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#### Mid-face location of primary basal cell carcinoma related to cancer aggressivity

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#### ABSTRACT

**Objective:** To study the aggressiveness of basal cell carcinoma (BCC) on the mid-face location. **Methods:** A total of 30 patients were diagnosed using specimen biopsy with hematoxylineosin stain at Moewardi Public Hospital in Surakarta, Central Java, Indonesia. The age, gender distribution, site of the lesion, as well as clinic-pathological appearance were analyzed.

**Results:** There were 30 patients consisting of 46.7% males and 53.3% females with ages ranging from 33 to 91 years old and with the most common occupation, such as farmers (53.6%) and housewives (26.7%). Morpheaform subtypes BCC were more frequent than other types. Based on the predilection, most of the BCC were found to be in the mid-face (76.7%) and using determined criteria of histopathological examination, the aggressive appearance was 77% and non-aggressive BCC was 23%. The BCC on the mid-face location was more aggressive than the other sites (P < 0.05).

**Conclusions:** BCC is the most common skin tumor in humans with rare metastases, which might cause significant damage due to its local recurrences and aggressiveness. BCC on the mid-face is significantly more aggressive than that on the other predilection sites.

#### 1. Introduction

Basal cell carcinoma (BCC) is the most common skin tumor in humans[1]. BCC is locally aggressive which may invade the skin and adjacent structure including the muscles and bones and it has the low metastatic potential[2]. The highest incidence of BCC is in Australia with the ratios of 1 041 in 100 000

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male population, and 745 in 100 000 female population. The incidence of skin cancer has markedly increased over the past decade. At this time, There are 2 up to 3 million of BBC that are non melanoma skin cancer[3]. In Indonesia, BCC is in the 3rd rank after breast cancer and cervix cancer[4]. In Moewardi Public Hospital, it is the most frequent of the skin cancers[5].

Ultraviolet B (UV-B, 290–320 nm wavelength) irradiation is a major etiologic and risk environmental factor in the pathogenesis of melanoma and non-melanoma skin cancer, including BCC[6]. Photocarcinogenesis follows a multistage model of cancer development in which UV-induced DNA damage leads to mutations resulting in activation of oncogenes

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or silencing of tumor suppressor genes[7]. UV-B proton induces DNA damage, particularly on neighboring pyrimidine bases thymine and/or cytosine. It stimulates several proinflammatory cytokines production, such as tumor necrosis factor-α, interleukin-1 and interleukin-6 in the skin and they are considered to be closely related to the progression of UV-induced carcinogenesis. Macrophage migration inhibitory factor is originally identified as a lymphokine that concentrates macrophages at inflammatory loci. Macrophage migration inhibitory factor inhibits p53-dependent apoptotic processes after UV-B exposure[8]. Lesions occur mainly on the sunexposed skin,in about 80% of patients. They appear in the heads and in half of the patients and affect the skins of cheeks and the noses[9].

The BCC classification is complex and lacks uniformity of terminology and clear definitions. There is considerable variability in the morphology of BCC and as a consequence, a number of histopathological subtype has been defined[10-11]. Clinical manifestation is various lesion with a pearl transparent rim, destructive ulcerative lesion called ulcus rodents, pale foci with various degrees of induration, erythematous foci with obvious telangiectasia or cystic nodules. The most common BCC was nodular, followed by superficial and sclerosing or morpheic form[10-11].

In this study, BCC was classified as aggressive and non-aggressive. BCC generally has a clinical course characterized by slow growth, minimal soft tissue invasion and a high cure rate. However, BCC behaves aggressively with deep invasion, recurrence and potential regional and distant metastasis. Several factors include tumor size, duration and histology and perineural spread have been postulated as markers of the aggressive BCC phenotype[12]. Although the mortality rate is low, BCC may grow aggressively through creating extensive tissue destruction. Its frequency of metastasis is less than 0.1%[13]. Though BBC is eminently curable when the diagnosis is made promptly and the lesion is treated in the early phase, it constitutes an enormous financial burden on the health care system[5].

This study mainly focused on the tumor aggressiveness and its correlation to its predilection. By determining the localization of tumor aggressiveness we can prevent and evaluate the risk of recurrence after BCC treatment.

#### 2. Materials and methods

A total of 30 BCC patients were diagnosed using specimen biopsy with hematoxylin-eosin. All patients were treated at the Moewardi Public Hospital in Surakarta, Central Java, Indonesia. The histologic pattern of BCC was divided into several major

types: superficial, nodular, morpheic, pigmented, basosquamous and mixed. BCC on the face was divided by three sections: upper-face, mid-face and lower-face. The upper-face area included anterior hairline until glabella. The mid-face area included glabella going down to sub-nasal and the lower-face area included sub-nasal to mentalis[13]. Aggressive BCC based on histologic examination showed damaged basal membrane from nested tumors in palisading form or noncircular nested tumor with a smaller degree of peripheral palisade or loss palisading, spiky and jagged, or atypical basaloid tumor cells. While, the characteristic of non aggressive BCC are circular nested tumor with greater degree peripheral palisading or undamaged basal membrane of nested tumor[14,15]. The results of the study were statistically analyzed with the Kruskal-Wallis test (P < 0.05).

#### 3. Results

In this study, we found BBC predominantly in females than males (54.3% and 46.7%, respectively). The age range of the patients was 33–91 years old with the most common occupation of farmers (53.3%) and housewives (26.7%). According to the duration of the illness, most patients had symptoms more than 3 years and affected people over 50 years old (Table 1).

**Table 1** The characteristics of patients. n (%).

Variable	Patients
Gender	
Male	14 (46.7)
Female	16 (53.3)
Age (years)	
30–39	1 (3.3)
40–49	2 (6.7)
50–59	12 (40.0)
60 years old or more	15 (50.0)
Occupation	
Farmer	16 (53.3)
Civil servant	2 (6.7)
Entrepreneur	3 (10.0)
Housewife	8 (26.7)
Others	1 (3.3)
Duration of disease (years)	
1–3	3 (10.0)
3–5	15 (50.0)
> 5	12 (40.0)

Based on histopathology analysis, we found morpheaform subtype BCC (40%) was more dominant than other subtypes, which was followed by basosquamous, nodular, qigmented, mixed and superficial subtype BCC with percentages of 24%, 16%, 8%, 8% and 4%, respectively.

Based on the predilection, the most common BCC was in the mid-face. There were 28 patients who had BCC in their mid-face, and 23 patients were categorized as aggressive BCC and 5 patients had not aggressive BCC. In addition, the predilection of

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