Irritated seborrhoeic keratosis masquerading as malignancy on $^{18}$F-fluorodeoxyglucose positron emission tomography–computed tomography

ABSTRACT
Seborrhoeic keratosis is a common benign skin tumor and can have a variable presentation. Irritated seborrhoeic keratosis can clinically mimic cutaneous malignancy and often warrant biopsy. $^{18}$F-fluorodeoxyglucose ($^{18}$F-FDG) positron emission tomography–computed tomography (PET-CT) can give false-positive results in many cutaneous pathologies. We present an interesting case of irritated seborrhoeic keratosis masquerading as skin cancer, clinically as well as on $^{18}$F-FDG PET-CT.

Keywords: $^{18}$F-fluorodeoxyglucose, malignancy, positron emission tomography-computed tomography, seborrhoeic keratosis

INTRODUCTION
Seborrhoeic keratosis is the most common benign epidermal skin tumor, most prevalent in people older than 50 years. It is caused by a benign proliferation of immature keratinocytes resulting in round or oval macules. Although it is a benign lesion with specific characteristics, there can be morphological overlap with malignancy. $^{18}$F-fluorodeoxyglucose ($^{18}$F-FDG) positron emission tomography–computed tomography (PET-CT) is now an integral part of cancer imaging. Unfortunately, $^{18}$F-FDG is a nonspecific radiotracer. False-positive $^{18}$F-FDG PET-CT findings have been seen for many benign skin lesions. We present an interesting case of a 55-year-old male with irritated seborrhoeic keratosis masquerading as cutaneous malignancy, clinically as well as on PET-CT.

CASE REPORT
A 55-year-old male with comorbidities of diabetes mellitus, chronic obstructive pulmonary disease, and hypertension presented at our hospital with a large area of irregular, ulcerated, inflamed, circumferential marked thickening in the skin of the lower half of the left leg, with hyperpigmentation and focal areas of bleeding. In addition, he complained of pruritus. While he gave a history of eczematous dermatitis at the same site of many years, there was a significant deterioration in the past few months. Apart from the skin lesion, clinical examination also revealed left inguinal lymphadenopathy. Suspecting skin malignancy based on clinical findings, a biopsy was done which was inconclusive. $^{18}$F-FDG PET-CT was then performed to characterize the skin lesion and assess extent of the disease [Figure 1a-d]. It showed $^{18}$F-FDG-avid ulceroproliferative circumferential cutaneous thickening involving the lower half of the left leg.
Sharma: PET-CT in seborrhoeic keratosis

Figure 1: On baseline positron emission tomography–computed tomography (a-d), the maximum intensity projection positron emission tomography image (a) shows focal areas of increased $^{18}$F-fluorodeoxyglucose uptake in the lower half of the left leg (arrow) and the left inguinal region (broken arrow). No other abnormal $^{18}$F-fluorodeoxyglucose uptake is seen in the rest of the body. Transaxial (b) and coronal (c) positron emission tomography–computed tomography images of the left leg demonstrate $^{18}$F-fluorodeoxyglucose avid, ulceroproliferative circumferential cutaneous thickening (arrows) without any definite involvement of underlying muscles and bones. Transaxial positron emission tomography–computed tomography images (d) also show left inguinal $^{18}$F-fluorodeoxyglucose-avid lymphadenopathy (broken arrow). The follow-up positron emission tomography–computed tomography done after 8 months (e-h) shows similar findings, but the reduction in $^{18}$F-fluorodeoxyglucose avidity of both cutaneous lesion (f, g, arrows) and left inguinal node (h, broken arrow).

leg, with a length of 19.7 cm and the maximum thickness of 1.9 cm (maximum standardized uptake value [SUVmax]: 11.5) along with $^{18}$F-FDG avid left inguinal lymphadenopathy, measuring 2.7 cm × 2.6 cm (SUVmax: 5.2). No other metastatic lesion was suspected in the rest of the body. The patient was then planned for surgical excision of the skin lesion with left inguinal nodal dissection, after on table frozen section. The patient refused surgery at that time and lost to follow-up. He presented eight months later with the same complaint, but increased oozing from the skin lesion. $^{18}$F-FDG PET-CT was again performed for restaging, before planning the surgery [Figure 1e-h]. The second PET-CT showed similar findings as before, with no significant change in length (18.9 cm) and some increase in the thickness of cutaneous lesion (2.1 cm) and no significant change in nodal size (2.6 cm × 2.5 cm); however, interval reduction of $^{18}$F-FDG uptake was seen at both sites (SUVmax: 9.1 and 4.6, respectively). Since there was a reduction of $^{18}$F-FDG uptake and relatively stable size without any anticancer treatment over a relatively long follow-up period, suspicion of some benign skin pathology was raised on PET-CT, and rebiopsy was advised. Repeat biopsy from the skin lesion showed hyperkeratosis, focal parakeratosis, acanthosis, papillomatosis consisting of horn cysts, and exocytosis in the epidermis, with dermis showing moderate perivascular and peridendneal chronic inflammatory infiltrate and edema, suggesting irritated seborrhoeic keratosis. There was no evidence of dysplasia or malignancy. Fine-needle aspiration cytology from the left inguinal node also showed inflammatory changes. The patient was then managed conservatively, with symptomatic improvement. He is scheduled for ablative therapy for the skin lesion.

