Tenacious Tumors: Basal Cell Nevue Syndrome in a 50-Year-Old Filipina*

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INTRODUCTION

Basal cell nevus syndrome is a rare autosomal dominant disorder with a prevalence of between 1 in 60,000 to 1 in 120,000. This disorder is associated with a panoply of phenotypic abnormalities that includes developmental anomalies and tumors particularly basal cell carcinoma. The genetic abnormality in almost all known cases is a mutation in the *PATCHED1* gene which is essential for normal body and limb patterning.[1,2]

We report a 50-year-old Filipina who suffered from multiple recurrent pigmented papules, plaques, nodules, and tumors on the face with the first tumor appearing at age 20.

Case Presentation:

This is a 50-year-old Filipino female who presented with multiple tumors on her face. Thirty years prior to consult, at age 20, a black "mole" appeared o n her right cheek. Initially marble-sized, it continued to enlarge for 3 years. Attributing its growth to sun exposure and manipulation, she would notice some scaling and bleeding on some occasions. An excision biopsy of the mass revealed basal cell carcin oma. The wound defect would require skin grafting.

Nine years prior to consult, gradually enlarging "moles" arose on her left cheek and forehead. After a year, these tumors grew with radial enlargement and increase in height. She underwent another skin excision and grafting. The biopsy had the same finding.

Two years prior to consult, she grew "moles" on her nose and left upper lip which both had a ring of redness. These eventualy drained purulent discharge and had some crusting. A year prior to consult, mu ltiple "moles" grew on her face, including the left lower eyelid. This eyelid tumor would cause her pain whenever she would open her eye.

Except for her mother who was diagnosed with basal cell carcinoma, she had an unremarkable medical history.

Examination revealed multiple black, variously-sized papules, plaques,nodules and tumors on the face with some lesions forming crusts (Fig. 1). Both hands showed palmar pits (Fig. 2). Dermoscopy of the lesions displayed blue-gray non –aggregated globules, large blue-gray ovoid nests, and arborizing telangiectasias (Fig. 3). The skin punch biopsy revealed findings consistent with basal cell carcinoma (Fig. 4). Chest x- ray (Fig. 5) showed a bifid left 3rd rib.

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.*

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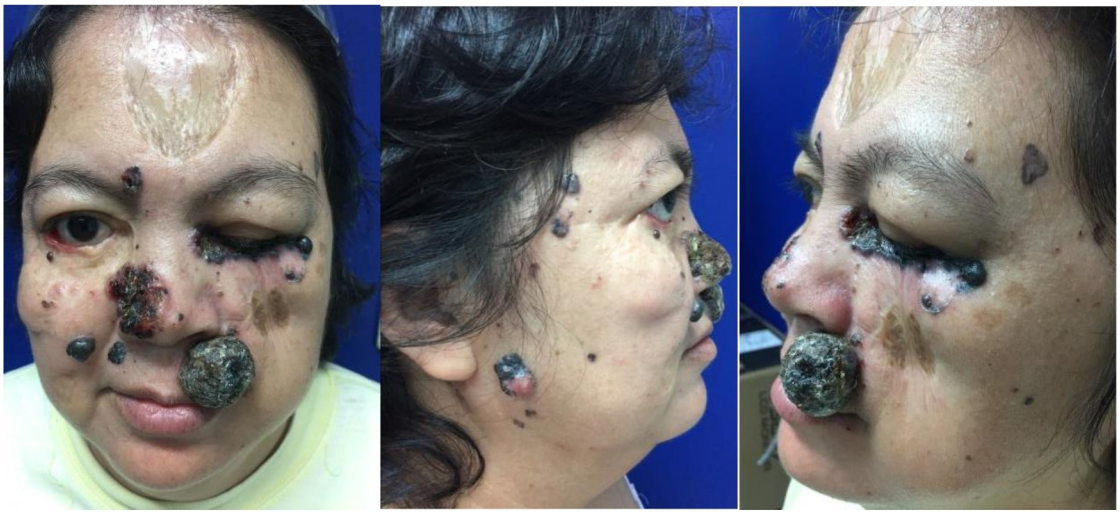
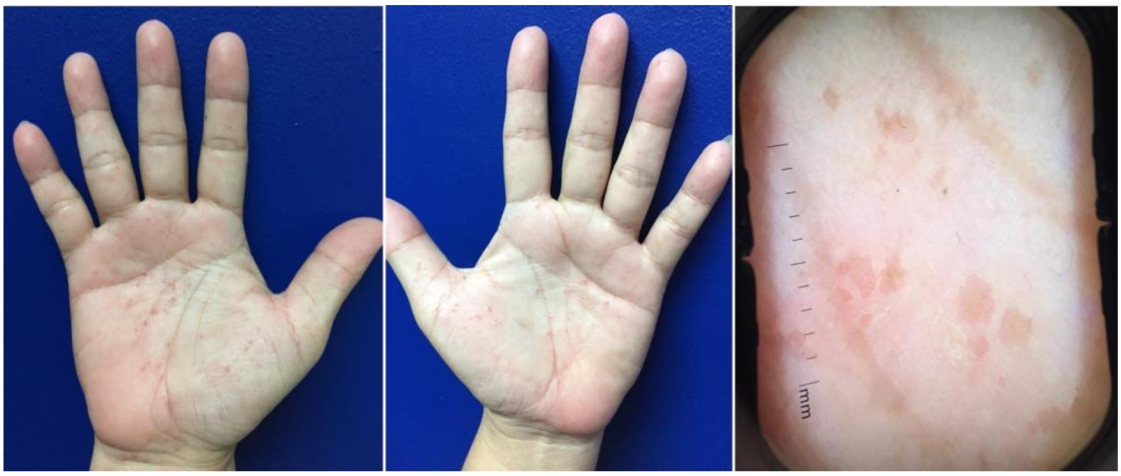


