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Squamous Cell Carcinoma with Co-infection of *Microsphaeropsis arundinis* and *Geotrichum candidum*: A Rare Case Report

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Abstract

BACKGROUND: Squamous cell carcinoma (SCC) is a non-melanoma skin cancer is a malignant carcinoma with an increasing incidence. The diagnosis of SCC is mainly based on clinical features and an excisional biopsy with histologic confirmation should be performed on all clinically suspected lesions to determine the prognostic and management of SCC. The first-line treatment of SCC of the skin is complete surgical excision. Microsphaeropsis arundinis and Geotrichum candidum are types of fungi that can infect the skin.

CASE REPORT: We report a case of a 46-year-old female patient that was diagnosed with SCC based on clinical, dermoscopy, and histopathological features. In addition, M. arundinis and G. candidum were also found on culture examination, where these fungi are rarely found, especially in cases of SCC.

CONCLUSION: The patient underwent tumor excision and amputation.

Introduction

Squamous cell carcinoma (SCC) is a cancer arising from the proliferation of epidermal keratinocytes. It is the second most common skin cancer after basal cell carcinoma (BCC); however, its incidence is relatively rare on the feet, heels, and other areas that are not exposed to sunlight [1]. SCC accounts for approximately 20% of skin malignancies and 75% of all skin cancer deaths, excluding melanoma [2]. Verrucous carcinoma is a variant of SCC with deep invasion of the underlying local structures [3]. Verrucous carcinoma rarely metastasizes but can be locally invasive and destructive. If left untreated, Lesions can significantly enlarge. This carcinoma in the plantar area can be irregular, well-defined, verrucous, and is also known as epithelioma cuniculatum. Management is usually palliative and includes extensive and aggressive tumor resection [4].

Microsphaeropsis arundinis is a dematiac-anamorphic fungus found in soil and freshwater. *M. arundinis* (fungi imperfecti) is a *coelomycete* that includes a new group of pathogens capable of causing soft tissue infections, mostly in immunocompromised human patients. The fungus usually penetrates the subcutis through trauma. The first reports of these organisms occurred more than 10 years ago [5]. *Geotrichum candidum* (teleomorph: *Galactomyces candidus*) is a dimorphic, *ascomycetous* species of the class *Saccharomycetes*. *G. candidum* is a commensal organism that can colonize one of them on the skin [6]. We report a case of a 46-year-old female patient with verrucous SCC with co-infection of M. arundinis and G. candidum that can lead to misdiagnosis and was treated with excision and subsequent referal to the orthopedic department.

Case Report

A 46-year-old female patient went to a dermatologist with complaints of mass and wound on the second and third fingers of the right foot for the past year. Initially, the patient had a history of moist feet that was covered by a white membrane. An enlarging mass that easily bled then appeared along with intermittent pruritus. The patient experienced pain especially if the lesion experienced friction. There is no history of fever and trauma.

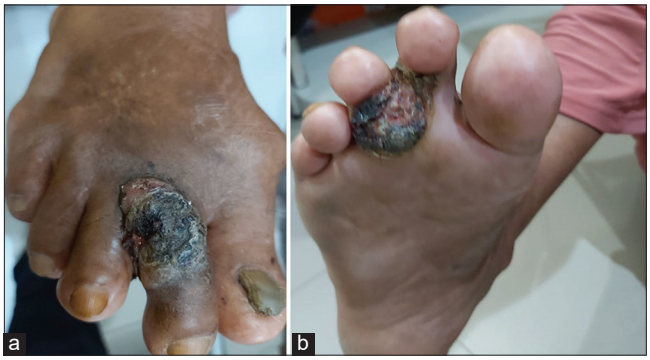

Figure 1: Clinical picture of the patient when she first came; (a) upper right toe (from dorsum) lesion, (b) lower right toe (plantar) lesion

On physical examination, vital signs were within normal limits, and no enlarged lymphadenopathy was observed. On the 2nd, 3rd and 4th digits of the right foot we found hyperpigmented verrucous nodule with the approximate size of 2.5 cm × 3 cm. Hyperpigmented plaque with thickness at around 2 cm was also found along with ulcers and crust (Figure 1). Dermoscopy found keratin/squama, blood spots, white structureless areas, and ulcerations (Figure 2).

