Multiple Bone Metastases in an Elderly Filipino with Basal Cell Nevus Syndrome*

Lyselle M. Desquitado, MD[1]

ABSTRACT

Basal Cell Nevus Syndrome (BCNS) is a rare autosomal dominant disorder characterized by a range of abnormalities, most notably multiple basal cell carcinomas (BCCs), odontogenic keratocysts, and palmar and/or plantar pits. BCC is the most common form of skin cancer globally. It is typically locally invasive and very rarely metastasizes, with distal metastases occurring in only 0.00028% to 0.55% of cases.

We present a case of a 68-year-old Filipino woman who was diagnosed with BCNS. She presented with multiple black nodules and plaques on her face and neck, histopathologically confirmed as BCCs. In addition, the presence of palmoplantar pits and calcification of the falx cerebri met three of the six major criteria for BCNS. Computed tomography (CT) and bone scans, revealed multiple bone metastases in the cranium, spine, sternum, and ribs. No previous cases of metastasis in a BCNS patient have been reported in the Philippines, making this the first documented case.

Keywords: *Basal Cell Nevus Syndrome, Basal Cell Carcinoma, Bone Metastases*

INTRODUCTION

Basal Cell Nevus Syndrome (BCNS), also known as Gorlin syndrome, is a rare autosomal dominant (AD) disorder characterized by a wide range of phenotypic abnormalities. The hallmark features of BCNS include multiple basal cell carcinomas (BCCs), palmoplantar pits, and odontogenic cysts. The diagnosis is made by fulfilling certain major and minor criteria, with confirmation possible through genetic analysis, particularly identifying mutations in the PTCH1 gene, which plays a critical role in the Hedgehog signaling pathway.[1]

BCC is the most common skin cancer and usually occurs on sun-exposed skin, predominantly in lighter-skinned individuals. It is generally locally invasive, with very rare distant metastasis, at 0.028% to 0.55%. The most common metastatic sites are the lymph nodes, lungs, and bones.[2] Although the BCCs associated with BCNS also rarely metastasize, the potential for metastasis underscores the need for vigilant monitoring.[3]

This report describes a Filipino woman with multiple black nodules and plaques on the face, neck, and trunk, diagnosed as multiple BCCs histopathologically. In addition findings of palmoplantar pits and calcification of the falx cerebri on imaging, met three of the six major criteria for basal cell nevus syndrome (BCNS). Further imaging revealed the rare occurrence of multiple bone metastases. We document a rare occurrence of bone metastases from BCCs in a person with BCNS.

Case Report

We present a 68-year-old Filipino woman, who worked as a seamstress from Bulacan. She had a 40-year history of multiple dark brown papules initially on the neck, which later involved the face and trunk. The lesions steadily increased in number over the years. At this time, the patient also noted the presence of asymptomatic multiple small pinkish pitting lesions on the bilateral palms and soles. Twenty years prior to consultation, she noted the onset of black nodules and plaques on the face and left arm, which gradually increased in size. There was no associated pain, tenderness, pruritus, bleeding nor discharge. There was no history of trauma prior to the appearance of lesions.

Eight years prior to consult, she noted new onset growth of a thick black plaque on the left preauricular area. Initially, no consult was done. She later noted new black nodules on the forehead and on the left angle of the lip that rapidly grew. These lesions were now associated with occasional pruritus (3/10) but no pain, bleeding or discharge. In the interim, she noted progressive enlargement of these new lesions still with no associated pain or bleeding.

Six years prior, she sought consult with a private surgeon in Bulacan, wherein the lesion on the forehead was completely excised but no biopsy was done. The patient only came back for removal of sutures and no further follow-up consult was done.