(a) (b) (c)

Figure 1. (a) and (b) Multiple, black, firm, shiny, smooth, and round papules, plaques, and tumors with measurements ranging from 0.5 x 0.5 cm to 1.5 x 1.5 cm scattered over the face; (c) Solitary black, firm, and dome-shaped tumor measuring 3 x 4 cm on the left upper lip, with a crater and yellowish crusts



(b) (b) (c)

Figure 2. (a) and (b) Florid palmar pits; (c) Dermoscopy of palmar pits

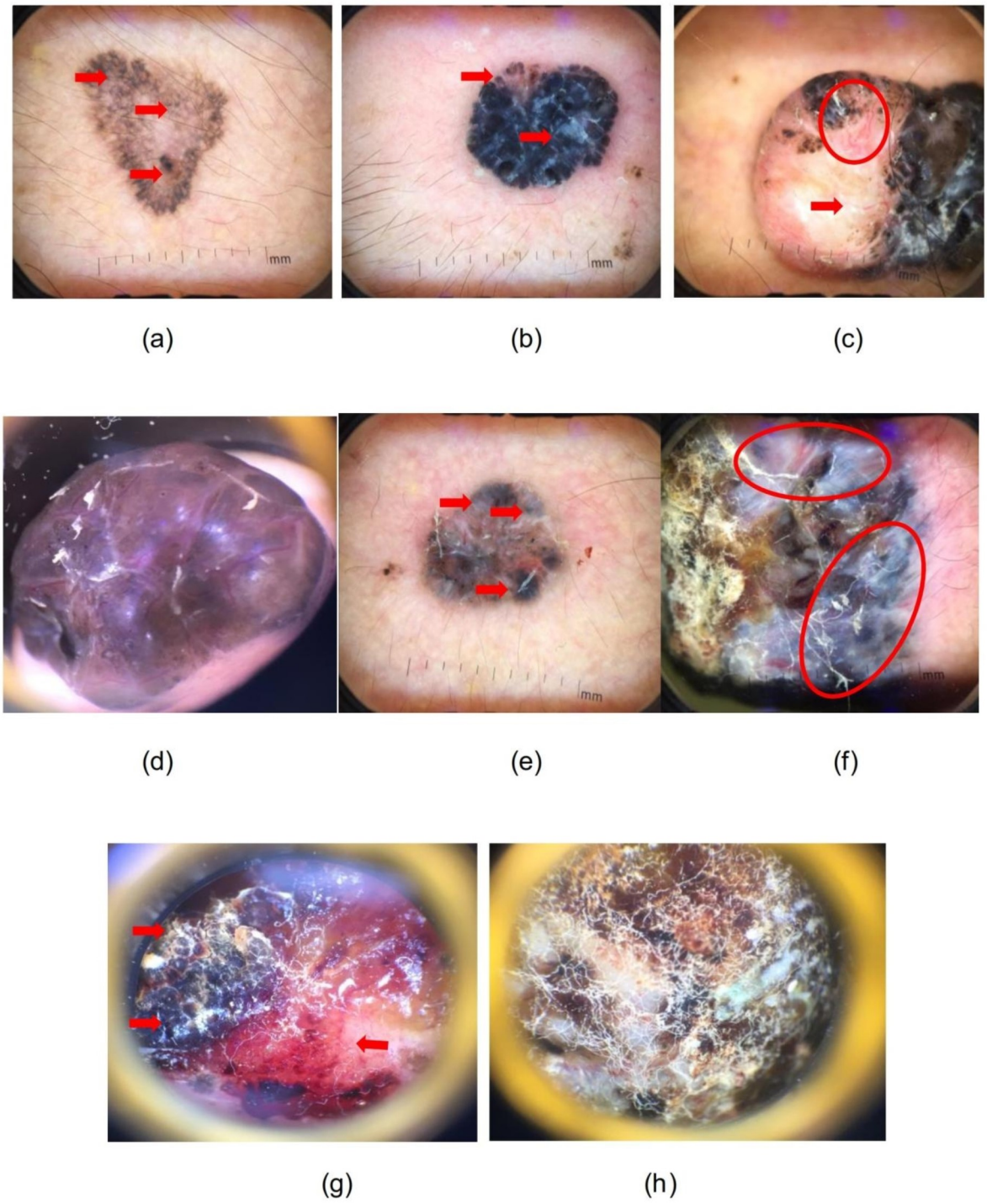