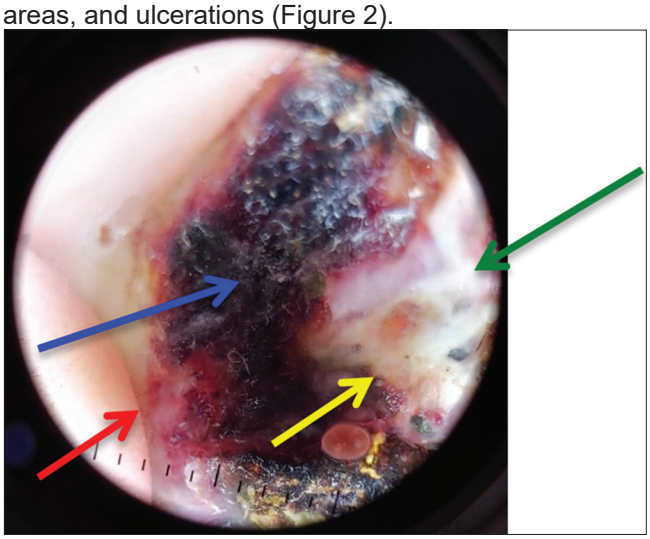

Figure 2: Dermoscopy of the lesion revealed keratin/scale (yellow arrow), blood spots (red arrow), white structureless areas (green arrow), ulceration (blue arrow)

The patient was suspected with a diagnosis of SCC accompanied by a fungal infection, so histopathological examination and fungal cultures were performed. On histopathological examination, the conclusion that SCC is well differentiated (Figure 3). Fungal culture found *M. arundinis* and *G. candidum* (Figure 4). The patient was then referred to the orthopedic surgery department because of suspicion of bone invasion and surgical excision, as well as amputation, were performed.

Discussion

SCC is the second most common skin cancer after BCC. The incidence of SCC continues to increase

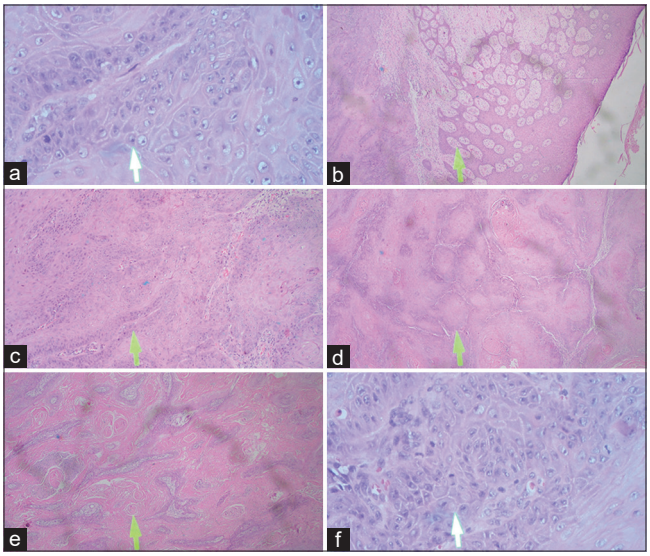

Figure 3: (a) Atypical nuclear squamous epithelial cell tumor nest, prominent nucleoli (40× magnification), (b) squamous epithelial cell tumor nest (4× magnification), (c) atypical nuclear squamous epithelial cell tumor nest, chaotic polarity with infiltrative growth (10× magnification), (d) squamous epithelial cell tumor nest (4× magnification), (e) horn pearl (4× magnification), (f) atypical nucleus squamous epithelial cell tumor nest, pleomorphic, prominent nucleoli, chaotic polarity (40× magnification)

worldwide, with a reported increase of 50–200% over the past 3 decades. The incidence of SCC increases with age and is more likely to develop in chronically injured skin, including chronic ulcers, burn scars, and radiation dermatitis. Chronic inflammatory disorders of the skin and mucosal tissue can also predispose to SCC [7].

