30	60%
Pigmented Nodular	5	10%
Adenoid	8	16%

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Infiltrative	3	6%
Morpheaform	3	6%
Superficial	1	2%
Total	**50**	**100%**

CD 10 Immunostain of BCC cases: The result of CD10 staining in the current study of 50 cases of BCC was variable, the staining was positive only in tumor cells 26 (52%) cases (P-value <0.05) which is statically significant, and only positive in stromal cells in 7 (14%) cases (P-value >0.05) which is statically not significant, and positive in both tumor and stromal cells in 14 (28%) cases (P-value <0.05) which considered statically significant, and negative in both tumor and stromal cells in 3 (6%) cases (P-value >0.05) i.e. statically not significant. Generally speaking, regarding tumor cells positivity: 16 (32%) cases were +2, 24 (48%) cases were +1 and 10 (20%) cases were negative, while regarding stromal cells staining: 7 (14%) cases was +1, 14 (28%) cases was +2 and 29 (58%) cases was negative (Figure 2, Figure 3, Figure 4, and Table 1). Regarding the single Trichoepithelioma case, the patient was female, 62 years old, the lesion located at the nose [13]. The CD 10 immunostain was +1 in the stromal cells and negative in the tumor cells (Figure 5).

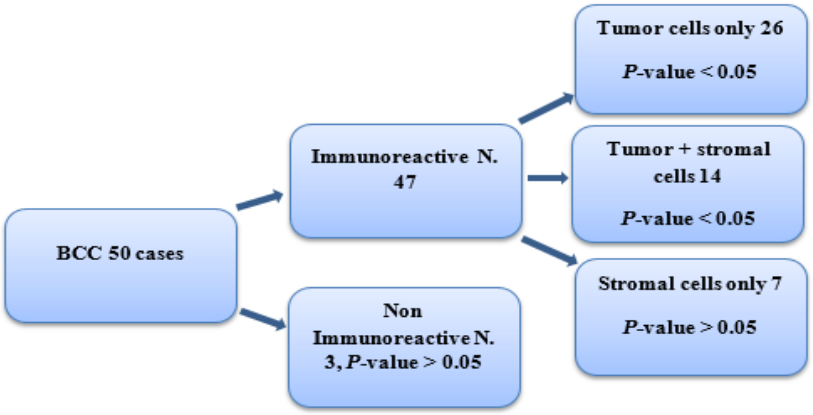

Figure 2. CD10 staining patterns of 50 cases of Basal Cell Carcinoma (BCC).

Table 1. CD 10 Expression pattern of BCC cases in both tumor and stromal cells

Components		Expression grade			Total
		+2	+1	0	
Tumor cells	Tumor cells only	10(20%)	16(32%)	10(20%)	50(100%)

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	Tumor+Stromal cells	6(12%)	8(16%)		
Stromal cells	Stromal cells only	3(6%)	4(8%)	29(58%)	50(100%)
	Tumor+Stromal cells	4(8%)	10(20%)		

