The case of the autoamputating toe: was it the SCC?

KEY WORDS
- Autoamputating
- Cutaneous Squamous Cell Carcinoma
- Toe
- Wound

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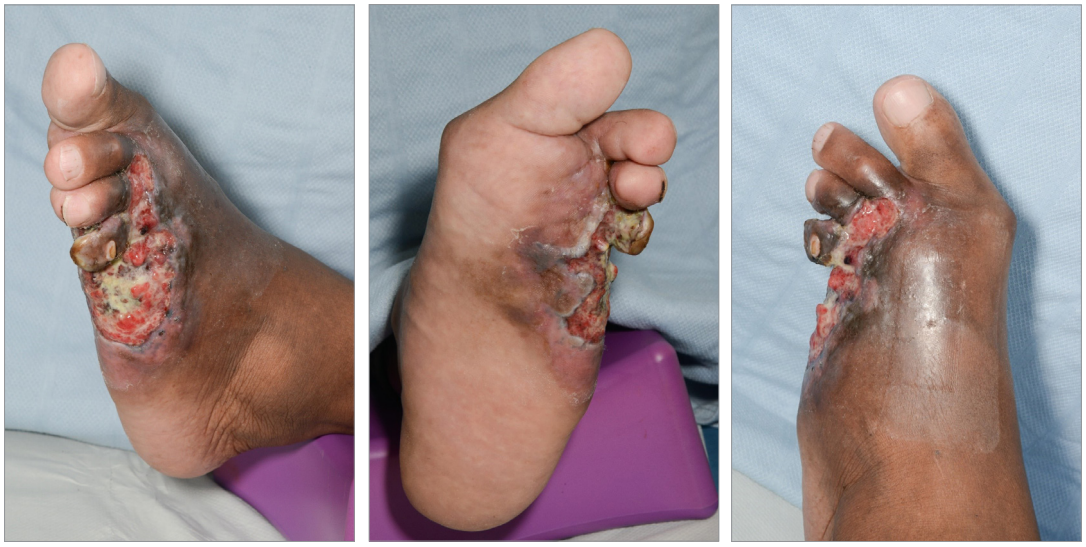
Cutaneous Squamous Cell Carcinoma (cSCC) is a rapidly growing tumour arising in the keratinocytes of the epidermis and is the most common skin cancer among African Americans and Asian Indians. We present the case of a 61-year-old Afro-Caribbean man who was referred to the Diabetic Foot Clinic with concerns about a superficial non-healing ulcer to the lateral aspect of the left foot of a 6-year duration. The patient reported autoamputation of the fifth digit at the time of presentation to our clinic. Over the previous years, he had been seen twice in primary care, and three times in secondary care services. Shortly after clinic review, he underwent incisional biopsy due to suspicion of Pyoderma gangrenosum, this showed an invasive squamous cell carcinoma. CT imaging was negative for metastatic visceral or nodal spread. Subsequently, he underwent amputation to the level of the ankle joint and analysis of intraoperative specimens confirmed poorly differentiated squamous cell carcinoma with infiltration of the skeletal muscle and bony tissue planes. The primary aim of this case report is to highlight the possibility of autoamputation due to invasive cSCC and the importance of biopsy in the case of non-healing and atypical ulcerative skin lesions.

Cutaneous squamous cell carcinoma (cSCC) is usually a rapidly growing tumour arising in the keratinocytes of the epidermis (Gordon, 2013). cSCC is the most common skin cancer among African Americans and Asian Indians, and the second most common skin cancer among Hispanics and Chinese/Japanese Asians thereby representing 30–65% of skin cancers in dark-skinned people and only 15–25% in whites (Gloster and Neal, 2006). In African-Americans, cSCCs have a greater tendency to occur in non-sun-exposed sites such as the feet, and often present at a more advanced disease stage at the time of diagnosis (Kim et al, 2009).

