

Malignant melanoma or diabetic foot syndrome?

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Clinicians need to be aware that unusual foot ulceration presenting in people with diabetes may not be diabetic foot syndrome, and alternative diagnoses may need to be considered. Most foot lesions in people with diabetes, neuropathy and/or peripheral arterial disease meet the criteria for diabetic foot syndrome. However, people with diabetes may also present with viral warts, allergic lesions such as rash, oedema and redness, or manifestations of systemic illness affecting their feet. The case described here highlights the risk of a cancer lesion presenting as an unusual foot ulcer.

Ulcer healing in people with diabetic foot is usually a long process (Tsourdi et al, 2013): neurogenic ulcers, for example, take 5–6 months to heal. No improvement in the affected area within this timeframe suggests the presence of osteolysis, insufficient blood supply or inadequate pressure offloading to the foot (Kruse and Edelman, 2006). Occasionally, standard management does not lead to healing of the ulcer. In these cases, referral to a dermatologist or oncologist is advised.

Case report

A 69-year-old man was referred to the diabetic foot clinic at the University Hospital in Warsaw (Centralny Szpital Kliniczny), Poland, in 2012. He had a 6-year history of diabetes and for the last 5 years had been treated with insulin.

He had been diagnosed with diabetes when he presented with a lesion on his left foot in 2006. The lesion had the appearance of a skin abrasion just below the left medial ankle, and over time it became raspberry coloured; however, there was no ulceration. He was treated by the dermatologist for 2 years (with ointments initially, and then with hyperbaric oxygen therapy), and then by the surgeon for 4 years (with surgical debridement).

In 2012 the patient fell from a chair and sustained a fracture of the left heel bone. On examination the area was found to be tender, swollen and reddened and the skin lesion was granulating. The orthopaedic

consultant withheld fixation owing to the presence of the lesion; the only treatment given was a cast to immobilise the foot. After the cast was removed, the patient returned to the surgical clinic for further treatment of the skin lesion.

In 2012 the patient complained of difficulty in walking, pointing to his left hip joint. Ultrasound examination revealed a hyperechogenic, vessel-rich mass (62 × 40 mm) compressing the left femoral artery and vein. This was thought to be a pathological lymph node. The differential diagnosis included lymphadenopathy due to a long-standing foot lesion, but lymphoma and melanoma also needed to be excluded. Another enlarged lymph node was found in the popliteal fossa (22 × 10 mm). Lymph node biopsy was ordered.

In the mean time the patient was referred to the diabetic foot clinic at the University Hospital in Warsaw. Examination revealed a lesion on the medial surface of the left foot just below the ankle and spreading to the plantar lateral part of the foot. It presented as a round, raspberry-coloured infiltration with no features of an ulcer (*Figure 1*). No surgical procedures were performed at that time.

Examination of skin sensation using a neurothesiometer revealed normal temperature sensation, minimal impairment of pain and pressure sensation, and severe impairment of vibration sensation on the side of the lesion (changes on the opposite side were minimal; *Table 1*).

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Article points

1. Unusual foot ulceration presenting in people with diabetes may not be diabetic foot syndrome, and other diagnoses, such as cancer (e.g. melanoma), may need to be considered.
2. Factors that suggest alternative diagnoses are significant delay or lack of treatment progress after standard management, asymmetry, unusual colour, and diameter and lymph node enlargement.
3. This case report describes a person with diabetes who presented with a foot lesion that was unusual because no typical ulceration was present, and which eventually proved to be nodular malignant melanoma.

Key words

- Diabetes
- Diabetic foot
- Malignant melanoma
- Ulceration

Authors

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Page points

1. Diabetic foot may present as ulceration, infection and destruction of tissue below the ankle in people with diabetes, with accompanying neuropathy and atherosclerosis.
2. Ulceration and infection are the most common presentations.
3. Neurogenic ulcers may be treated by debridement, achieved surgically (by scalpel or waterjet), biologically (by *Lucilia sericata* larvae) or, rarely, enzymatically.
4. Foot lesions presenting in people with diabetes that lack the typical features of ulceration should always point to an alternative diagnosis, especially if the response to standard treatment (ischaemia exclusion, antimicrobial therapy, pressure offloading) is slower than expected.

Blood flow in the arteries of the left foot was estimated by mini-Doppler. This revealed middle membrane stiffness (increased ankle-brachial pressure index, increased blood pressure in the arteries of the left foot, vessels non-compressible).

Transdermal measurement of arterial partial pressure of oxygen was optimal for ulcer healing (mean tpO_2 , 59.48 mmHg).

Bone X-ray showed malformation of the left talus, cuboid and heel bone (irregular outline and heel bone remodelling) consistent with previous fracture (Figures 2–5). However, these features are also suggestive of resorption typical of neuroarthropathy. There were no laboratory findings indicating inflammation (white blood cell count and C-reactive protein level were within normal limits) or renal failure (serum creatinine level was 0.77 mg/dL). Urine was negative for protein. Glycated haemoglobin level indicated relatively satisfactory glycaemic control of diabetes (HbA_{1c} 7.4% [57 mmol/mol]). At the time, the patient was being managed with intensive insulin therapy (human insulin) and a full dose of metformin (1000 mg three times a day).