DISCUSSION

Seborrhoeic keratosis results from benign clonal expansion of epidermal keratinocytes, with a possible correlation with fibroblast growth factor receptor 3 and or PIK3CA oncogenes. There are various subtypes of seborrhoeic keratosis, including acanthotic, hyperkeratotic, clonal, adenoid, irritated, and melanoacanthoma. Sudden appearance of multiple seborrhoeic keratoses, also called a sign of Leser–Trelat, is a hallmark of internal malignancy. As seborrhoeic keratosis is easily identifiable on clinical examination and dermatoscopy, biopsy is usually not performed. However, for lesions presenting with atypical features or in irritated seborrhoeic keratosis, the biopsy is done to rule out malignancy.

On $^{18}$F-FDG PET-CT, seborrhoeic keratosis can have a variable appearance, though literature in this regard is sparse. Kariya et al. have reported that high $^{18}$F-FDG avidity can be seen in some seborrhoeic keratoses, which is associated with high expression of glucose transporter 1 and 3 (GLUT 1 and GLUT 3), while poor expression of GLUT 1 and GLUT 3 is seen in non-$^{18}$F-FDG-avid seborrhoeic keratosis and normal skin. Among GLUT 1 and GLUT 3, the latter was more specifically expressed in $^{18}$F-FDG-avid seborrhoeic keratosis. Merklen-Djafri et al. have also...
reported a case where false-positive high $^{18}$F-FDG uptake was seen in seborrhoeic keratosis in a case of esophageal carcinoma, raising suspicion of metastasis.[7] However, no GLUT 1 expression was seen in that case. The reasons for this variable GLUT expression in seborrhoeic keratosis remain unknown. As irritated seborrhoeic keratosis also shows dermal perivascular and periadnexal inflammatory cells infiltrate, it is expected to demonstrate high $^{18}$F-FDG uptake, as was seen in the present case. High $^{18}$F-FDG uptake by inflammatory cells is a widely known phenomenon,[8] and has expanded the scope of PET-CT to infective and inflammatory diseases. However, in the present case, to what extent de novo epidermal changes and dermal inflammatory cells contributed to the total $^{18}$F-FDG uptake is unclear, warranting further research.

Most of the patients with seborrhoeic keratosis do not need any treatment; however, it is often opted for because of cosmetic reasons. The treatment modalities include removal of the lesion with cryotherapy, laser or shave excision, or application of topical agents such as hydrogen peroxide.[3,5]

In conclusion, irritated seborrhoeic keratosis can mimic skin cancer, clinically as well as on PET-CT and should be kept in mind as a differential diagnosis when evaluating $^{18}$F-FDG-avid suspicious cutaneous lesions.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Hafner C, Vogt T. Seborrheic keratosis. J Dtsch Dermatol Ges 2008;6:664-77.
2. Metser U, Tau N. Benign cutaneous and subcutaneous lesions on FDG-PET/CT. Semin Nucl Med 2017;47:352-61.
3. Jackson JM, Alexis A, Berman B, Berson DS, Taylor S, Weiss JS. Current understanding of seborrhoeic keratosis: Prevalence, etiology, clinical presentation, diagnosis, and management. J Drugs Dermatol 2015;14:1119-25.
4. Narala S, Cohen PR. Cutaneous T-cell lymphoma-associated Leser-Trelat sign: Report and world literature review. Dermatol Online J 2017;23:13030/qt0w01b1t3.
5. Karadag AS, Parish LC. The status of the seborrhoeic keratosis. Clin Dermatol 2018;36:275-7.
6. Kariya T, Kato Y, Kanzaki A, Kanda Y, Ohara T, Tsuboi R. [(18) F]-Fluorodeoxy-d-glucose uptake-positive seborrhoeic keratosis on positron emission tomography may result from high expression of glucose transporter. Br J Dermatol 2016;175:175-7.
7. Merklen-Djafri C, Truntzer P, Hassler S, Cribier B. Increased glucose uptake by seborrhoeic keratosis on PET scan. Ann Dermatol Venereol 2017;144:378-82.
8. Basu S, Ranade R. 18-fluoro-deoxyglucose-PET/computed tomography in infection and aseptic inflammatory disorders: Value to patient management. PET Clin 2015;10:431-9.