SKIN

BRIEF ARTICLE

Multiple Basal Cell Carcinomas Mimicking Segmental Neurofibromatosis: A Clinical Conundrum

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ABSTRACT

Basal cell carcinomas (BCC) are the most common type of skin cancer, typically presenting as pearly pink papules on areas of the body with chronic ultraviolet (UV) exposure. Sporadic segmental BCC has been rarely reported in the literature and can often be mistaken for other skin conditions, such as segmental neurofibromatosis or inherited segmental basal cell nevus syndrome. A comprehensive clinical history, a detailed physical examination with dermoscopy, and maintaining a high index of suspicion for biopsy allowed us to achieve an accurate diagnosis. Initiating targeted therapy with Vismodegib resulted in rapid clinic improvement and a significant enhancement in the patient's quality of life.

INTRODUCTION

Basal cell carcinoma (BCC), the most common type of skin cancer, is caused by prolonged exposure to ultraviolet (UV) radiation.[1] BCCs can present as localized, pearly lesions often accompanied by telangiectasias. In contrast, neurofibromatosis (NF) is a multisystem disorder with a wide range of clinical manifestations including cutaneous neurofibromas, which are discrete, well-circumscribed skin colored to pink to brown papules to nodules.[2] While these are distinct dermatological conditions with unique pathologies, both can pose diagnostic challenges due to their potential to exhibit a segmental distribution of skin lesions.

Segmental BCC presents as clusters of lesions in a broad, contiguous area, often resembling a linear or band-like pattern across a dermatome or nerve distribution. This form of BCC can resemble segmental neurofibromatosis (SNF), a condition marked by unilateral neurofibromas or café-au-lait macules without systemic involvement or family history.[3] Misdiagnosis can lead to inappropriate management strategies, which may delay necessary timely treatment for patients with sporadic segmental BCC.

CASE PRESENTATION

We report the case of a 65-year-old male with a significant medical history of multiple basal cell carcinomas (BCC) and squamous cell carcinomas (SCC), along with a familial history of melanoma in his son. The patient presented for a routine skin check, reporting several asymptomatic lesions on his forearms that have persisted for at least two years. These lesions had been previously evaluated by dermatology, where they were presumed to be cutaneous neurofibromas.

He also had a history of extensive, chronic UV exposure due to his decades-long career as a truck driver, during which he frequently rested his left arm outside ethe vehicle window to cool off, resulting in significant actinic damage.

On examination, numerous pink to skin-colored papules and nodules, ranging from 4 to 15mm, were observed on the left forearm and arm in a segmental distribution (**Figure 1 and Figure 2**). Additionally, a 10 x 9 mm pink nodule was noted on the central upper chest (**Figure 3**). Shave biopsies were performed on three lesions: a 10 mm pink plaque on the left medial forearm, a 15 mm pink nodule on the left lateral forearm, and the central upper chest nodule. Histology of the left forearm lesions confirmed nodular BCC with cystic degeneration, with immunohistochemistry