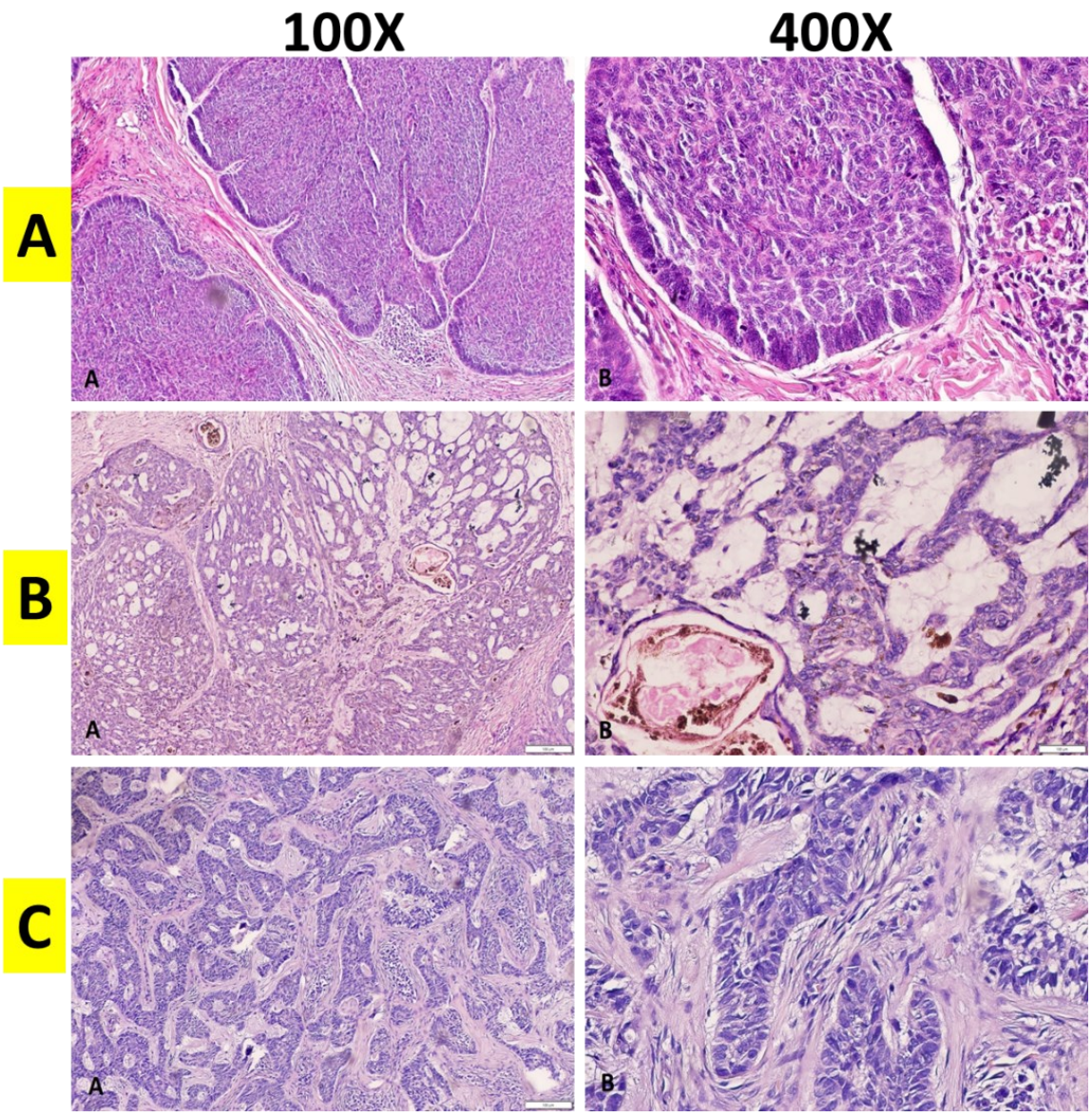

Figure 3. H&E stained section of [A] Nodular variant of BCC, [B] Pigmented Adenoid variant of BCC, [C] Morpheaform variant of BCC