The clinical presentation can be variable ranging from a small nodule, ulcerating sloughing plaque or an exophytic lesion (Alam and Ratner, 2001; Ridky, 2007; Potter et al, 2009; Mirigliano et al, 2011). Autoamputation due to SCC has previously described in the literature, however, these cases have reported on autoamputation of the penis (Hasham, 1975; Chiu et al, 2009; Garg et al 2018) and tongue (Patel et al, 2001). The aetiology of autoamputation of the digits (specifically of the fifth toe) has been previously reported and is most frequently attributed to gangrene (due to diabetes, peripheral vascular disease, vasculitis, cryoglobulinaemia (Fang and Huang, 1997; Ott et al, 1998; Al Wahbi, 2008; Zhang et al 2021) ainhum and pseudoainhum (Morand and Lightburn, 2002; Arkush et al, 2016) frostbite (Poulakidas et al 2008) and acute constriction ring syndrome (Singh et al, 2008).

To our knowledge, and following a literature search, cSCC invasion involving the foot with digit autoamputation (in the absence of osteomyelitis) has not been reported. We cannot definitively state that the cutaneous malignancy was the cause of the autoamputation, however, this is our clinical suspicion. Therefore, we report herein an unusual case of a 61-year-old Afro-Caribbean man presenting with an extensive ulceration lesion of the left foot plus autoamputation of the fifth toe, with no plausible aetiology other than invasive cSCC of six-year duration.

"...the nail of the fifth toe came away, the toe subsequently decreased in size until complete autoamputation 36 months later."



Figures 1. The left foot demonstrating a large fungating wound covering the lateral to mid-dorsum of the left foot measuring 93mm x 56mm to a depth of 2mm, note absence of the fifth digit

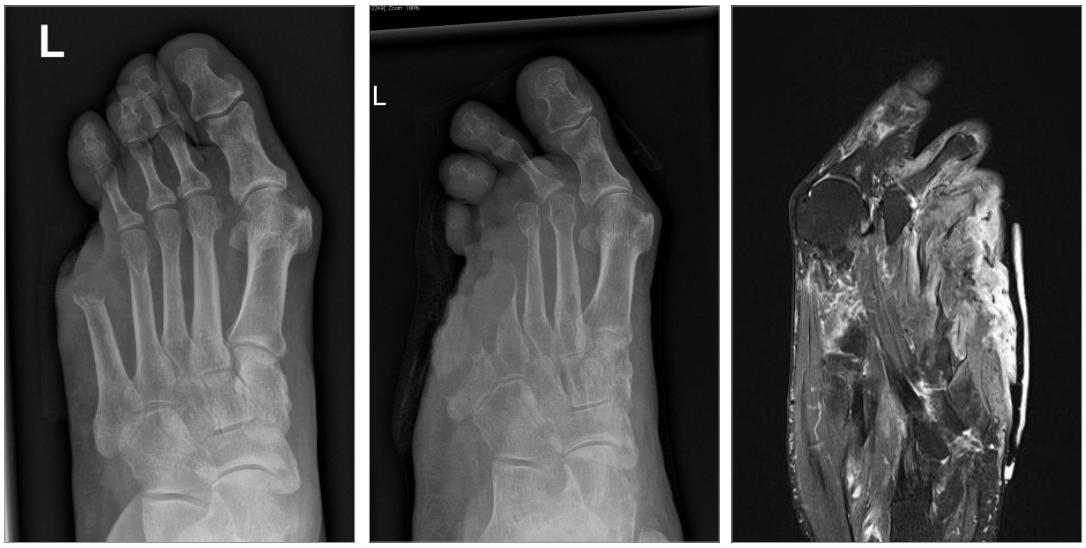


Figure 2. Plain AP radiograph of the left foot. A from December 2019 showing amputation of the distal phalanx of the 5th digit with destruction of the head of the 5th metatarsal plus associated skin defect and swelling of local soft tissues. B from June 2021 showing destruction now extending to the base of the 5th metatarsal with new destructions of the 4th metatarsal, head and neck of the 3rd metatarsal, and phalanges of the 3rd and 4th digits. C from June 2021 (axial view, Fat sat PD sequence) showing destruction of the 3rd, 4th and 5th metatarsals with destruction of the 3rd, 4th and 5th digits with an extensive ill-defined soft tissue mass replacing normal foot architecture

CASE PRESENTATION

A 61-year-old Afro-Caribbean man with a history of inflammatory oesophagitis, hydrocele repair and sigmoid colectomy (for invasive adenocarcinoma T1bN0Mx), was referred to the Diabetic Foot Clinic in May 2021 with concerns about a superficial non-healing ulcer to the lateral aspect of the left fifth foot.

