A rapidly growing skin nodule

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CASE

A man, aged 67 years, living in Queensland, Australia, was referred for excision of a biopsy-proven left forearm nodular basal cell carcinoma (BCC). He had no significant medical history, other than several keratinocyte skin cancers treated previously. He was not taking any medications, drank 3–4 standard alcoholic drinks and smoked approximately 10 cigarettes each day.

On examination, in addition to the diagnosed BCC, we noted significant solar damage to his skin, and three other head and neck keratinocyte cancers. Excision was planned for three weeks later. On return for the excision, he reported the appearance of a rapidly growing nodule, also on his left forearm, since the initial consultation (Figure 1). On specific questioning, the patient reported doing renovation work in an old farm building and thought he might have scratched his arm. The lesion caused some pain but was not discharging, had no associated systemic features and there was no fever.

The new lesion was dome shaped, 22×18 mm, with a crusted surface (Figure 1). There was no ulceration, but there was mild surrounding erythema, and the lesion was tender to touch. A clinical diagnosis of keratoacanthoma was made and the lesion was excised as an ellipse with 3-mm margins.

QUESTION 1

What it the most likely cause of the new skin nodule?

QUESTION 2

What differential diagnoses of the nodule need to be considered?

QUESTION 3

What other potential diagnoses should be considered?

QUESTION 4

What are the criteria for diagnosis of a blastomycosis-like pyoderma?

QUESTION 5

What are the management options for a blastomycosis-like pyoderma?

ANSWER 1

A rapidly growing skin nodule is an important and potentially serious presentation, with a range of infectious, inflammatory and neoplastic causes.

Squamoproliferative conditions including keratoacanthoma (KA) and poorly differentiated squamous cell carcinoma (SCC) are important and common considerations. This is particularly so in patients with a history of repeated keratinocyte cancers and sun damaged skin. Nodular melanoma must always be considered. We promptly performed an excision biopsy in consideration of these possibilities. In retrospect, it would have been useful to also send part of the excised specimen for culture, considering an infective cause. However, the histopathology report diagnosed 'blastomycosis-like pyoderma' and noted 'no convincing features of neoplasia'.

Blastomycosis-like pyoderma, also called pyoderma vegetans, is a rare disease[1] manifesting as vegetating skin lesions and elicits an impressive verrucous epidermal reaction. It is most seen in malnourished patients or in those in a general poor state of health.

The true incidence is not known as there are very little data available. This disease is

Figure 1. A rapidly growing pink nodule on extensively sun damaged skin.

thought to be an abnormal, exaggerated tissue reaction to a skin infection, of which most frequent causative agents include *Staphylococcus aureus*, beta-haemolytic streptococci, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Escherichia coli* and *Candida albicans*.[2]

ANSWER 2

A differential diagnosis to consider is KA. This is a low-grade, rapidly growing dome-shaped skin tumour with a centralised keratinous plug, which can be locally destructive. Although recognised as low-grade malignant lesions, KA shares histopathological features with squamous cell carcinoma (SCC) and requires active treatment.[3]

SCC is one of the most common forms of skin cancer,[4] caused by malignant transformation of normal epidermal keratinocytes and caused mainly by chronic sun exposure.

A nodular melanoma would be another differential diagnosis to consider. These appear as a round, raised lump on the surface of the skin that is pink, red, brown or black and feels firm to touch. It might develop a crusty surface that bleeds easily.[5]

'The lesion presents as a nodule that has been rapidly enlarging over the previous weeks to months. It can arise de novo in normal-appearing skin, or within an existing nevus, or melanoma of another type'.[5,6] Nodular melanoma can penetrate deep within the skin within a few months of its first appearance.

Other malignancies worthy of consideration, albeit uncommon, include Merkel cell carcinoma, atypical fibroxanthoma and cutaneous metastasis from a distant primary tumour.

ANSWER 3

Other potential diagnoses are listed in Table 1.