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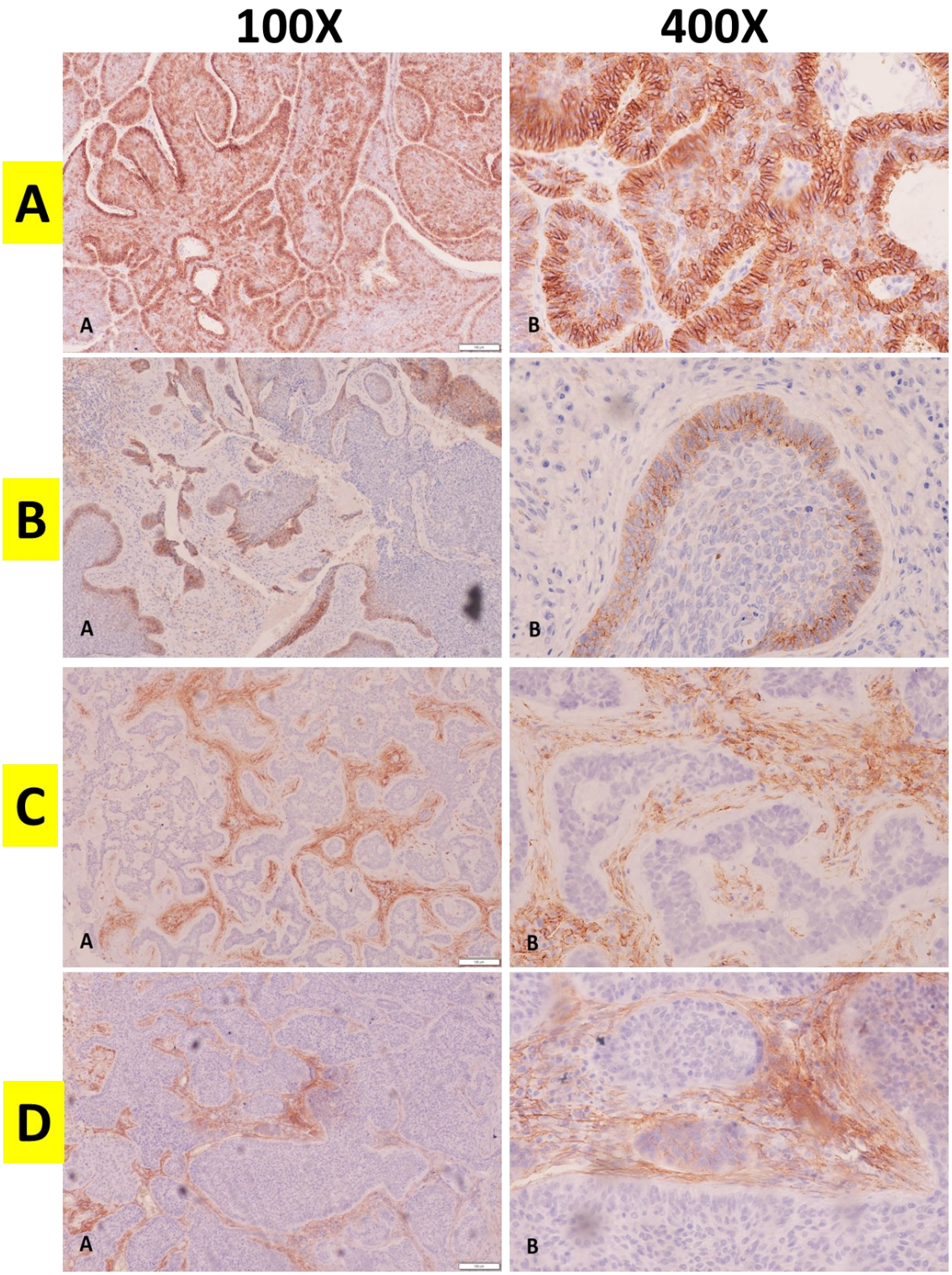

Figure 4. CD10 stain of tumor cells of [A] Nodular BCC(++), [B] Nodular BCC (+), [C] stroma of Morpheaform BCC (++), [D] both tumor cells (+) and stroma (++) of Nodular BCC.

