CASE REPORT

Marjolin's squamous cell carcinoma of the hallux following recurrent ingrown toenail infections

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SUMMARY

Marjolin's squamous cell carcinoma (SCC) affecting the toe is rare. Due to resemblance with benign conditions it can often result in misdiagnosis. We report a case of Marjolin's SCC affecting the proximal hallux in a patient with recurrent ingrown toenail infections. A 58-year-old woman with a background of wedge resections for ingrown toenail and distal phalanx amputation for osteomyelitis presented with pain and hyperkeratotic raised ulcer around the proximal phalanx. MRI scan revealed soft tissue mass infiltrating the proximal phalanx with biopsies confirming a SCC. The patient underwent first ray amputation and made a good clinical recovery and remains disease free. Due to clinical similarities with benign conditions, awareness of Marjolin's SCC as a potential diagnosis when treating patients with recurrent ingrown toenail is imperative. We recommend patients with recurrent ingrown toenail or ulceration with a background of chronic infection have biopsies performed to exclude potential malignancy.

BACKGROUND

Marjolin's ulcer is a rare and aggressive form of squamous cell carcinoma (SCC) arising from chronic non-healing wounds. SCC affecting the toe is rare.¹ Of all cases of SCC involving the lower extremity, only 2.3% of cases affect the toe.² Approximately 94% of SCC of the toe affects a single toe with two-thirds of cases involving the hallux. It is twice as common in men as it is in women. In approximately 50% of cases the exact aetiology is unknown, while other causes for SCC of the toe include distant metastases, human papilloma virus (HPV) or chronic infection.³ Other risk factors include chemical or physical microtrauma, excessive sunlight exposure and immunosuppression.³

Patients with subungual SCC may present with a variety of symptoms including chronic pain, swelling, dyschromia of the nail plate and onycholysis. A verrucous appearance of the nail bed and nail dystrophy may be seen along with nodularity, bleeding and ulceration of the lesion.^{4,5} Biopsy of the lesion is the gold standard for the histological diagnosis of SCC.

Due to lack of awareness among physicians, resemblance to benign conditions and the indolent course of the disease, it often results in either misdiagnosis or delayed diagnosis.

We report a case of SCC affecting the proximal hallux in a patient with a 15-year history of

recurrent wedge resection for ingrown toenail and distal phalanx amputation for late-onset osteomyelitis of the distal phalanx.

CASE PRESENTATION

A 58-year-old woman presented with an 8-year history of recurrent ingrown toenail of the right hallux following four failed attempts at wedge resections in the community. She was otherwise healthy, with no history of diabetes or immunosuppressant use. On examination, only the medial two-thirds of the nail plate was present and a chronic malodorous ooze was discharging from the wound (figure 1).

On referral to the orthopaedic clinic, the nail was dystrophic and the wound had failed to heal from previous surgeries despite management in the specialist wound healing clinic. There was a history of recurrent infections for which she had antibiotic treatment over the previous years. Wound swabs had demonstrated a light growth of coliform species, mixed anaerobes and coryneform sensitive to metronidazole. Despite this, the wound still discharged and required daily dressings. This regime had finally brought the inflammation under control and she was referred for definitive treatment (figure 1).

Due to the history of infection, osteomyelitis was suspected and was investigated with inflammatory markers and imaging. The white blood cell, C-reactive protein and an MRI scan excluded infection and she subsequently underwent nail ablation and excision of the germinal epithelium. Following this,

Figure 1 Clinical photographs demonstrating remnant of the medial two-thirds nail plate and chronic malodorous ooze from medial nail bed.

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Figure 2 Postoperative clinical photograph following nail ablation and excision of germinal epithelium.

the patient developed a postoperative infection for which she was treated with metronidazole following the growth of coliform species, mixed anaerobes and mixed coagulase negative staphylococcus growth. Following antibiotic therapy, the patient had appeared to make a good recovery and discharged to the general practitioner (GP) (figure 2).