Table 1. Features of the differential diagnoses of blastomycosis-like pyoderma

Condition	Pathophysiology	Clinical features
Neoplasia		
Keratoacanthoma	• Low-grade neoplasm that arises from the infundibulum of hair follicles • The specific pathogenetic mechanisms are unclear, with likely mutations in the tumour suppressor gene, *TP53* • They have a tendency to spontaneously involute	• Dome-shaped, sharply demarcated, firm lesion, which grows rapidly • They can be erythematous or skin-coloured with a central hyperkeratotic plug • If left untreated, it will regress spontaneously
Squamous cell carcinoma	• Caused by the cumulative exposure of the skin to ultraviolet light[7,8] resulting in abnormal, accelerated growth of squamous cells	• Flesh toned to erythematous papule or nodule with variable degrees of scale, crusting, ulceration and hyperkeratosis • Can be painful or tender • A Marjolin ulcer is a squamous cell cancer that develops in a long-standing ulcer or scar
Nodular melanoma	• Melanoma arises when melanocytes undergo malignant transformation of the dermal–epidermal junction • Nodular melanoma grow vertically from the start and develop depth of invasion more rapidly than other radial growth phase melanomas[8]	• Usually symmetric, uniform in colour, have regular borders and small diameters • Nodular melanoma will begin to ulcerate, crust and bleed over time[9]
Autoimmune		
Halogenoderma	• Uncommon dermatosis that develops following exposure to halogens (iodine/bromide) • The exact pathogenesis is unknown • Likely caused by type 2 delayed hypersensitivity reaction	• Papulonodular eruptions with an acneiform appearance[10] • Can also present as a vegetating nodule or necrotic ulcer • Mucous membranes might be involved • There might be systemic signs and symptoms of halogen toxicity
Actinic comedonal plaque	• It is a variant of Favre–Racouchot syndrome, characterised by solar elastosis and basophilic degeneration of the connective tissue	• The plaque is characterised by papules, cysts and comedones forming a yellowish plaque in areas of chronic sun exposure[3] • More common in smokers

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Table 1. Features of the differential diagnoses of blastomycosis-like pyoderma (cont'd)

Condition	Pathophysiology	Clinical features
Infective		
Cutaneous botryomycosis	• Chronic granulomatous inflammatory response to bacterial pathogens, most commonly caused by *Staphylococcus aureus* and *Pseudomonas aeruginosa*[11]	• Chronic suppurative infection of the skin • Presents as subcutaneous nodules, abscesses, large verrucous lesions, fistulae, ulcers and sinuses with purulent discharge[12] • The pus might contain yellow grains • More common in immunocompromised patients
Blastomycosis	• Fungal infection caused by *Blastomyces dermatitidis*	• Cutaneous blastomycosis presents in two forms: verrucous or ulcerative • Lesions start as pustules that evolve into necrotic ulcers or verrucous plaques on sun-exposed areas • More common in immunocompromised patients
Atypical mycobacterial infection	• Non-tuberculous mycobacterium which is commonly found in soil, water and animals • Most commonly involved are: *Mycobacterium fortuitum*, *Mycobacterium chelonae*, *Mycobacterium abscessus*, *Mycobacterium marinum* and *Mycobacterium ulcerans*[13]	• Erythematous plaques/nodules that progressively ulcerate, or ecthyma that resembles cellulitis • A Buruli ulcer is a painless area of soft tissue swelling that slowly ulcerates with a poorly defined and irregular border
Other		
Pyogenic granuloma	• Benign lesion, proliferation of capillary vessels in the skin • Most common in children and younger adults • Causes include trauma, infection, hormonal changes and some medications[15]	• A fleshy, red, painless nodule that grows rapidly in a few weeks, which is typical • The lesion is usually friable and bleeds easily

Blastomycosis-like pyoderma is rare in immunocompetent patients. If this is diagnosed in a patient without known immunosuppression, careful consideration should be given to factors such as alcoholism, malnourishment, undiagnosed human immunodeficiency virus (HIV) infection, neoplasia and diabetes.

Local factors might contribute including previous radiotherapy, foreign body and tattoos.

ANSWER 4

There are six criteria for the diagnosis of blastomycosis-like pyoderma and these include:[3,13,14]

- clinical presentation of a large verrucous plaque with multiple pustules and an elevated border
- pseudoepitheliomatous hyperplasia and abscesses diagnosed histologically
- identification of bacteria diagnosed by tissue culture
- negative culture for fungi and mycobacterium
- negative fungal serology test
- normal bromide and iodide blood levels.[3,14,15]

ANSWER 5

The most effective management option includes systemic corticosteroids and oral antibiotic therapy[15] for a prolonged period (up to 3–4 weeks). Physical therapies, such as curettage, intralesional steroid injection and carbon dioxide laser can also be considered.[16] Oral acitretin therapy has been successful in some cases.

Doses of prednisolone 1 mg/kg/day were reported to be successful to control inflammation and relieve pain in some cases. This dose should be continued until the lesions show evidence of healing and then gradually decreased. Agents such as minocycline, dapsone, rifampicin, vancomycin or clofazimine might be added to enhance *S. aureus* killing by inhibiting bacterial synthesis.[16]

Skin nodules, especially new and rapidly growing ones, should be given urgent attention. They usually require complete excision biopsy to exclude aggressive and dangerous malignancy. However, 'common things are common' and many such lesions are low grade malignancies such as KA and well-differentiated SCC. Further, occasionally uncommon causes like this case do occur.

