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Multiple Scalp Lesions in a Patient with Keratitis, Ichthyosis and Deafness Syndrome Mimicking Metastatic Squamous Cell Carcinoma on 18F-FDG PET/CT

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We report the case of a 17-year-old girl with keratitis, ichthyosis, and deafness (KID) syndrome. As a complication of her KID syndrome she developed squamous cell carcinoma at the left index finger. Additional clinical features were multiple soft tissue lesions over the scalp mimicking metastatic disease on 18F-FDG PET/CT. To our knowledge, this is the first case report about the uptake pattern of KID syndrome associated skin lesions on whole body PET/CT with 18F-FDG.

Introduction

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Abbreviations: CT, computed tomography; F, fluorine; FDG, fluorodeoxyglucose; KID syndrome; keratitis, ichthyosis, and deafness syndrome; MRI, magnetic resonance imaging; PET, positron emission tomography; SUV, standardized uptake value

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Keratitis ichthyosis deafness syndrome is a rare congenital, autosomal dominant ectodermal dysplasia. The syndrome is characterized by congenital bilateral sensorineural deafness, progressive defects of the cornea due to keratitis and corneal neovascularization which may lead to blindness, scarring alopecia with thin or absent scalp hair, nail dystrophy and focal disfiguring reddish hyperkeratosis. The spectrum of skin lesions in these patients ranges from erythrokeratoderma, hyperkeratosis, chronic cheilitis, and infections of the skin and mucocutaneous to squamous cell carcinoma of the skin and the oral mucosa.

To our knowledge, there are no reports in the literature about the uptake pattern of KID syndrome associated skin lesions on whole body PET/CT images with 2-[18F] Fluor-2-deoxyglucose (18F-FDG). In this report, we present the case of a patient with squamous cell carcinoma of the distal left index finger as a complication of her KID syndrome. Interesting findings in our case were multiple soft tissue lesions over the scalp with increased 18F-FDG uptake mimicking metastatic disease.

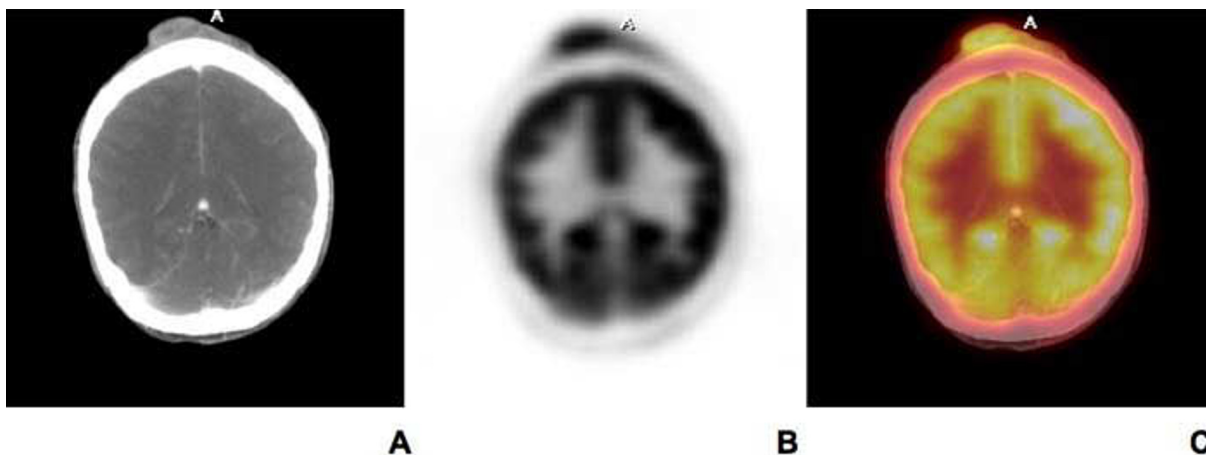


Figure 1. 17-year-old girl with invasive squamous cell carcinoma at her distal left index finger and congenital keratitis, ichthyosis, deafness (KID) syndrome. **A**, CT image depicts several soft tissue lesions over the frontal scalp. **B**, 18FDG-PET and **C**, 18FDG-PET/CT, show multiple subcutaneous soft tissue lesions over the scalp and posterior to the left pinna with increased metabolic activity and measured standardized uptake values up to 7.4. There is no evidence of erosion or other bony changes of the calvarium subjacent to these soft tissue lesions. These lesions are proven benign by histopathology and are a complication of her KID-syndrome. **D** (facing page), Whole body 18FDG-PET scan with increased radionuclide uptake at the distal left index finger (arrow) (SUV 3.1) and at multiple soft tissue lesions over the scalp (SUV 7.4).