Two years later, the patient reattended with a heavy malodorous discharge from the wound. Clinical examination and investigation confirmed osteomyelitis of the distal phalanx. Plain radiographs revealed a cyst at the base of the proximal phalanx. After discussion with the patient, amputation of the distal phalanx was chosen and the patient underwent amputation through the interphalangeal joint. Postoperatively the wound again developed a severe infection with a heavy growth of mixed anaerobes and light growth of non-haemolytic streptococcus that required operative debridement and metronidazole. After 8 weeks the wound had healed and the patient was again discharged back to the care of her GP.

Five years following the partial amputation, the patient re-presented with pain around the proximal phalanx of the hallux. Clinical examination of the proximal phalanx demonstrated an area of hyperkeratotic skin ulceration with hard raised edges (figure 3). Inflammatory markers and plain radiographs were unremarkable. An MRI scan revealed a soft tissue mass infiltrating the proximal phalanx that had encased the distal flexor tendon and extended to the skin on the lateral aspect of the toe (figure 4). There was no clinical or radiographic evidence of infection.

The patient underwent debridement and curettage of the proximal phalanx. On this occasion, she presented without inflammation and discharge for the first time in 10 years and

Figure 3 Clinical photographs demonstrating a hyperkeratotic ulcer with hard raised edges at the proximal phalanx of hallux.

Figure 4 Coronal and sagittal MRI scans demonstrating soft tissue mass at the proximal phalanx.

inflammatory markers were normal. Therefore, samples were sent for histopathology as well as microbiology as there was no overt evidence of infection. Microbiology specimens revealed no growth. The histopathology specimens revealed nests of malignant squamoid cells infiltrating the bone and adipose tissue, with mitoses and foci of necrosis; features consistent with SCC. The patient was immediately referred to the tertiary orthopaedic oncology unit. Clinical examination revealed no regional lymphadenopathy either in the popliteal or groin region and staging CT of the chest, abdomen and pelvis did not demonstrate any metastases. The patient successfully underwent a first ray amputation for the Marjolin's SCC of the great toe without requiring neoadjuvant chemotherapy or radiotherapy.

OUTCOME AND FOLLOW-UP

At 9-month follow-up, the wound has healed with no recurrence of infection. The patient is mobilising pain free with the aid of an in-shoe prosthesis (figure 5).

DISCUSSION

Marjolin's ulcer is a rare and aggressive form of SCC arising from chronic non-healing wounds and constitutes only 2% of all SCC. The mean age of diagnosis tends to be near 50 years of age with a 2:1 male-to-female ratio.⁶

Of all cases of SCC involving the lower extremity, only 2.3% of cases affect the toe.² Despite subungual SCC of the toe being a rare occurrence, it is the most common type of malignancy associated with the nail unit.⁷ Dalle *et al* reviewed 35 patients with subungual SCC and reported only seven cases involving the toe, with the remainder involving the finger.⁸ Riddel *et al* reviewed 103 patients with ungual SCC and periungual SCC and reported only eight cases of SCC presenting in the toes.⁹

Valero *et al* reported only 36 cases of SCC affecting the toe from January 1994 to December 2011 with 94% (n=34) of cases affecting a single toe and 69% affecting the hallux. Furthermore,

Figure 5 Clinical photograph following first ray amputation.

the authors reported a 2:1 male-to-female ratio with an average age of presentation of women and men of 52 and 62 years, respectively.³

In approximately 50% of cases reported, the aetiology of subungual SCC was reported as unknown, with the remaining cases due to distant metastases, HPV or chronic infection. Other risk factors for subungual SCC include chemical or physical microtrauma, excessive sunlight exposure and immunosuppression.³

Subungual SCC may originate from a variety of toe locations including the nail bed, nail matrix, nail groove or the lateral nail folds.¹⁰ Patients with subungual SCC may complain of a variety of symptoms from chronic pain, swelling, dyschromia of the nail plate and onycholysis. Patients commonly present with a verrucous appearance of the nail bed and nail dystrophy. Nodularity, bleeding and ulceration can suggest subungual SCC.^{4,5}

Due to the clinical similarities of subungual SCC with several benign conditions including verruca vulgaris, ingrown toenail and onychomycosis, diagnosis can be challenging.^{1,11,12} Furthermore, masking of tumour by nail plate and low awareness by physicians can often lead to initial misdiagnosis and delayed diagnosis.^{4,13} In chronic nail disorders unresponsive to antifungal treatment, biopsy of nail bed should be performed to enable early diagnosis of subungual SCC.

