Numerous Basal Cell Carcinoma: A Case Report in a Suspected Nonsyndromic Patient

Arinia Kholis Putri[1], Adhimukti T. Sampurna[1], Larisa Paramitha Wibawa[1], Roro Inge Ade Krisanti[1]
[1]*Departement of Dermatology and Venereology Faculty of Medicine Universitas Indonesia, Dr. Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia*

Keywords: Basal cell carcinoma, numerous, multiple, nonsyndromic, nonmelanoma skin cancers

Abstract: Basal cell carcinoma (BCC) is the most common cancer in humans. BCC usually occurs as a solitary lesion on sun-exposed areas. Various syndromes have been defined in which basal cell carcinoma exists in multiple localizations in a single patient. Multiple BCC is often related with inherited conditions such as Gorlin syndrome, Rombo syndrome, etc. Multiple BCC without history and clinical examination that are not consistent with those syndromes is considered as nonsyndromic BCC. It is still unclear what environmental and genetic factors contribute to the development of multiple nonsyndromic BCC. A case of numerous basal cell carcinoma with multiple localizations without signs and symptoms which is classified as a syndrome is described in this case report. Dermoscopic evaluation aids the diagnosis of and evaluation for people with history of nonmelanoma skin cancer.

1 INTRODUCTION

BCC is the most frequent cutaneous neoplasm, with slowly progressive nature and locally invasive behavior, that arise from non-keratinizing cells within the basal layer of the epidermis (Tcherney et al., 2017; Carucci et al., 2012; Totonchy and Leffell, 2017). The malignancy accounts for approximately 75% of all nonmelanoma skin cancers (NMSC) and almost 25% of all cancers diagnosed in the United States (Carucci et al., 2012).

BCC usually occurs as a solitary lesion on sun-exposed areas. There have been very few cases reported in the literature so far of multiple BCC. This condition occur mostly in several genetic syndromes, but can also happens as a sporadic feature. Among several syndromes, the most commonly known is Gorlin syndrome or nevoid basal cell carcinoma syndrome, an autosomal dominant trait caused by PTCH gene mutation (Satolli et al., 2018). It is still unclear what environmental and genetic factors contribute to the development of multiple nonsyndromic BCC (Tcherney et al., 2017). Risk factors for BCC have been well characterized (Totonchy and Leffell, 2017). The most significant risk factor involved in the pathogenesis is ultraviolet (UV) which triggers mutations in tumor suppressor genes (Kim et el., 2017). Increasing age, male, white race, exposure to ionizing radiation, arsenic, and polyaromatic hydrocarbons have also been correlated with higher rates of BCC (Totonchy and Leffell, 2017; Kim et al., 2017). Both genetic predisposition and exposure to environmental risks are involved in the pathogenesis of the malignant transformation in BCC (Tcherney et al., 2017). The early detection and eradication of these tumors are of importance for treatment effectiveness and quality of life because BCC could have an aggressive course and behavior which can lead to severe disfiguration and destruction (Tcherney et al., 2017; Carucci et al., 2012; Totonchy and Leffell, 2017; Kim et al., 2017).

BCC comprising several lesions is not uncommon, but nonsyndromic with numerous lesions are rare entities. We present a patient, came with numerous BCC without any signs and symptoms of a specific syndrome as we discuss the potential triggering risk and the further appropriate therapeutic options.

2 CASE

A 56-year-old female patient with Fitzpatrick skin type IV was admitted to the dermatological unit with a complaint of three ulcerated pigmented skin lesions with painless sensation on the face. The patient had

Putri, A., Sampurna, A., Wibawa, L. and Krisanti, R.
Numerous Basal Cell Carcinoma: A Case Report in a Suspected Nonsyndromic Patient.
DOI: 10.5220/0008159004280432
In *Proceedings of the 23rd Regional Conference of Dermatology (RCD 2018)*, pages 428-432
ISBN: 978-989-758-494-7

previously received Mohs micrographic surgery (MMS) for a BCC lesion, with diameter approximately 3 cm, on the upper lip at our hospital 4 years ago. But she was loss to follow up after the treatment for the flap from plastic reconstruction surgery unit. The patient was a scavenger and was constantly exposed to direct sunlight for most of her lifetime. She denied any history of sunburn, family history of skin cancer, past history of radiotherapy, and exposure to chemical substances including arsenic.