The patient reported that six years before clinic attendance, the nail of the fifth toe came away, the toe subsequently decreased in size until complete autoamputation 36 months later. The patient denied any history of trauma to the nail or toe, long-standing wounding or inflammation, or chronic infection. Of note, the patient denied any pain associated with

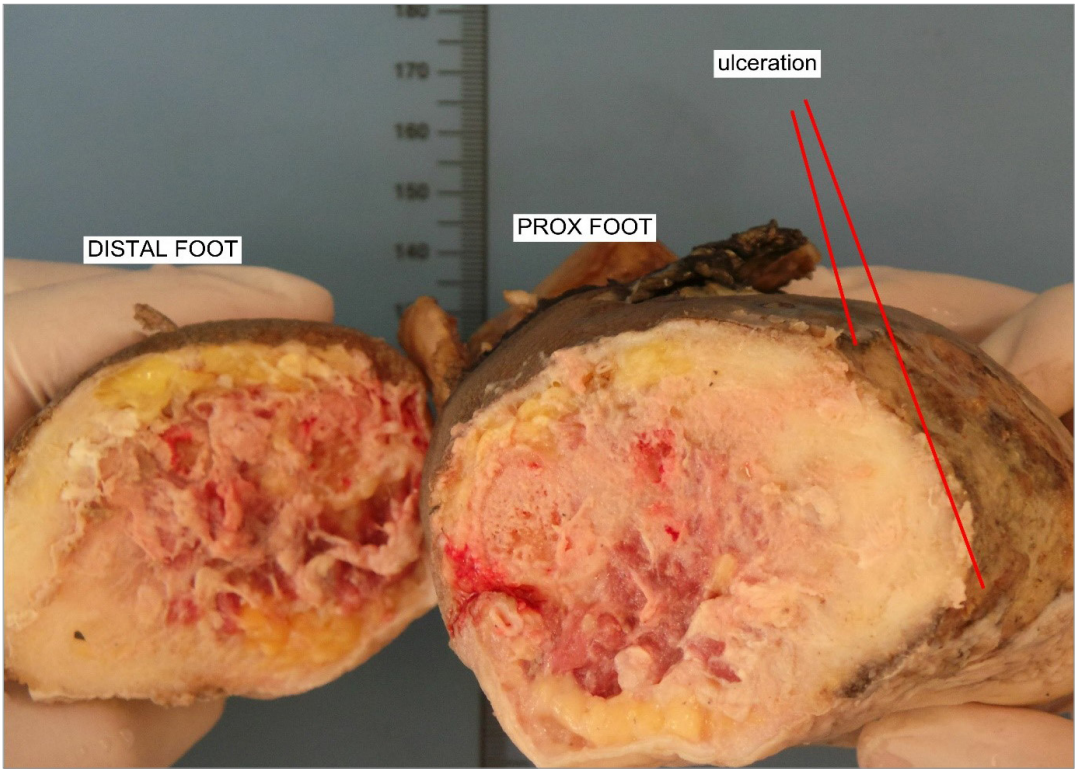


Figure 3. Macroscopic view of the amputated foot. Image shows a single coronal slice through the mid-foot

autoamputation or the non-healing skin lesion.

Over the 6-year period, the patient presented twice to his GP and three times to various secondary services. Diagnoses included diabetic ulcer, osteomyelitis, peripheral vascular disease and pyoderma gangrenosum. However, inflammatory markers were within normal range, HbA1c showed pre-diabetes only, and there was no neurovascular deficit of the distal lower limbs on assessment in vascular clinic. Vasculitis, blood-borne virus and haematological malignancy screens were negative.

On clinical examination in the diabetic foot clinic, there was a large fungating wound covering the lateral to mid-dorsum of the left foot measuring 93mm x 56mm to a probing depth of 2mm, with noted absence of the fifth digit *(Figure 1)*.