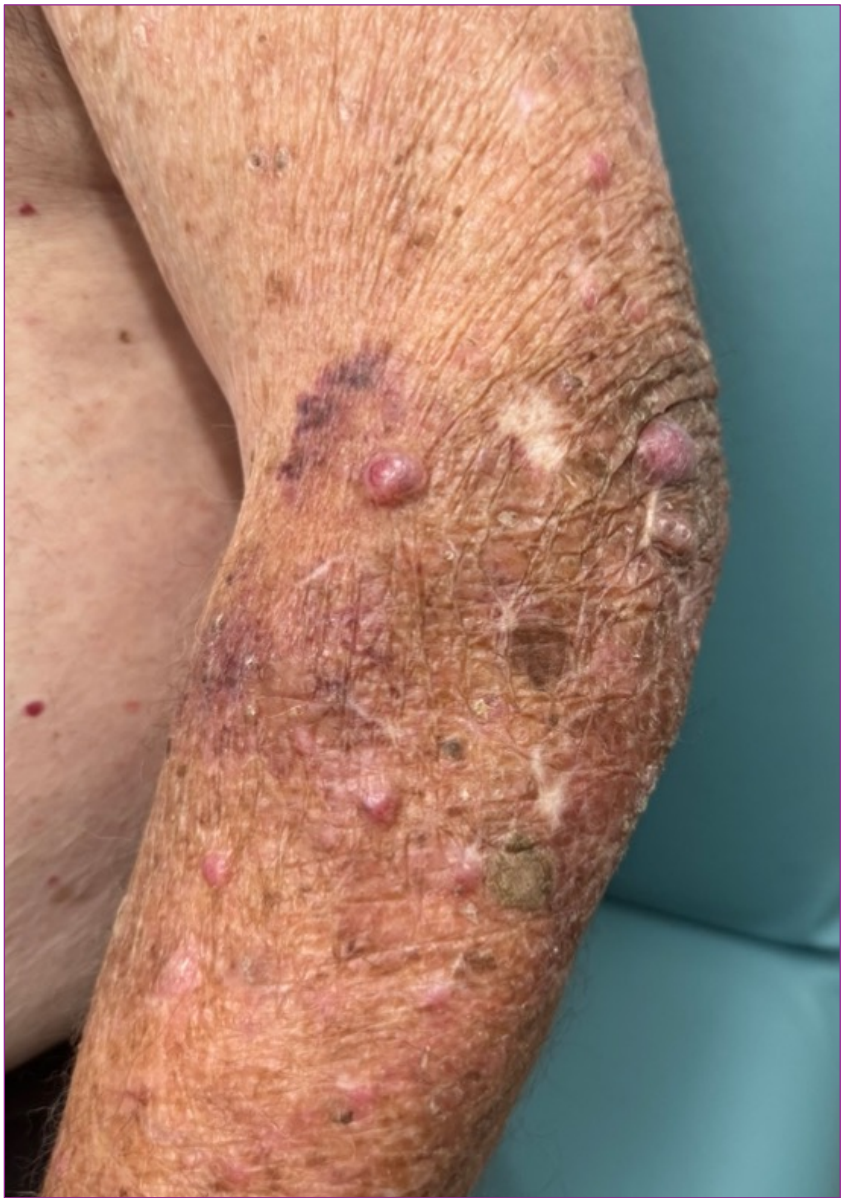

Figure 1: Pink to skin-colored papules and nodules, ranging from 4 to 15 mm, were observed in a segmental distribution on the left forearm and were subsequently diagnosed as basal cell carcinomas.

staining positive for BER-EP4 and chromogranin but negative for CK20 and synaptophysin, effectively ruling out Merkel cell carcinoma or neurofibroma. Chromogranin positivity has been reported in 27% of basal cell carcinomas.[4] The central chest lesion was diagnosed as a neurofibroma, characterized by spindle cells with wavy nuclei within a loose, myxoid stroma.