She had hypertension, which is controlled with medications and showed no regional lymphadenopathy. The laboratory blood tests and imaging diagnostic procedures did not revealed any abnormalities nor signs for systemic involvement. No symptom and sign such as mandibular cyst, palmar and plantar pitting, skeletal abnormalities, keratocystic odontogenic tumors, ectopic calcification of the dura, macrocephaly, and mental retardation.

On physical examination of the face, three ulcerations were observed, one measuring approximately 1 x 1 x 0,5 cm located on the tip of her nose. The second and third one measuring approximately 1,5 x 1 x 0,5 cm and 0,5 x 0,5 x 0,1 cm were located on the right cheek. Those three lesions showed pigmented pearl-like edges, bleeding surface, and irregular borders. These lesions were in accordance clinically, dermoscopically, and histopathologically for BCC in different stages of invasion (figure 1). We also found 21 pigmented lesions on her face and head, also 54 pigmented lesions were noted on her neck, which she did not notice nor have any complaints. All of these lesions have size ranging from 0,4 mm to 1,5 cm and demonstrated similar clinical signs such as irregular borders with pearl-like edges, with dermoscopic appearance also suggestive for BCC (Figure 2b – g).

Electrosurgery was performed for more than twenty superficial tumors on the neck. After the procedure, the wound sites were re-examined using a dermoscope to ensure there were no visible pigmented lesions left. Furthermore, the patient is still regularly come to our clinic to remove her remainder BCC lesions gradually with excision and electrosurgery. We plan to do periodic checkup for early detection of NMSC after all the lesions are removed.

3 DISCUSSION

BCC is the most common human cancer that usually occurs as a single lesion. The vast majority of BCC were located on the head and neck (Carucci et al., 2012; Kim et al., 2017). Recent reports show that the number of patients who develop more than one BCC is increasing (Tcherney et al., 2017). According to the clinical, dermoscopic, and histopathologic findings, our patient was diagnosed as having multiple BCC that mostly located on the scalp, nose, and neck. Multiple BCCs are not uncommon as there is a 36%–50% increased risk of development of additional BCCs after the first lesion within 5 years (Kim et al., 2017). The total number of NMSC is a risk factor for recurrence of previous tumor, as well as for the formation of new ones (Tcherney et al., 2017). This patient also had a history of MMS for a large BCC on her upper lip 4 years ago.

UV is thought to be the most important environmental factor in its pathogenesis, although it is not always possible to correlate the sites where exposure is most intense to those where lesions are most frequently found (Kobacas et al., 2010). An Italian study indicated the important role of sunburns, and therefore intense sun exposure, rather than that of prolonged sun exposure to increase the risk of BCC (Tcherney et al., 2017). Increasing age, Northern-European ancestry, male, immunosuppression, and arsenic exposure are the other established risk factors (Carucci et al., 2012; Kim et al., 2017). Our patient was 56 year-old female with Asian descendant. Although she is a scavenger and was constantly exposed to direct UV for most of her lifetime, she has Fitzpatrick skin type IV which rarely burns and tans easily, and denied any history of sunburn. Other factors include exposure to ionizing radiation, arsenic, and polyaromatic hydrocarbons, which appear to be involved in mutations of regulatory genes and alterations in immune surveillance (Carucci et al., 2012; Kim et al., 2017). From history taking this patient denied exposure of ionizing radiation, arsenic, and polyaromatic hydrocarbons.