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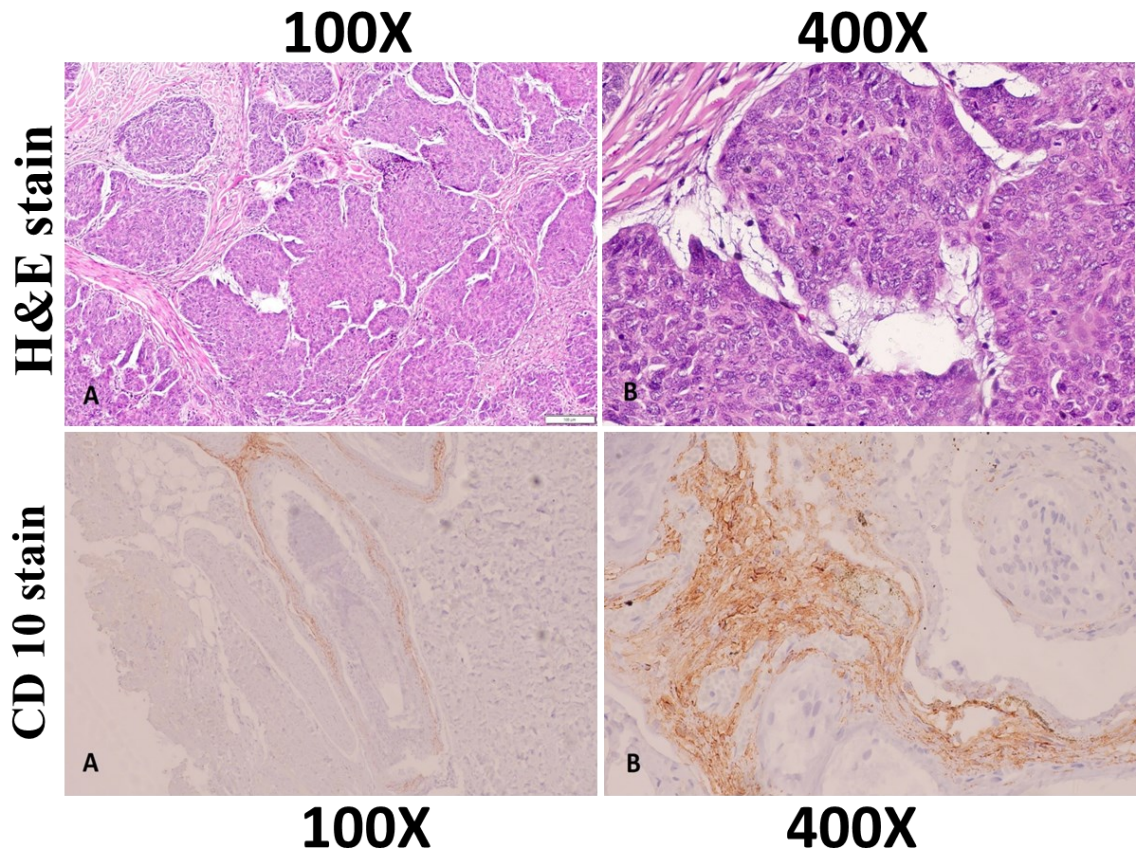

Figure 5. Trichoepithelioma by H&E stain and CD 10 stain of the stroma of trichoepithelioma.

Discussion

Basal cell carcinoma is the most common skin cancer that mainly affect old age group [14]. According to the current study ,which was done on 50 cases of BCC, the Patients' age was ranged from 41 years to 85 years with a mean ± SD 63 ± 5.3 years, the P-value ≤ 0.05 which is statically significant. This result is nearly in agreement with several studies as Heidarpour M. et al at Iran in 2011 [15], Mohammad S et al in 2016 at Iraq , Al-Qarqaz F. et al in 2018 at Jordan [16] and Mohammed HL. et al at Iraq in 2019 , while in a study done by Wu S. et al in 2013 at USA the mean age was 66 years and was 75 year in a study done by Devine C. et al in 2017 at United Kingdom [17]. So, the mean age of BCC patient is lower in the middle east in general, this may be due to the higher level of UV light at this area including our locality, and BCC will develop in younger age.

Regarding the gender, in this study Male:Female ratio of BCC cases is 1:1.27, i.e. there is female predominance in the incidence of BCC in our locality this is in agreement with a study done by Hussein M.R et al in 2022 at Egypt in which the ratio of M:F was 1:1.36, while in other studies the ratio is reversed, i.e. there is male predominance in BCC cases such as a study done by Boon F. et al in 2010 at Malaysia in which M:F ratio was 1.04:1 [18] and the ratio was 1.75:1 in a study done by Aslani FS. in 2013 at Iran , and in a study done by Astarci HM. et al in 2015 at Turkey the M:F ratio was 2.54:1 , while the ratio was 1.76:1 in a study done by Al-Qarqaz F. et al in 2019 in Jordan [19]. The

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explanation of this difference in M:F ratio in the current study may be due to higher concern of cosmetic aspects in females than males so the female will seek a medical advice whenever she see abnormal lesion while usually the male neglect it [20].

In our study 88% of the cases located in head and neck and 12% of the cases located in other sites of the body, P-value<0.05 which is statically significant. In comparing with other studies: in a study done by Boon F. et al in 2010 at Malaysia: 82.8% of the cases located in sun-exposed area, in another study which was done by Aslani FS in 2013 at Iran the percent was 96% [21], while in a research done by Devine C. et al in 2017 at United Kingdom the percent was 91%, and the percent was 80% and 94.73% in a study done by Al-qarqaz F. et al in 2018 at Jordan and in a study done by Mohammed HL. et al at Iraq in 2019, respectively [22]. The reason behind this high percent of the cases in head and neck is that this area receives the highest concentration of sun light which contain the carcinogenic effect of its UV light [23].