Due to a rich arteriovenous network located in the subungual bed, subungual SCC is associated with a higher risk of local invasion and metastasis.³ The overall metastatic rate and presence of lymphadenopathy of Marjolin's ulcer are 27.5% and 24.4%, respectively.¹⁴ Marjolin's ulcer with a background of osteomyelitis has a 14% metastatic rate.¹⁵

Biopsy of the suspicious lesion is the gold standard for the diagnosis of SCC followed by CT or MRI to exclude a metastatic process. Patients with SCC without bone invasion undergo wide local excision due to low recurrence rate while those with bone invasion usually undergo distal phalanx amputation.¹⁶

In the absence of metastases, the overall survival for patients with Marjolin's ulcer is 65%–75% at 3 years following diagnosis, but can fall to 35%–50% in the presence of metastatic disease.¹⁷

Pavlovic *et al* report a case of a 51-year-old woman with type 1 diabetes who had initially been diagnosed with an ingrown toenail and underwent repeated resection without resolution. The patient underwent complete removal of the entire nail 6 years prior to presentation for presumed chronic osteomyelitis of the right hallux. During her recent presentation, examination revealed an irregular area of granulation tissue in the nail bed with erythema and tenderness. A punch biopsy of the lesion revealed features of Marjolin's ulcer; an aggressive ulcerating SCC presenting in chronically inflamed or traumatised skin with the patient undergoing radiotherapy followed by Mohs micrographic surgery.¹⁸

David and colleagues reported a case of verrucous type SCC of the left great toe presenting with a 6-week history of pain and erythema. The toenail was hypertrophic and plain radiographs revealed severe erosive changes at the medial aspect of the distal phalanx. A total nail plate avulsion was performed revealing white fibrotic soft tissue in the nail bed which was later identified as SCC following histopathology. Following exclusion of metastatic disease, an interphalangeal hallux amputation was performed and the patient did not require further oncological intervention.¹⁹

Holgado and coworkers reported a case of SCC of the hallux in a 75-year-old patient presenting with a hyperkeratotic ulcer at the nail bed of the right hallux. A biopsy revealed poorly differentiated SCC. He previously developed an ulcer over this

region 30 years ago following minor trauma. The patient underwent a hallux disarticulation at the first metatarsophalangeal joint (MTPJ).²⁰

We report a rare case of Marjolin's SCC of the proximal hallux unusually presenting in a female patient with no previous risk factors besides trauma secondary to recurrent surgery for ingrown toenail and distal phalanx amputation. The patient underwent the gold standard biopsy of the hyperkeratotic lesion revealing histopathological features consistent with SCC. Clinical examination revealed no regional lymphadenopathy and staging CT chest, abdomen and pelvis excluded distant metastases and therefore the patient underwent a first ray amputation.

The patient underwent more than 10 years of management for recurrent infections in an ingrowing toenail and had been applying daily dressings for many years prior to her first referral to orthopaedics. Marjolin's SCC was not suspected during this time as the toe was always infected and discharging as one would expect with an ingrowing toenail. However, she failed to settle despite radical debridement and even partial amputation. Each surgery was complicated by a postoperative infection.

When she re-presented there was no overt infection and so MRI scan was requested that revealed a mass without signs of infection. Histopathology samples were therefore taken and these confirmed the presence of malignancy.

This case confirms the importance of investigation with bloods, MRI and most importantly histopathology in cases of long-standing infection no matter whether the appearances are consistent with the expectations for the condition.

Learning points

- ▶ Marjolin's ulcer is a rare and aggressive form of squamous cell carcinoma (SCC). SCC affecting the toe is rare accounting for only 2.3% of SCC cases involving the lower extremity.
- ▶ In 50% of cases, the exact aetiology is unknown, while other causes for SCC affecting the toe include microtrauma, distant metastases, human papilloma virus or chronic infection.
- ▶ Clinical presentation includes chronic pain, swelling, dyschromia of the nail plate and onycholysis. A verrucous appearance of the nail bed and nail dystrophy may also be seen along with nodularity, bleeding and ulceration of the lesion.
- ▶ Due to clinical similarities to benign conditions including ingrown toenail, it is important to be aware of Marjolin's SCC as a potential differential diagnosis when treating patients with recurrent ingrown toenail.
- ▶ We recommend that patients with recurrent ingrown toenail or ulceration with a background of chronic infection and inflammation have biopsies performed to exclude potential malignancy including Marjolin's SCC.