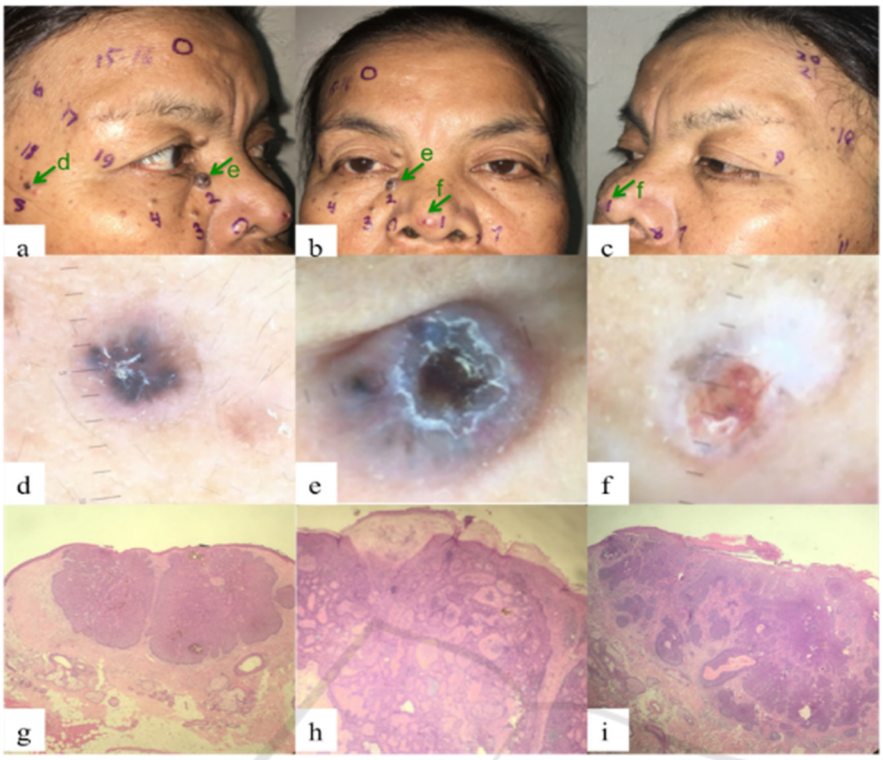

Figure 1. Preoperative photography shows that the lesions (circles) were located on the face (a-c). Dermoscopy appearance showed ulceration, leaf-like structures, blue-black globules and dots, and arborizing vessels (d-f). Histopathology with hematoxylin and eosin (H&E) staining with 40x magnification, showed the 3 lesions have basaloid epithelium with peripheral palisade layer under an ulcerated epidermis, with artefactual cleft, and mucinous stroma deposit on the border and central tumors (g-i)

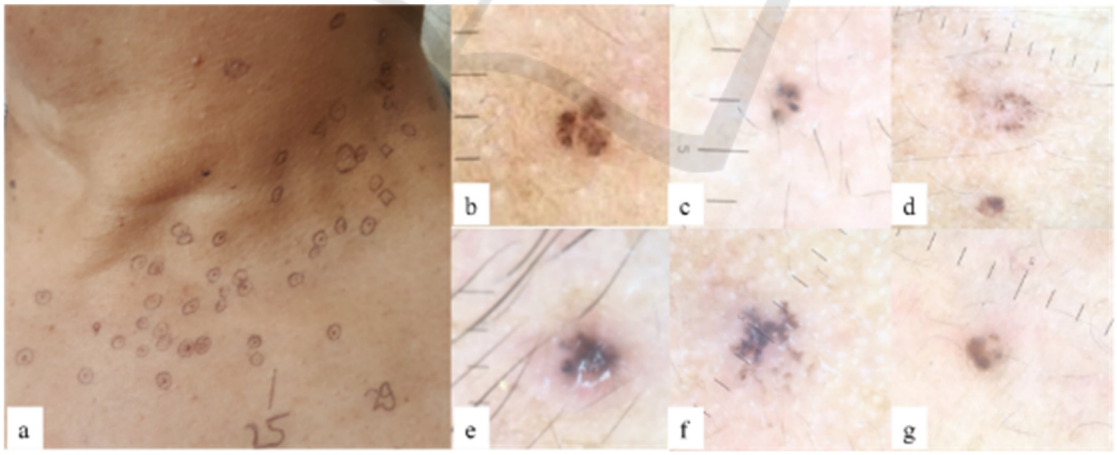

Figure 2. Pigmented lesions (circles) were located on the neck (a). Dermoscopy appearance showed leaf-like structures, blue-black dot, globules, and arborizing vessels (b-g).