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References

1. Cecchi R, Bartoli L, Brunetti L, Pavesi M. Blastomycosis-like pyoderma in association with recurrent vesicular hand eczema: Good response to acitretin. Dermatol Online J 2011;17(3):9. doi: 10.5070/D30DS6984N.
2. Borra SK, Peter DCV, Balakrishnan N, Pulimood S, Bhindra M. Blastomycosis-like pyoderma: Novel use of potassium iodide. Indian J Dermatol Venereol Leprol 2017;83(6):720–21. doi: 10.4103/ijdvl.IJDVL_260_17.
3. Zito PM, Scharf R. Keratoacanthoma. StatPearls Publishing LLC, 2024. Available at www.ncbi.nlm.nih.gov/books/NBK499931 [Accessed 12 June 2024].
4. Knoxville Dermatology Group. The universal threat of skin cancer. Knoxville Dermatology group, 2018. Available at www.knoxderm.com/?s=+Squamous+cell+carcinoma++skin+cancer [Accessed 17 December 2023].
5. Cancer Council Victoria. Melanoma. Cancer Council Victoria, 2024. Available at www.cancervic.org.au/cancer-information/types-of-cancer/melanoma/melanoma-overview.html [Accessed 26 March 2024].
6. Oakley A. Nodular melanoma. Dermnet NZ, 2011. Available at https://dermnetnz.org/topics/nodular-melanoma#:~:text=In%20nodular%20melanoma%2C%20melanoma%20cells,existing%20melanoma%20of%20another%20type [Accessed 17 December 2023]
7. Hadian Y, Howell JY, Ramsey ML, Buckley C. Squamous cell skin cancer. StatPearls Publishing LLC, 2024. Available at www.ncbi.nlm.nih.gov/books/NBK441939 [Accessed 12 June 2024].
8. Heistein JB, Acharya U, Mukkamalla SKR. Malignant melanoma. StatPearls Publishing LLC, 2024. Available at www.ncbi.nlm.nih.gov/books/NBK470409 [Accessed 12 June 2024].
9. Kelly JW, Chamberlain AJ, Staples MP, McAvoy B. (Nodular melanoma: No longer as simple as ABC. Aust Fam Physician 32(9):706–09. Available at www.racgp.org.au/getattachment/559858aa-43ef-448e-9e8a-25a677a72af3/attachment.aspx [Accessed 12 June 2024].
10. Onalaja-Underwood AA, Hurley MY, Sokumbi O. Diagnosis and management of bullous disease. Clin Geriatr Med 2024;40(1):37–74. doi: 10.1016/j.cger.2023.09.002.
11. Weinstein M, Ott H, Hoeger PH. Cutaneous infections in immunocompromised children. In: Hoeger P, Kinsler V, Yan A, et al, editors. Harper's textbook of pediatric dermatology. John Wiley & Sons Ltd, 2019; p. 684–92. doi: 10.1002/9781119142812.ch56.
12. Thummanapally N, Lawdyavath K, Guruva C, Enumula D, Sastry PVK. A review on common Staphylococcal bacterial skin infections in pediatrics and their management. Acta Scientific Pharmaceutical Sciences (ASPS) 2023;7(5):23–32. Available at www.actascientific.com/ASPS/pdf/ASPS-07-0950.pdf [Accessed 17 June 2024].
13. Winburn B, Sharman T. Atypical mycobacterial disease. StatPearls Publishing LLC, 2024. Available at www.ncbi.nlm.nih.gov/books/NBK556117 [Accessed 16 June 2024].
14. Hongal AA, Gejje S. Blastomycosis-like pyoderma – A rare case report. J Clin Diagn Res 2016;10(10):WD03–04. doi: 10.7860/JCDR/2016/20468.8610.
15. Sahli F, Litaiem N, Gara S, Charfi O, Rammeh S, Zeglaoui F. Blastomycosis-like pyoderma in an immunocompetent patient. Clin Case Rep 2022;10(2):e05479. doi: 10.1002/ccr3.5479.
16. Jevremović L, Ilijin I, Kostić K, Mijušković Z, Tufegdžić I, Sekulović LK. *Pyoderma vegetans* – A case report. Serbian Journal of Dermatology and Venereology (SJDV) 2017;9(1):22–28. doi: 10.1515/sjdv-2017-0004.

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