The majority of the BCC was of Nodular variant (70%), 16% of cases was of adenoid variant, 6% for each of the infiltrative and morpheaform variant and 2% was of superficial variant. In comparing other studies regarding the BCC variants: in a study done by Heidarpour M. et al. at Iran in 2011 which included 30 cases of BCC: 13 solid type, 5 morphea type, 6 adenoid type and 6 pigmented type [24], while in another study done in Iraq by Mohammad S et al in 2016 the results was as following: pigmentonodular BCC 53.2%, pigmented BCC 27.42%, superficial BCC 6.45%, ulcerative BCC 4.83%, asosquamous carcinoma 3.22%, ulcerative BCC 3.22 and morpheaform BCC 1.6% . Another study done by Mohammed HL. et al at Iraq in 2019 the percentage of the variant was as following: 84.21% were mixed, 7.89% were nodular, 3.95% were pigmented and 3.95% were superficial [25].

The staining was positive only in tumor cells in 52% cases (P-value <0.05), and only positive in stromal cells in 14% cases (P-value >0.05), positive in both tumor and stromal cells in 28% cases (P-value <0.05), and negative in both tumor and stromal cells in 6% cases (P-value >0.05). So, The positivity of CD 10 in BCC biopsy in tumor cells only or in both tumor and stromal cells will support the diagnosis of BCC in doubtful cases.

Comparing our results with others: in a study done by Aslani FS in 2013 at Iran in which 55 cases of BCC included in the study and their staining by CD10 the results was as following: the staining was positive only in tumor cells in 21 cases and only positive in stromal cells in 12 cases and positive in both tumor and stromal cells in 21 cases and negative in both tumor and stromal cells in 1 case. In total, tumor cells is positive (+2)in 34.5% of cases, 41.8% of cases were +1 and only 23.6% of cases were negative, and about the stroma stain: 18.2% were +2, 41.8% were +1 and negative in 40% of cases [26].

Other study done by Astarci HM. et al in 2015 at Turkey which involved 51 cases of BCC stained by CD10: 59% of cases were positive in the tumor cells peripherally and 25.6% of cases with tumor cells positive centrally, 28.2% were positive in stromal cells and 17.9% of the cases were negative for CD10 immunostain [8].

Another study done by Ilyas M. et al in 2020 at Pakistan a total 38 cases of BCC were included in the study, 24% of cases were strongly tumor cells positive (+2) whereas 52.6% were positive (+1) and 23.7 % were negative (-) for CD 10 [27].

The result of the single case of Trichoepithelioma which included in this study is positive (+1) stromal cells stainig by CD 10 and negative in the tumor cells. Regarding other studies which used CD10 to stain Trichoepithelioma cases: in a study done by Heidarpour

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M. et al. at Iran in 2011 83.3% of trichoepithelioma cases was positive CD10 staining of the stroma and negative in the tumor cells [28], in another study done by Aslani FS in 2013 at Iran 100% of trichoepithelioma cases was positive stromal cells staining by CD10 and negative in tumor cells [29], while in a study done by Astarci HM. et al in 2015 at Turkey 60% of the cases was positive stromal staining by CD10, 46.6% with positive tumor cells stain (26.7% peripherally and 20% centrally) and 20% with negative stain . The above results, including the result of the current study, reflect the importance of positivity of stromal cells with CD 10 immunostain in supporting the diagnosis of Trichoepithelioma [30].

Conclusion

The higher rate of BCC frequency is in the range of 51-70 years old patient, i.e. the middle aged group. There is female predominance in BCC incidence. The sun-exposed areas (i.e. head and neck) have higher risk for developing BCC. The nodular variant of BCC is the most common one while the superficial variant is rare. CD 10 positivity in tumor cells only of BCC biopsies or in both in tumor and stromal cells will support the diagnosis of BCC, while stromal cells will be positive in trichoepithelioma. Further studies with larger number of patients may be needed to prove the potent evidence of CD10 immunostain in the diagnosis of BCC and its mimics. Other immunostains may be needed beside CD10 stain to be sure about the diagnosis of BCC and differentiate it from its mimics.

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