Figure 3. Dermoscopy of the lesions: (a) and (b) blue-gray non-aggregated globules and large blue-gray ovoid nests; (c) arborizing telangiectasias; (d) and (e) blue-gray ovoid nests; (f) blue-white veil; (g) and (h) ulceration and crusts

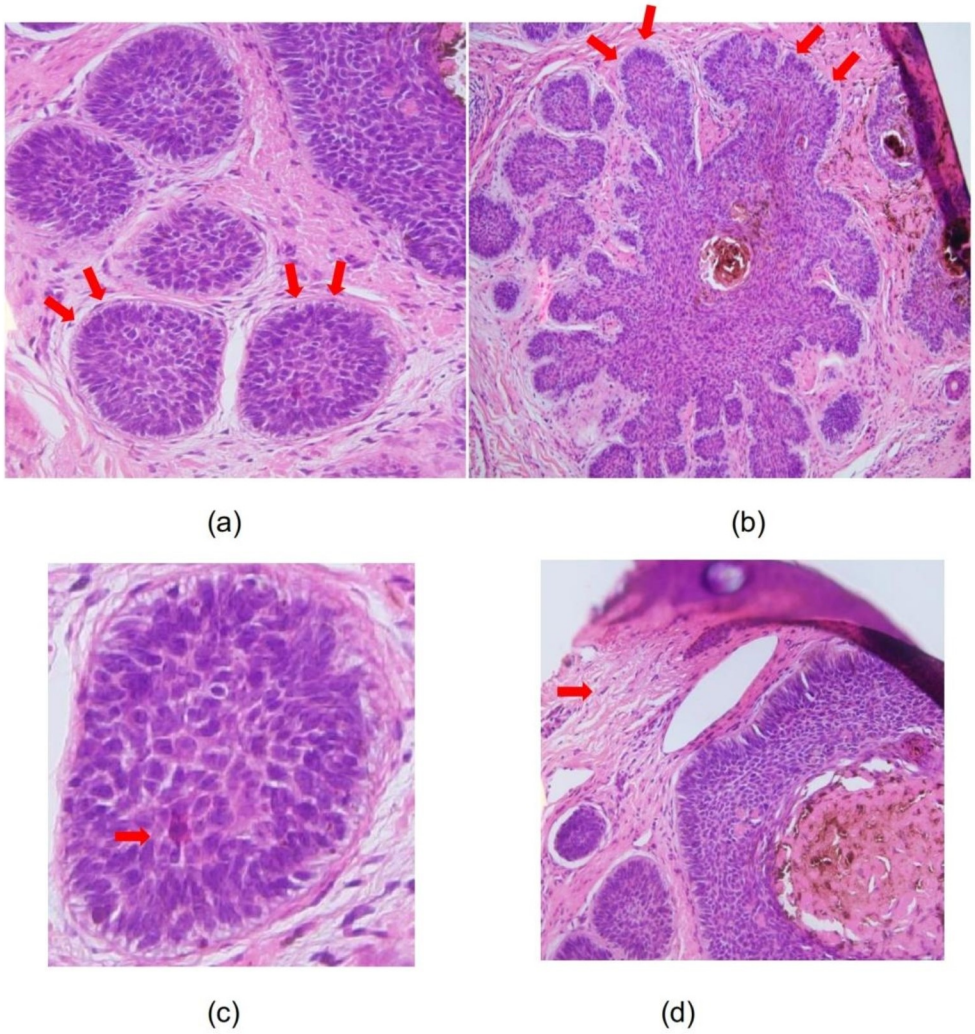


Figure 4. Histopathology: (a) and (b) islands of tumor cells showing peripheral palisading; (c) mitotic figures and (d) clefting artifact between the epithelium and the stroma