Disclosures: *The author has formally acknowledged and signed a disclosure affirming the absence of any financial or other relationships (including personal connections), intellectual biases, political or religious affiliations, and institutional ties that could potentially result in a conflict of interest.*

***3rd Place, 31th Philippine Medical Association Residents' Research Case Report Presentation, May 17, 2025**

[1]Department of Dermatology, Jose R. Reyes Memorial Medical Center

Four years prior, she noted a new rapidly growing black nodule on the same area as the previously excised lesion on the forehead. The nodule grew in size to approximately 2x2cm, associated with minimal pruritus (3/10), bleeding upon minimal trauma, but no pain. In the interim, there was new growth of multiple rapidly growing asymptomatic black nodules and plaques on the face. There was no associated weight loss, malaise, loss of appetite, or bone pains. No consultation was done. One week prior to consultation, still with the above lesions, the patient sought consultation at a private hospital and was given mupirocin ointment which she applied twice daily for one week, with no noted change in the lesions. She was then advised to consult a dermatologist for biopsy.

The patient previously had Stevens-Johnson syndrome secondary to allopurinol intake for her hyperuricemia in 2012. She was diagnosed to have bilateral cataracts in 2024. The patient had no history of radiation therapy. The patient had no history of seizures, mental retardation, cleft lip/palate or syndactyly. One of her sisters was diagnosed with ovarian cancer, while the other sister with thyroid cancer. There is no history of any family members with the same lesions or increased number of nevi. There is no known family history of skin cancer.

The patient is a non-smoker, non-alcoholic beverage drinker. She previously worked as a caretaker of a fishery, with approximately four hours daily sun exposure from 8AM-12NN and with no use of sunscreen or any sun protection. She had no history of sunburns and tans easily to a moderate brown.

Cutaneous examination showed multiple, well-defined, round to irregularly shaped, dark brown to black nodules and plaques, some topped with ulcerations, hemorrhagic crusts and white scales on the forehead, left preauricular area, left upper lip area. There were multiple, discrete, round, dark brown papules on the face, neck, central chest, abdomen and central back (Figure 1). There were also multiple, discrete, round to irregularly shaped, small, 1-2mm, pinkish, depressed papules on the bilateral palms and soles (Figure 2). The patient had a head circumference of 77cm.

There were no nail and mucosal changes noted. Her hair was white streaked with black and gray hair, with no thinning and no alopecia. There were no palpable cervical nor axillary lymphadenopathies detected.

A four-millimeter skin punch biopsy was done on five representative sites on the face (Figure 3). All five sites (central forehead, left forehead, left temporal, preauricular, and perioral) showed absent epidermis, dermis presenting with islands of basaloid cells with peripheral palisading and artifactual clefting. There was mucin deposition within tumor islands. There were melanophages within tumor islands and surrounding stroma, as well as mild infiltrates of lymphocytes and histiocytes (Figure 4).

Laboratory tests showed decreased hemoglobin and hematocrit, elevated uric acid at 12.6mg/dl and elevated creatinine at 9.8mg/dl. Multiple radiographs were done to screen for other specific skeletal malformations and radiologic changes however radiographs of the chest, thoracic cage, bilateral hands and feet were found to be unremarkable.

However, cranial and facial CT scans without contrast showed mixed sclerotic and lytic changes which involved the bones of the cranium, face, 1st and 2nd posterior ribs representing osseous metastasis. There were multiple, calcific densities seen in the falx cerebri as well as bilateral cerebellar tentorium. Plain chest CT revealed mixed sclerotic and lytic changes involving the thoracic spine, sternum and ribs, representing osseous metastases. The bone scan of the skull revealed a photopenic defect in the maxilla and mandible which suggests an osteolytic lesion from osseous metastasis.

Due to the detection of distal metastasis, the patient was referred to medical oncology and subsequently to radiation oncology. However, the patient's acute kidney injury needed to be addressed first before any management of metastasis. She was advised for genetic testing and a positron emission tomography (PET) scan. However, due to logistical challenges, the patient was unable to maintain consistent follow-up and succumbed to the disease six months after the initial diagnosis.