Contributors WA was responsible for writing the paper, collecting photographs, and radiographs. BJON was responsible for editing the paper and literature review. AP was responsible for planning and conceptualisation of the paper, and is the consultant treating this particular patient.

Competing interests None declared.

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REFERENCES

- 1 Patel DU, Rolles R. Squamous cell carcinoma of the nail bed. *J Am Podiatr Med Assoc* 1995;85:547–9.
- 2 Arlen D, Kott ET. Squamous cell carcinoma. A case history. *J Am Podiatr Med Assoc* 1994;84:409–10.
- 3 Valero J, Gallart J, Gonzalez D, *et al.* Subungual squamous cell carcinoma and exostosis in third toe—case report and literature review. *J Eur Acad Dermatol Venereol* 2014;28:1292–7.
- 4 Meesiri S. Subungual squamous cell carcinoma masquerading as chronic common infection. *J Med Assoc Thai* 2010;93:248–51.
- 5 Ruiz Santiago H, Morales-Burgos A. Cryosurgery as adjuvant to Mohs micrographic surgery in the management of subungual squamous cell carcinoma. *Dermatol Surg* 2011;37:256–8.
- 6 Kowal-Vern A, Criswell BK. Burn scar neoplasms: a literature review and statistical analysis. *Burns* 2005;31:403–13.
- 7 Carroll RE. Squamous cell carcinoma of the nail bed. *J Hand Surg Am* 1976;1:92–7.
- 8 Dalle S, Depape L, Phan A, *et al.* Squamous cell carcinoma of the nail apparatus: clinicopathological study of 35 cases. *Br J Dermatol* 2007;156:871–4.
- 9 Riddel C, Rashid R, Thomas V, Val T. Ungual and periungual human papillomavirus-associated squamous cell carcinoma: a review. *J Am Acad Dermatol* 2011;64:1147–53.
- 10 Yip KM, Lam SL, Shee BW, *et al.* Subungual squamous cell carcinoma: report of 2 cases. *J Formos Med Assoc* 2000;99:646–9.
- 11 Gómez Vázquez M, Navarra Amayuelas R, Martín-Urda MT, *et al.* [Subungual squamous cell carcinoma. presentation of two cases]. *Actas Dermosifiliogr* 2010;101:654–6.
- 12 Lai CS, Lin SD, Tsai CW, *et al.* Squamous cell carcinoma of the nail bed. *Cutis* 1996;57:341–5.
- 13 Kelly KJ, Kalani AD, Storrs S, *et al.* Subungual squamous cell carcinoma of the toe: working toward a standardized therapeutic approach. *J Surg Educ* 2008;65:297–301.
- 14 Kerr-Valentic MA, Samimi K, Rohlen BH, *et al.* Marjolin's ulcer: modern analysis of an ancient problem. *Plast Reconstr Surg* 2009;123:184–91.
- 15 Tobin C, Sanger JR. Marjolin's Ulcers: A Case Series and Literature Review. *Wounds* 2014;26:248–54.
- 16 David MG, Stumph J, David BM. Primary squamous cell carcinoma of the distal hallux. *J Am Podiatr Med Assoc* 2013;103:149–51.
- 17 Lack W, McKinley T. Marjolin's ulcer: incidental diagnosis of squamous cell carcinoma on hemipelvectomy for recalcitrant pelvic osteomyelitis. *Iowa Orthop J* 2010;30:174–6.
- 18 Pavlovic S, Surowiec D, Branicki M. Marjolin's ulcer of the hallux. *J Am Podiatr Med Assoc* 2013;103:250–3.
- 19 David MG, Stumph J, David BM. Primary squamous cell carcinoma of the distal hallux. *J Am Podiatr Med Assoc* 2013;103:149–51.
- 20 Holgado RD, Ward SC, Suryaprasad SG. Squamous cell carcinoma of the hallux. *J Am Podiatr Med Assoc* 2000;90:309–12.

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