Plain radiographic imaging of the left foot in 2019 reported amputation of the distal phalanx of the 5th toe, destruction of the head of the 5th metatarsal with associated skin defect and swelling of local soft tissues *(Figure 2A)*, likely representing osteomyelitis. Repeat radiography in June 2021 showed local progression *(Figure 2B)*. MRI at the same time *(Figure 2C)* demonstrated an extensive lytic process involved the 3rd, 4th and 5th toes with mid-shaft amputation of the 4th and 5th metatarsals, erosion of the 3rd metatarsal and marked soft tissue oedema on the anterolateral part of the foot. Again, the findings were erroneously reported as long-standing osteomyelitis with pastoperative amputations.

The patient subsequently underwent an incisional biopsy due to suspicion of pyoderma gangrenosum. Histopathological examination of a 6x5mm strip of tissue revealed an invasive moderate to poorly differentiated squamous cell carcinoma of at least 1.7mm in depth. CT imaging was negative for metastatic visceral and nodal spread.

He was discussed with the Dermatology and Plastic Surgery teams and a recommendation for foot amputation under spinal anaesthesia to achieve local control was made. Intraoperatively, the patient received intravenous antibiotics and a 2cm margin around the tumour was marked. The patient underwent a successful Syme procedure with amputation to the level of the ankle joint with preservation of the heel pad and creation of a standing cone deformity. *Figure 3* shows the macroscopic specimen of the amputated foot. Intraoperatively, approximately 200mls of blood loss was recorded. The wound was sutured closed and a 12F drain was left *in situ* for 96 hours postoperatively. He made an uneventful recovery

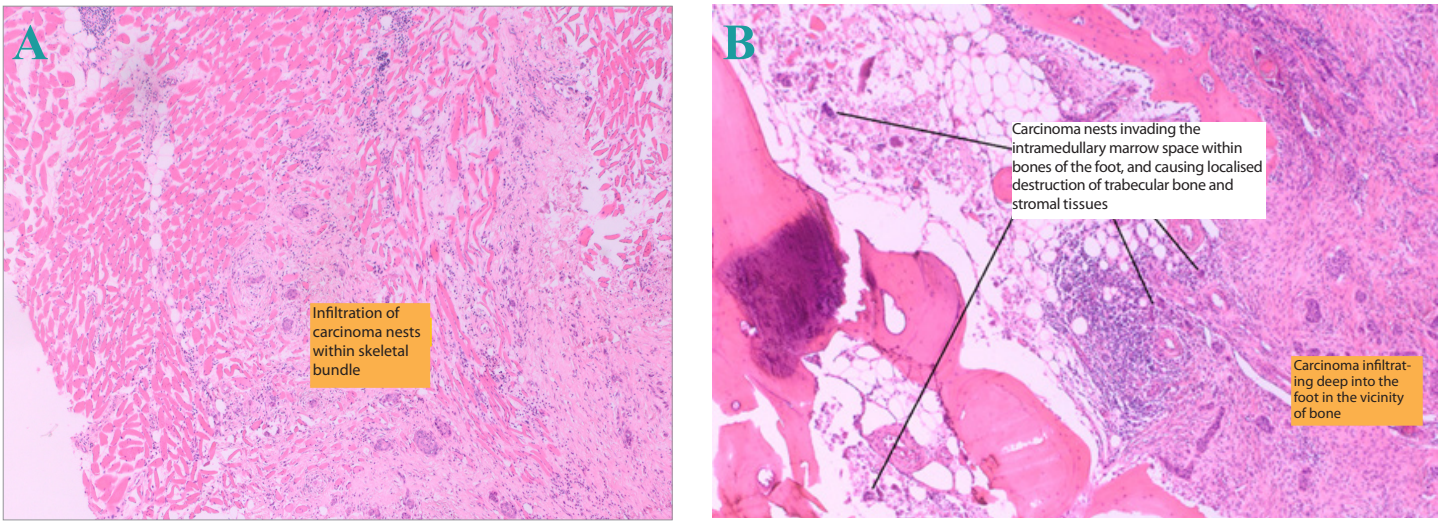


Figure 4. Microscopic x40 magnification, H&E stained histological specimen. Shows a poorly differentiated squamous cell carcinoma composed of small nests and clusters of destructive, malignant cells. There is infiltration into skeletal muscle (A) and bony tissue planes, including the intramedullary space (B)

and is undergoing regular dressings with the Plastics team will be reviewed by the operating surgeon 6 weeks postoperatively.