Figure 1. Multiple, well-defined, round to irregularly shaped, dark brown to black nodules and plaques, some topped with hemorrhagic crusts and white scales on the forehead, left preauricular area, left upper lip area. Also noted were multiple, discrete, round, dark brown papules on the face, neck, central chest, abdomen and central

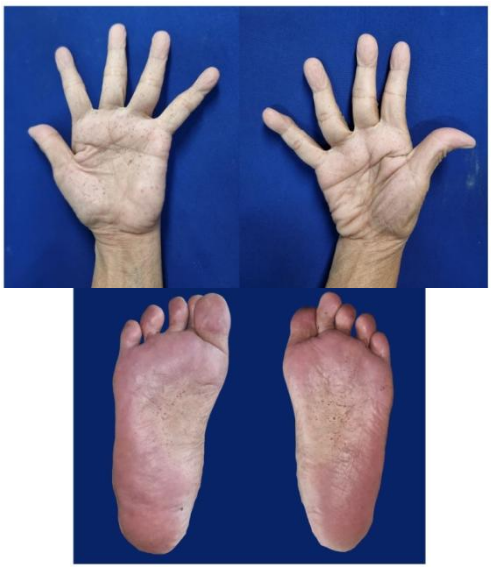

Figure 2. Multiple, discrete, round to irregularly shaped, small, 1-2mm, pinkish, depressed papules on the bilateral palms and soles.

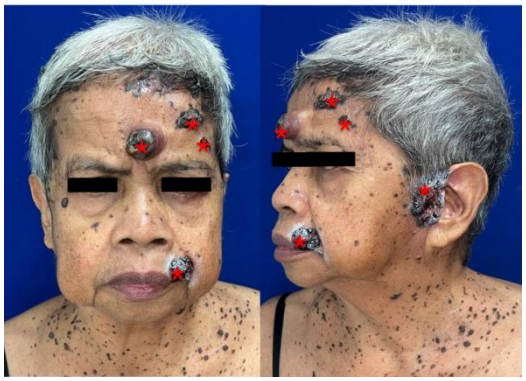

Figure 3. Five sites and lesions where 4mm skin punch biopsies were done (red asterisks).

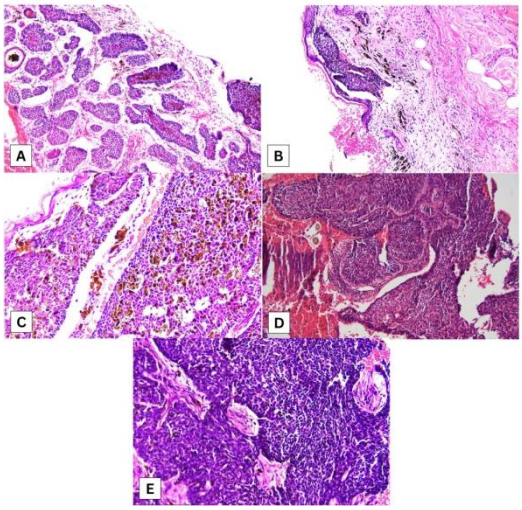

Figure 4. Histopathologic imaging of lesions of the A) center forehead, B) left forehead, C) left temporal, D) periauricular, and E) perioral areas. All findings consistent with basal cell carcinoma.

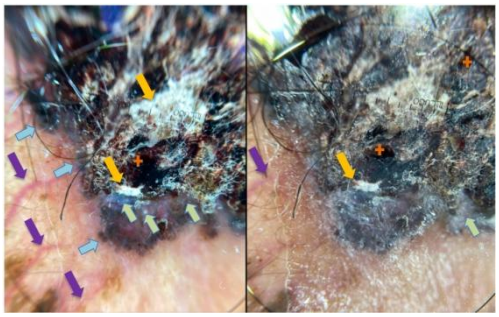

Figure 5. Dermoscopy showed ulcerations (orange cross), blue gray globules (blue arrows), white blotches (green arrows), arborizing vessels (violet arrows) and white scales (yellow arrows).