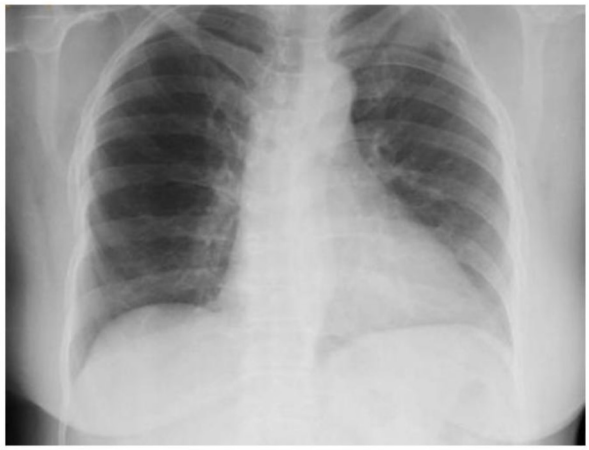
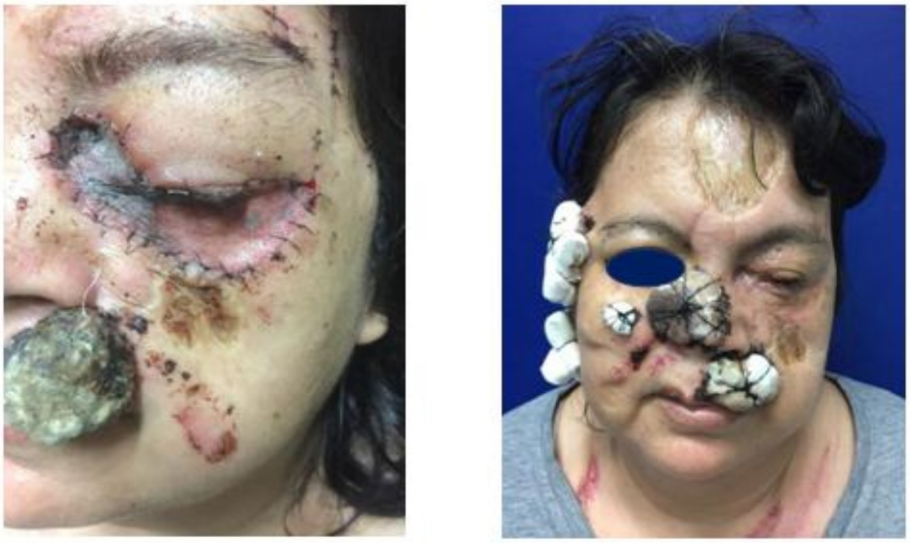


Figure 5. Chest X-ray: bifid 3rd rib, left.

She was referred to the ophthalmology service and subsequently underwent excision of the left lower lid tumor with complex reconstruction and skin grafting (Fig. 6a). Four months after, she underwent excision (Fig. 6b) of the remaining tumors on her face done by otorhinolaryngology-head and neck surgery service. She had an uneventful recovery.



(a) (b)

Figure 6. Post-operative photos showing: (a) The patient after undergoing excision of left lower lid tumor with complex reconstruction and skin grafting and; (b) post- excision of multiple basal cell carcinomas on the face still covered with gauze.

DISCUSSION

Basal cell nevus syndrome (BCNS) is a rare autosomal dominant disorder showing high penetrance and variable expressivity. It is caused by a mutation of the *PATCHED1* tumor suppressor gene resulting in uncontrolled upregulation of the Sonic Hedgehog pathway and carcinogenesis.[7]

The disease is characterized by multiple basal cell carcinomas (BCC) of the skin, skeletal abnormalities, palmar and/or plantar pits, bifid ribs, ectopic calcification of the falx cerebri, and multiple keratocystic odontogenic tumors in the jaw. The last two that were mentioned were not seen in our patient. Because of the variety of systemic symptoms, early diagnosis in most cases may be difficult.[4]

The Philippine Dermatological Society reported only 9 cases of BCNS in the Philippines from a 7-year registry (2011-2017).[6]

Eyelid BCCs are the most common ocular finding in BCNS. Aside from eyelid BCCs, these tumors may arise on the neck, chest, back, arms and elsewhere on the face. Eyelid lesions are often multiple and generally start to appear in the post-pubertal period, usually by age 35. However, their indolent nature can result in considerable delay in diagnosis and local recurrences are common.[3]

BCC subtypes share common histologic characteristics: malignant basal cells with large nuclei and relatively little cytoplasm, absence of mitotic figures, and a slit-like retraction of the stroma from tumor islands, creating peritumoral lacunae.[2] Our patient's biopsy showed islands of tumor cells with prominent palisading pattern.