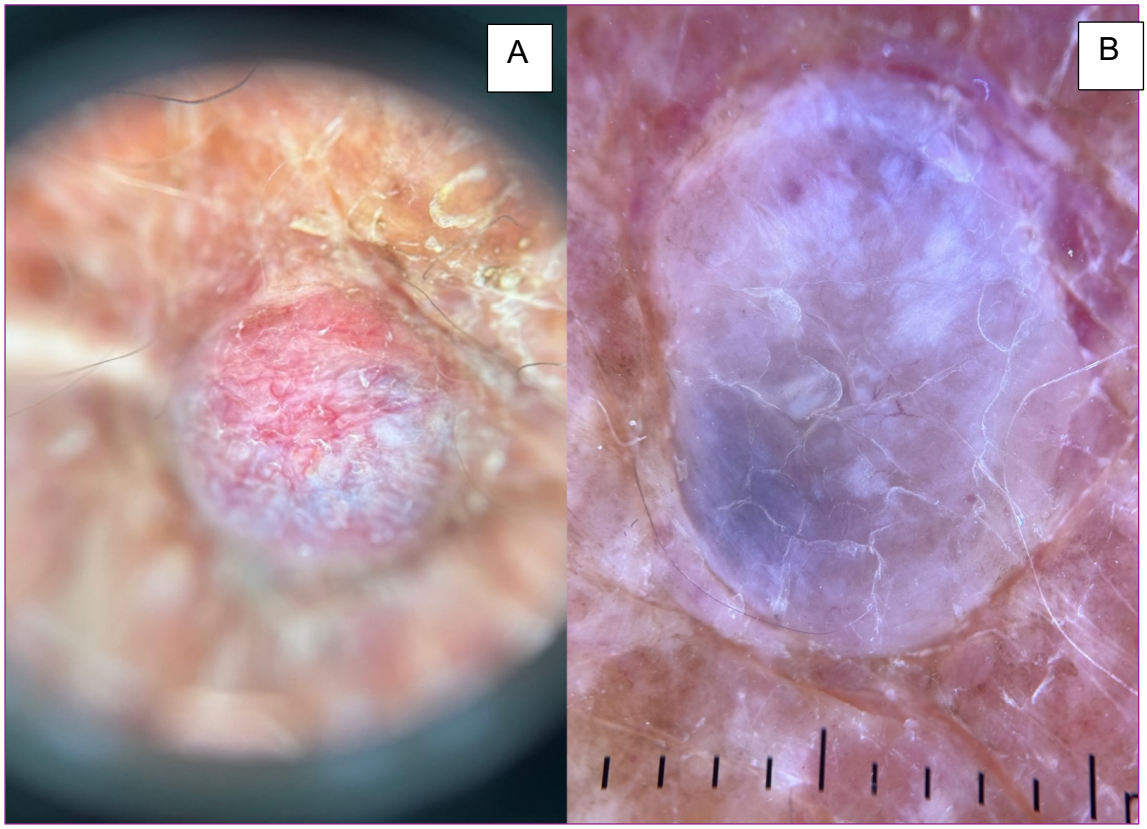

Figure 2: Dermoscopy of A shows an erythematous papule with arborizing vessels and shiny white steaks (chrysalis structures). Dermoscopy of B shows eccentric blue-gray ovoid nests with shiny white steaks (chrysalis structures). These dermoscopic findings are consistent with basal cell carcinoma, the diagnosis for both lesions.

At a one-month follow-up, three additional 5-6 mm pearly nodules on the left forearm were biopsied, with results consistently indicating BCC. These findings, in conjunction with earlier biopsies that also raised concerns for multiple BCC, suggested multiple BCCs with a segmental pattern of distribution, as opposed to the prior diagnosis of segmental NF. Various treatment options were discussed with the patient, including surgical excision, electrodessication and curettage (ED&C), or systemic chemotherapy. After discussion, the patient opted for starting vismodegib, a smoothened pathway inhibitor, and was referred to oncology for management.

At a two- month follow up after starting vismodegib, significant improvement was observed, with marked shrinkage of the nodules and papules on the left arm and no evidence of new lesions. Given the patient's high burden of actinic damage, he continues to be followed closely with regular skin checks to detect any new lesions.

Figure 3: A 10 x 9 mm compressible pink to skin-colored nodule was observed on the central upper chest, subsequently diagnosed as a neurofibroma, surrounded by brown to black, stuck-on papules and plaques consistent with seborrheic keratoses.

DISCUSSION

This case underscores the importance of a thorough clinical history, detailed physical examination with dermoscopy, and maintaining a high index of suspicion for biopsy, particularly in patients with an extensive history of NMSC. The patient's chronic and significant UV exposure as a truck driver further increased his risk, particularly due to his habit of placing his left arm outside the window to cool off. In the western world, where left-hand driving is common, studies have shown that UV exposure with closed windows is five times greater on the left arm and up to 20 times greater on the left side of the face.[5] This risk is amplified when the window is open, allowing 25-31% UV radiation to penetrate, compared to only 3-4% with a closed window.[5]

This patient's presentation can be mistaken for segmental basal cell nevus syndrome (BCNS), which is an inherited autosomal dominant genodermatosis typically caused by germline mutations in PTCH1, PTCH2, or SUFU, and rarely in smoothened (SMO).[6] Segmental BCNS is significantly less common than the generalized form and may present with additional skin findings, such as unilateral palmar pits, comedones, frontal bossing, short digits, with or without systemic involvement.[7] A family history of autosomal dominant inheritance and the presence of associated skin findings can help differentiate segmental BCNS from sporadic segmental

BCC. Currently, the standard routine dosing regimen for BCNS is vismodegib 150 mg daily for 12 weeks with an 8-week break.[8]

The coexistence of BCC and NF which may mimic each other's presentations through segmental distribution. Patients with NF1 are at an increased risk of developing BCC and SCC, likely due to activation of RAS/MAPK pathway and subsequently should be closely monitored with regular skin checks.[9] In this case, a prior diagnosis of sporadic NF could have resulted in missed biopsies, delaying the identification and treatment of malignancies. Reassessing the earlier benign diagnosis allowed the initiation of targeted therapy, which led to rapid clinical improvement and enhanced patient safety and quality of life.

Conflict of Interest Disclosures: None

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