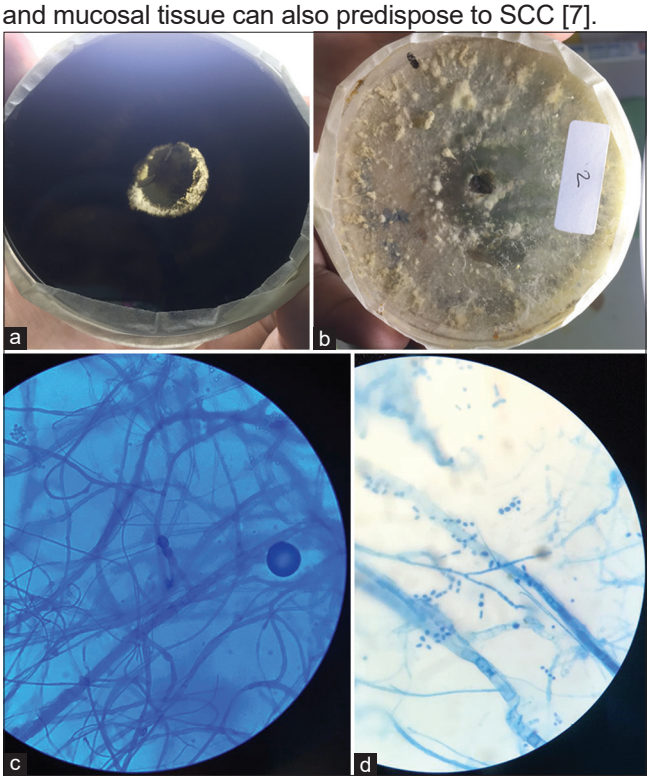

Figure 4: (a) Microsphaeropsis arundinis (macroscopic), (b) Geotrichum candidum (macroscopic), (c) Microsphaeropsis arundinis (microscopic), (d) Geotrichum candidum (microscopic)

Around 1% of skin cancers arise in chronically inflamed skin (e.g., burn scars, chronic ulcers, sinuses,

inflammatory skin diseases) [1]. Verrucous carcinoma is a rare variant of SCC. Locations in the intertriginous region of the foot and bone invasion are rare. The etiology of verrucous carcinoma remains unclear, but as it can develop in areas of chronic inflammation, we suspect the lesion in our case is due to continuous maceration [8]. Macerated white membrane occurred one year prior that resulted in wound formation and possibly lead to SCC development.

The clinical manifestation of SCC varies and depends on the histologic subtype and the location of the tumor. Typical locations of verrucous SCC include the oral cavity, the genitoanal area, the plantar area, commonly referred to as the epithelioma cuniculatum [7]. The location of verrucous carcinoma in the interdigital is still very rare [8]. Dermoscopy examination was typical for invasive SCC, where we found keratin/scale, blood spots, white circles, white structureless areas, hairpin, and linear-irregular vessels, perivascular white halos, ulceration. Keratin/squama is a strong predictor of well-differentiated and moderately differentiated SCC, whereas the presence of blood vessels in more than half of the tumor surface with a diffuse distribution of blood vessels and bleeding was a predictor of poorly differentiated SCC [2].

The diagnosis of SCC was confirmed histologically. The superficial verrucous resembles a verruca with parakeratosis, acanthosis, and prominent stratum granulosum [7]. Histopathology of epithelioma cuniculatum showed hyperkeratosis, acanthosis with undulations, keratinization, well-differentiated squamous epithelium [2].

Interestingly, in our case, there was also the presence of fungal growth in culture that can lead to misdiagnosis. This was mentioned in a case report that found *Candida parapsilosis* in a SCC patient [9]. In addition, another case report mentioned seven patients. With SCC due to chronic chromoblastomycosis. The malignant lesions occurred independent of the antifungal therapy and all patients underwent curative amputation [10]. *M. arundinis* is a rare fungal infection in humans, and there have only been eight cases previously described in the literature. The clinical manifestations of *M. arundinis* are described in the literature as crusted indurated plaques that can be mistaken for other conditions such as SCC. Management of *M. arundinis* infection includes surgical excision, thermotherapy, and antifungal drugs including terbinafine, amphotericin, and azole antifungals such as itraconazole, posaconazole, and voriconazole [11]. There is still limited references regarding *M. arundinis* colonization in SCC lesions.

Geotrichum is a species of fungus that can be found in the environment and is abundant in soil, water, and in the air. In addition, it is also found in plants and dairy products, it has also been shown to be found in normal human flora (mucus and feces). *G. candidum* is mostly a saprophyte that can cause a disease called Geotrichosis [12]. *G. candidum* is a commensal organism that can colonize human skin, tracheobronchial tree, and digestive tract. It is rare to be pathogenic in human and is of low virulence. These organisms are usually acquired through ingestion or inhalation [6]. We have not obtained literature describing the presence of *G. candidum* in SCC lesions.

The management of SCC is either surgical or non-surgical [7]. This patient was consulted to the orthopedic department because of suspicion of bone invasion. In cases with difficult to distinguish borders, amputation may be performed, where complete excision of the tumor rarely results in recurrence [4]. The prognosis for verrucous carcinoma is generally good but local invasiveness and metastatic potential can occur [1].

Conclusion

The co-infection of *M. arundinis* and *G. candidum* in a patient diagnosed with SCC is a rare case and can lead to misdiagnosis. We hypothesize that the SCC lesion arised due to chronic inflammation caused by maceration. Treatment in this patient includes surgical excision and subsequent amputation.

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