Subsequent histological analysis showed a poorly differentiated squamous cell carcinoma, composed of small nests and clusters of destructive, malignant cells, present within the ulcer base, underlying the ulcer and further infiltrating within deeper tissue planes of the amputation specimen. Central necrotic debris and abnormal keratin formation were noted in many of these malignant nests, the latter of which confirmed the aetiology to be that of a squamous cell carcinoma. Tumour was confirmed to infiltrate skeletal muscle *(Figure 4A)* and bony tissue planes, including the intramedullary space *(Figure 4B)*.

DISCUSSION

cSCC is the most frequently encountered malignancy of the distal lower extremity (Alam and Ratner, 2001; Ridky, 2007; Potter et al, 2009; Mirigliano et al, 2011). The differential diagnoses for cSCC of the foot include actinic keratosis, keratoacanthoma, squamous cell carcinoma *in situ*, basal cell carcinoma, verruca plantaris, pyoderma gangrenosum, psoriasis, repetitive trauma, infection (bacterial and/or fungal), amelanotic melanoma, sarcoma and Hodgkin's disease (Alam and Ratner, 2001; Ridky, 2007; Mirigliano et al, 2011; Monaco et al, 2015). Importantly, cSCC of the lower extremity has a high likelihood for metastases (up to 30%) and early diagnosis is critical with regional lymph node involvement occurring in 85% of cases.

Bone invasion of SCC is well-documented as a sequelae of oral cavity SCC (OCSCC) (Gilbert et al, 1986; Pandey et al 2007), however, bony invasion by SCC to regions other than the head and neck, is very rare. A small number of studies have reported on the finding of bony invasion of locally invasive cSCCs (Essig et al, 2013; Dika et al 2015; Li et al, 2015; Handler and Goldberg, 2018), however, these studies commonly report bony invasion in the presence of underlying osteomyelitis (Altay et al, 2004; Li et al 2014; Jiang et al, 2020). No previous studies have reported on digit autoamputation as a complication of locally invasive cSCC. Possible cellular and molecular mechanisms of osteoinvasion as reported in studies of invasive OCSCC include increased expression of interleukin (IL)-6, IL-11, tumour necrosis factor-α (TNF-α) and parathyroid hormone-related protein (PTHrP) (Jimi et a, l2011). Increased expression of these cancer-related cytokines lead to expression of receptor activator of NF-jB ligand (RANKL) or suppression of osteoprotegerin (OPG) leading to increased osteoclastogenesis (Jimi et al, 2011).

Given our findings, plain film radiography to assess for bony involvement is paramount in the setting of limb cSCC. Furthermore, magnetic

resonance imaging and computed tomography should be performed to assess tumour margins and to determine local, regional or distal involvement. Possible treatment modalities of cSCC of the distal extremities include electrodessication and curettage, cryosurgery, wide surgical excision, Mohs micrographic surgery, amputation and radiotherapy. If indicated, amputation should attempt to achieve R0 excision with preservation of limb function, however, the level of amputation will depend on the tumour grade and size. Importantly, intraoperative lymph node biopsy or dissection is indicated if there is suspicion, or confirmation of, metastasis (Altay et al, 2004; Ridky, 2007; Ross and Schmults, 2006).

CONCLUSION

Cutaneous squamous cell carcinoma is a rare lesion found in the lower extremity and studies have reported different aetiologies (Altay et al, 2004; Potter et al, 2009), however, a unifying feature appears to be that of diagnostic delay, with a range of 4 to 50 years reported (Altay et al, 2004). cSCC can have devastating implications when there is a delay in diagnosis and treatment as demonstrated in this case, whereby digit autoamputation was likely a direct consequence of bony invasion of undiagnosed and untreated cSCC. Non-healing and atypical ulcerative skin lesions of long duration should raise clinical suspicions and a biopsy should be performed to exclude underlying malignancy. WUK

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