Year	Authors	Age/Sex	
2009	Ledesma-Pacia et al.	67/F	Multiple BCCs, palmoplantar pits odontogenic cysts, Basal cell carcinoma from a palmar pit
2013	Sabido et al.	11/F	Multiple BCCs, palmoplantar pits
2017	Magbuhat et al.	46/F	Multiple BCCs, palmoplantar pits, odontogenic cysts, calcification of the falx cerebri
2020	Habaluyas et al.	48/M	Multiple BCCs, palmoplantar pits, odontogenic cysts, calcification of the falx cerebri First degree relatives with multiple BCCs
2020	Balatibat et al.	50/F	Multiple BCCs, palmoplantar pits, Bifid

Table 1. A summary of the reported cases of Basal Cell Nevus Syndrome in the Philippines and the phenotypic abnormalities they presented with.

BCCs are the most prevalent cancers in humans. It would most often develop on the sun-exposed skin of lighter-skinned individuals and is relatively rare in dark skin due to inherent photoprotection of melanin and melanosomal dispersion. Cumulative exposure to ultraviolet (UV) is the main causal factor in the development of BCC.[1] The number of BCCs present in BCNS would vary from 50 to hundreds more often affecting the thorax, cervicofacial area, neck and, abdomen. There is also a high risk of recurrence for BCCs in this syndrome.[11]

Metastasis for BCCs is a very rare occurrence with rates varying from 0.00028% to 0.55%. The most common sites of metastasis are the regional lymph nodes (53%), lungs (33%), and bone (20%).[2] Similar to sporadic BCCs, the BCCs involved in BCNS rarely metastasize.[3] The rarity of metastasis in BCNS-related BCCs makes this case particularly notable, especially given the extensive bone involvement.

In the literature there are only five published reports describing BCNS with distal or distant metastasis and only one case report of BCNS with multiple bone metastasis.[11-15]

Year	Authors	Age/Sex	Metastatic sites
1968	Taylor et. al.	65/F	Lung
1987	Winkler et. al.	48/M	Lung, pleura, diaphragm, pericardium, epicardium and myocardium
2010	Lamon et al.	54/M	Bone
2011	Bajon et. al.	34/M	Submandibular lymph node
2014	Bilir et. al.	50s/M	Lung

Table 2. A summary of the reported cases of distal or distant metastasis accompanying Basal Cell Nevus Syndrome globally.

One case report by Lamon et al. revealed a similar scenario of bone metastasis from BCCs in a 54-year-old male patient with BCNS. A total of 21 interventions were done for this patient including surgical excisions, external radiotherapy and photodynamic therapy. However, the disease continued to progress and lesions recurred. Further workup with MRI, bone scan and vertebral bone biopsy revealed metastasis at the 12th thoracic vertebra. Six months later, bone scintigraphy revealed new metastases at the parietal bone, chest wall, right shoulder, left scapula, and thoracic rachis.[11]

Although surgical excision remains the gold standard for BCC, the extensive number of lesions that occur with BCNS necessitates consideration of alternative therapies. Radiotherapy is relatively contraindicated in patients with BCNS as it is associated with an increased risk of BCCs in the irradiated area.[15] A study by Sekulic et al. demonstrated that vismodegib, a hedgehog pathway inhibitor, is effective in treating advanced BCC and BCNS, with response rates of 30% for metastatic and 43% for locally advanced BCC. It offers a promising option for managing advanced diseases such as in this case.[16]

Conclusion and Recommendations

We report a rare occurrence of bone metastases from BCCs in a patient with BCNS, a rare AD disorder. A high level of suspicion and early recognition are crucial for effective disease management. Early detection allows a holistic approach to diagnostics and the prompt initiation of targeted interventions, which can significantly improve patient outcomes. By identifying a condition at its onset, healthcare providers can implement preventive measures to halt disease progression, monitor the patient's status, and swiftly initiate multidisciplinary medical care.

Future studies should focus on the genetic and molecular mechanisms underlying BCNS-associated metastases to improve risk stratification. Additionally, establishing standardized protocols for long-term monitoring of patients with BCNS, including regular imaging and multidisciplinary collaboration, may aid in earlier detection of rare complications such as bone metastases.