Evans and Kimonis et al formulated the criteria for diagnosing BCNS. The major criteria are the following: 2 or more BCCs, keratocystic odontogenic tumors in the jaw, 3 or more palmar and/or plantar pits, bi-lamellar calcification of the falx cerebri, and family history. The minor criteria are bifid ribs and various skeletal abnormalities. To diagnose BCNS, 2 major criteria or 1 major and 2 minor criteria must be present.4 Our patient had multiple BCCs, a parent with BCC, palmar pits, and a bifid rib satisfying the diagnosis of BCNS.

The burden of BCNS lies with the recurrent nature of BCCs on the face and/or odontogenic tumors and its impact on quality of life.[5]

Vismodegib is an oral sonic h edgehog pathway antagonist approved in 2012 by the US Food and Drug Administration for metastatic, locally advanced, or inoperable BCC[7]. Its high cost made it inaccessible for our patient.

The BCC's anatomic location determines the approach to therapy. Treatment includes standard surgical excision, Mohs micrographic surgery, destruction by various modalities, and topical chemotherapy. The best chance to achieve cure is to adequately remove the primary tumor. Surgery and radiotherapy appear to be the most effective treatments with surgery having the lowest failure rate. Standard surgical excision offers the advantage of histologic evaluation of the removed specimen compared to non -surgical techniques. Our patient underwent standard surgical excision.

Non-surgical approaches may be aggressively pursued in a BCNS patient. The key is to convince the patient to accept frequent treatments. Minimization of discomfort and prevention of scarring are major goals.[1]

CONCLUSION

This rare case illustrates how a case of BCNS was diagnosed through the recognition of distinctive clinical, histopathologic, and radiologic findings: BCCs at a young age, a parent with BCC, biopsy findings, palmar pits, and a bifid rib. BCNS should be suspected in a patient who has multiple and recurrent BCCs starting at a young age

REFERENCES

1. Oro AE, Tang JY. Basal Cell Nevus Syndrome. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, eds. Fitzpatrick's Dermatology in General Medicine. 8th ed. New York: McGraw-Hill; 2012. p. 1304-11.
2. Carucci JA, Leffell DJ, Pettersen JS. Basal Cell Carcinoma. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, eds. Fitzpatrick's Dermatology in General Medicine. 8th ed. New York: McGraw-Hill; 2012. p. 1294-1303.
3. Wolkow N. Basal Cell Nevus Syndrome as a Hereditary Ocular Disease. The University of Arizona Health Sciences [Internet]. 2017 [Cited 2017 Dec 26] Available from: http://disorders.eyes.arizona.edu/disorders/basal -cell-nevus-syndrome
4. Jung E-J, Shin H, Baek J-A, Leem D-H, Ko S-O. Nevoid Basal Cell Carcinoma Syndrome: A Case Report and Review of Korean Cases. Maxillofac Plast Reconstr Surg [Internet]. 2014 [Cited 2014 Nov 12]; 36(6):292-297. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4283538/DOI:10.14402/jkamprs.2014.36.6.292
5. Akbari M, Chen H, Guo G, Legan Z, Ghali G. Basal cell nevus syndrome (Gorlin syndrome): genetic insights, diagnostic challenges, and unmet milestone s. Pathophysiology [Internet]. 2018 [Cited 2017 December]; 25:77-82. Available from: https://www.pathophysiologyjournal.com/article/S0928-4680(17)30134-7/pdf
6. Philippine Dermatological Society Health Information Systems. Philippine Dermatological Society. C2011. [updated December 1, 2017; cited January 28, 2018]. Available by request from: pdshis@outlook.com
7. Yang X, Dinehart S. Intermittent Vismodegib Therapy in Basal Cell Nevus Syndrome. JAMA Dermatol [Internet]. 2016 [Cited 2015 Oct 28]; 152(2):223-224. Available from: https://jamanetwork.com/journals/jamadermatology/fullarticle/2466922 DOI: 10.1001/jamadermatol.2015.3210