Inherited conditions such as the nevoid BCC syndrome (Gorlin syndrome), Rombo syndrome, unilateral basal cell nevus syndrome, and Bazex syndrome are common inherited conditions with multiple BCC manifestations. Nonsyndromic but hereditary multiple BCC have been reported in literatures, but they were ruled out based on the negative family history (Tcherney et al., 2017; Kim et al., 2017). In our case, history and clinical examination were not consistent with these

syndromes that related to multiple BCC. Also, there was no sign and symptom of the lesions at a younger age, nor a positive family history. Thus, this case does not fit into any of the syndromes seen with basal cell carcinoma such as Gorlin syndrome or Bazex syndrome. There was no history of exposure to arsenic, irradiation, dry ice and no evidence of keratoacanthoma or xeroderma pigmentosum in this patient. However, considering the financial status of the patients, we could not perform polymerase chain reaction (PCR) assay to rule out this genotype. Moreover, the treatment plan would not be affected by the PCR result. Hence, we categorized our cases as nonsyndromic and nonhereditary type of multiple basal cell carcinomas worth mentioning.

In some literature, multiple BCC in one patient increases the risk of recurrence and they often develop new BCC with similar or different histological appearance (Tcherney et al., 2017). As also proven, not all instances of multiple BCC are due to genetic syndromes. Multiple superficial BCCs without associated anomalies are distinct from the Gorlin syndrome and could be explained by an autosomal dominant phenotype. Alternatively, this nonsyndromic phenotype might have a polygenic basis. Furthermore, a recent article has revealed that multiple BCC can be also part of the BAP 1 mutation (Satolli et al., 2018). We concluded that our patient had a high number of basal cell carcinoma lesions without a syndrome.

Despite the low metastatic potential, local tissue destruction and disfigurement caused by the tumor can be enormous if not completely eradicated by early diagnosis and treatment (Tcherney et al., 2017). Most basal cell carcinomas can be treated with any of a number of treatment modalities, including electrodessication and curettage, cryosurgery, surgical excision, or MMS. While surgical interventions such as MMS and surgical excision are the standard of care and yield the highest cure rates, the number of non-surgical interventions approved for the treatment of BCC continues to expand (Totonchy and Leffell, 2017). Standard surgical excision with 4-mm margins is the recommended treatment for BCC with non-aggressive histology, size of less than 2 cm, and occurrence on low-risk sites where tissue sparing is not critical (trunk and extremities). BCC of the face demonstrates high rates of incomplete excision, and greater efficacy has been demonstrated using MMS as compared with standard excision. MMS is recommended in cases of aggressive histology, recurrent BCC, critical areas of skin (head, neck, genitalia, hand/feet, nipples) and for tumors of large size (more than 2 cm) (Totonchy and Leffell, 2017; Fahradyan et al., 2017).

Current management options are numerous and focus on tumor eradication while maximizing cosmetic and functional capacity. The choice of treatment depends on the tumor type, tumor location, cost, recurrence rates, and potential cosmetic disfigurement (Kocabas et al., 2010). Our patient was treated with 3-4 mm margin excision and performing histopathologic examination, for lesions that were bigger than 1 cm on high risk area. But for approximately 20 small superficial lesions less than 1 cm in size, located not on the high risk area, and demonstrated with leaf-like structures and arborizing vessels with the dermoscope, we performed electrosurgery. After the procedure, the wound sites were re-examined using a dermoscope to ensure that there were no visible lesions left. Excision and histopathology examination for all the BCC lesions will not be cost-effective for this patient. The early detection and eradication of these tumors are of importance for treatment effectiveness and quality of life (Kim et al., 2017). The patient were asked to avoid sun-exposure as much as she could possible do. We plan to do regular checkup for this patient for the rest of her life to early detection of NMSC.

4 CONCLUSIONS

We have described a patient with multiple nonsyndromic basal cell carcinoma and had undergone Mohs micrographic surgery, wide excision, and electrosurgery. The early detection and eradication of these tumors are of importance for treatment effectiveness and quality of life. Our case illustrates the importance of diagnose and treatment multiple basal cell carcinoma at early stage. Performing dermoscopic evaluation will improve in early detection of BCC.

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