REFERENCES

1. Kang S, Amagai M, Bruckner AL, Enk A, Margolis DJ, McMichael AJ, Orringer JS. Fitzpatrick's dermatology. New York: McGraw Hill Education; 2019.
2. Wysong A, Aasi SZ, Tang JY. Update on metastatic basal cell carcinoma: A summary of published cases from 1981 through 2011. JAMA Dermatol. 2013;149(5):615. doi:10.1001/jamadermatol.2013.3064
3. Fernandez LT, Ocampo-Garza SS, Elizondo-Riojas G, Ocampo-Candiani J. Basal cell nevus syndrome: An update on clinical findings. Int J Dermatol. 2021;61(9):1047–1055. doi:10.1111/ijd.15884
4. Schierbeck J, Vestergaard T, Bygum A. Skin cancer associated genodermatoses: A literature review. Acta Derm Venereol. 2019;99(4):360–369. doi:10.2340/00015555-3123
5. Bree AF, Shah MR. Consensus statement from the first international colloquium on basal cell nevus syndrome (BCNS). Am J Med Genet A. 2011;155(9):2091–2097. doi:10.1002/ajmg.a.34128
6. Del Prado-Lu JL. Anthropometric measurement of Filipino manufacturing workers. Int J Ind Ergon. 2007;37(6):497-503. doi:10.1016/j.ergon.2007.02.004
7. Ledesma-Pacia AG, King-Ismael D, Reyes-Cacas TM, Tan ED. Basal cell carcinoma arising from a palmar pit in a Filipino with nevoid basal cell carcinoma syndrome.
8. Magbuhat DC, Matsuo JM, De la Cruz RA. Basal cell carcinoma, odontogenic cysts, brain and skeletal abnormalities (Gorlin Goltz syndrome) in a 46-year-old woman. Philipp J Head Neck Surg. 2017;32(2):38-42.
9. Sabido PW, Jamora MJ, Encarnacion LA. Multiple basal cell carcinomas in an 11-year-old Filipino-American girl with basal cell nevus syndrome. J Philipp Dermatol Soc.
10. Habauyas KE, Ciriaco-Tan C. Basal cell nevus syndrome in a 48-year-old male. J Philipp Dermatol Soc. 2020.
11. Lamon T, Gerard S, Meyer N, Losfeld B, Abellan van Kan G, Balardy L, Vellas B. Exceptional bone metastasis of basal cell carcinoma in Gorlin-Goltz syndrome. Dermatology. 2009;220(1):57–59. doi:10.1159/000264669
12. Taylor WB. The nevoid basal cell carcinoma syndrome. Autopsy findings. Arch Dermatol. 1968;98(6):612-614. doi:10.1001/archderm.98.6.612

13. Winkler P, Guyuron B. Multiple metastases from basal cell naevus syndrome. Br J Plast Surg. 1987;40(5):528-531.doi:10.1016/0007-1226(87) 90089-0
14. Bajon T, Adamiak E, Krawczyński M. Metastasis of basal cell carcinoma to lymph nodes in a patient with Gorlin syndrome – and literature review. Contemp Oncol (Pozn). 2011;2:107-110. doi:10.5114/wo.2011.21815
15. Bilir Y, Gokce E, Ozturk B, Deresoy FA, Yuksekkaya R, Yaman E. Metastatic basal cell carcinoma accompanying Gorlin syndrome. Case Rep Oncol Med.2014;2014:1–7. doi:10.1155/2014/362932
16. Verkouteren BJA, Cosgun B, Reinders MGHC, Kessler PAWK, Vermeulen RJ, Klaassens M, et al. A guideline for the clinical management of basal cell naevus syndrome (Gorlin-Goltz syndrome). Br J Dermatol. 2021 Nov 8;186(2):215-26. doi: 10.1111/bjd.20700
17. Sekulic A, Migden MR, Oro AE, Dirix L, Lewis KD, Hainsworth JD, et al. Efficacy and safety of vismodegib in advanced basal-cell carcinoma. N Engl J Med.2012 Jun 7;366(23):2171-9. doi: 10.1056/NEJMoa1113713.