Histopathological examination of a tissue sample from the lesion revealed malignant melanoma with necrosis. The lesion was resected, along with

inguinal, iliac and obturator lymph nodes. The final histopathological diagnosis was nodular malignant melanoma type pT4bN3 with ulceration, angioinvasion, Breslow depth 14 mm, without lymphocytic invasion or symptoms of regression. Metastases to inguinal, iliac and obturator lymph nodes were found.

The excision wound was covered with Codogard® polyurethane absorption dressing (Figure 6). The patient is currently under the care of the oncology clinic.

Discussion

Diabetic foot may present as ulceration, infection and destruction of tissue below the ankle in people with diabetes, with accompanying neuropathy and atherosclerosis (International Working Group on the Diabetic Foot/Consultative Section of the IDF, 2007). Ulceration and infection are the most common presentations.

Neurogenic ulcers may be treated by debridement, achieved surgically (by scalpel or waterjet), biologically (by *Lucilia sericata* larvae) or, rarely, enzymatically (Tantawi et al, 2007).

This case report describes a lesion that was unusual for diabetic foot syndrome because no typical ulceration was present. Such lesions should always point to an alternative diagnosis, especially if the response to standard treatment (ischaemia exclusion, antimicrobial therapy, pressure offloading) is slower than expected.

Only 4% of all malignant skin lesions are melanoma; however, melanoma carries a high mortality of 80% (Franke et al, 2000; Torres et al, 2010). Diabetes increases the risk of melanoma, especially in women (Bell et al, 1987). A correlation has been shown between the presence of glycation products and their receptors and the incidence of melanoma and its metastases (Abe et al, 2004).

An ABCD(E) system has been proposed for the early diagnosis of melanoma, where A stands for asymmetry, B for irregular borders, C for irregular pigment distribution and D for a diameter of >5 mm or rapid growth (Dynamic); E is occasionally used to describe elevation of the lesion (Garbe et al, 2008).

Another indication for histopathological examination is persistent lymphadenopathy without inflammation within the lesion. The patient described here had these unusual features. Long-



Figure 1. Appearance of the lesion on the left foot at admission.

Table 1. Sensation assessment using a neurothesiometer

Area tested	Result (volts)	Normal value (volts)	Area tested	Result (volts)	Normal value (volts)
Left toe	220	15.0	Right toe	35	15.0
Left medial ankle	145	20.0	Right medial ankle	100	20.0
Left lateral ankle	160	25.0	Right lateral ankle	70	25.0

lasting course, atypical macroscopic presentation and lymphadenopathy require further investigation.

According to the American Cancer Association/International Union Against Cancer, a suspected melanoma should be excised completely and examined. Fine- or core-needle biopsy, or other partial sampling of the lesion, should be avoided because of unreliable results (Balch et al, 2009). Standard treatment of skin melanoma consists of surgical excision and biopsy of the sentinel node. No additional treatment is required (Krzakowski et al, 2011). Quarterly follow-up with complete skin examination is recommended for the next 2 years.

A separate issue in this case described here is the radiological studies. The images may suggest bone resorption due to diabetic neuroarthropathy, but it is known that the patient sustained a fracture, which can directly trigger bone resorption. The persistent nature of the lesion and the presence of inflammation could also contribute to osteolysis. The radiological appearance could result from all these factors. The observed abnormalities disappeared 22 months after the fracture, suggesting that they were not melanoma-related.

Conclusion

Unusual presentation and biology of foot ulceration should point away from a diagnosis of diabetic foot syndrome and prompt consideration of other conditions, including cancer (e.g. melanoma).

Factors that suggest alternative diagnoses are significant delay or lack of treatment progress after standard management (exclusion of ischaemia, antimicrobial therapy, pressure offloading), asymmetry, unusual colour, and diameter and lymph node enlargement. People with diabetes are at risk of developing melanoma. Delay in diagnosis may lead to the spread of lesions, or limb amputations in the case of distal changes. ■

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Figure 2. X-ray of the left foot 8 months post fracture.



Figure 4. X-ray of the left foot 22 months post fracture.

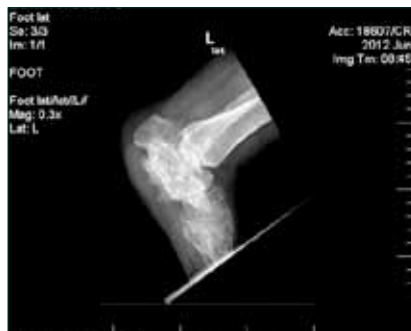
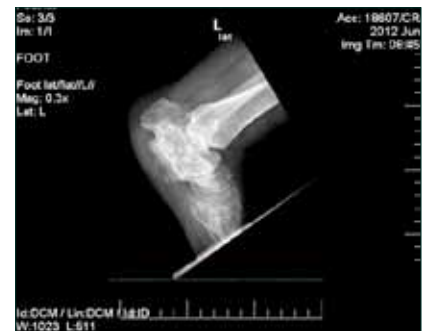


Figure 3. X-ray of the left foot 8 months post fracture.



Figure 5. X-ray of the left foot 22 months post fracture.



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Figure 6. Excision wound covered with Codogard® following oncological treatment of the lesion.