Case Report

A 17-year-old girl with known KID syndrome presented at our Pediatric Clinic with complaints of strange sensations at the end of the left index finger, followed by gradual destruction of the nailbed and a two-day period of rapid swelling. This patient first noticed redness and swelling on her left index finger approximately two months prior to admission and a nodular appearance soon appeared thereafter. Initially it was treated with caps on bacitracin and amoxicillin with no relief of symptoms. Physical examination revealed ulceration of the nail bed at the left index finger and chronic mucocutaneous candidiasis of the first, third, fourth and fifth nail beds also on the left hand. Candidiasis was also found on all toes which were treated with topical antifungal and antibacterial medication. Physical examination revealed furthermore, abnormal shortening of the fourth and fifth metacarpal bones, which may be associated with KID syndrome. In addition, the patient's other complaint was some mild tenderness of some of the scalp cystic lesions which had recently increased in size. The scalp lesions appeared clinically to be infected but needed to be followed since they were proliferative

and therefore could be cancer and could metastasize. Furthermore, she had also scattered nevi which appeared benign via epi-luminescence. Metastatic spread was clinically not evident at this time. The cervical, axillary, inguinal and popliteal areas were examined and no lymphadenopathy was noted. A complete blood count was drawn and found to be within normal limits. Debridement of the distal left index finger was performed and the pathology revealed invasive squamous cell carcinoma, which was interpreted as a known complication of her KID syndrome.

The Pediatric Multidisciplinary Tumor Board reviewed her case and initiated a staging evaluation to include an MRI and PET/CT. The MRI of the left hand showed marked soft tissue swelling and gadolinium enhancement at the distal aspect of the second digit with associated ulceration and defect of the nail bed. There was evidence of gadolinium enhancement of the prominent tissues of the distal second digit, extending proximally to near the proximal interphalangeal joint. There was a six millimeter focus of enhancement in the palmar aspect of the distal second proximal phalanx, which could represent extension of tumor or infection. In addition, the first, third, fourth, and fifth nail beds showed a diffuse gadolinium enhancement without a



focal lesion, which was related to the patient's chronic mucocutaneous candidiasis. There was no evidence of abnormal enhancement at the level proximal to the carpal bones.

Subsequently, the patient underwent a whole body PET/CT with 2-[18F] Fluoro-2-deoxyglucose (18F-FDG). An increased, focal 18F-FDG uptake was found in the distal second digit of the left hand, measuring up to 3.1 SUV's (Fig. 1). Other foci of low level uptake were identified within the left and right hands, with SUV values of less than 1.2 SUV. Additionally, multiple subcutaneous soft tissue lesions over the scalp and posterior to the left pinna were identified. These lesions demonstrated increased 18F-FDG uptake with measured SUV's up to 7.4. Therefore, metastatic disease could not be excluded at these sites. A biopsy of the soft tissue lesions over the scalp was performed by dermatologic surgeons to determine the cause of increased glucose activity in this region. The histopathology showed multilocular follicular cysts with the morphology of vellus hair cysts, enveloped by a dense suppurative and granulomatosis.

The patient then underwent a left index finger tip amputation to include the distal interphalangeal joint. Pathology of the left index finger tip revealed well to moderately differentiated invasive squamous cell carcinoma extending into the deep dermis, as well as prominent ichthyosis involving the entire specimen. However, there was no clear invasion of bone, cartilage or skeletal muscle and the resection margins were negative for tumor. Another MRI of the hands showed no evidence of residual squamous cell carcinoma two months post amputation of the left index finger tip on follow-up. To exclude metastasis to regional lymph nodes, surgical resection of two left axillary sentinel lymph nodes and three non-sentinel lymph nodes was performed after they were identified on a lymphoscintigram. The pathology of all lymph nodes was negative for metastatic disease.

The management plan was to follow up on other gadolinium-enhancing regions in this hand and survey the contralateral hand by MRI imaging in approximately two months.

Discussion

Keratitis ichthyosis deafness syndrome is a rare congenital ectodermal dysplasia with the major criteria (1) vascularizing keratitis, (2) erythrokeratoderma and (3) neurosensory deafness [1]. The skin of KID patients is focally thickened, dry and scaly especially on the palms and soles, compatible as an ichthyosis. Furthermore, KID patients have an increased susceptibility to bacterial, viral and fungal skin and mucocutaneous infections and may develop abnormalities of the teeth, hair (scarring alopecia), nails and heat intolerance [1]. To date, less than 100 previous cases have been reported since 1915, with a male to female ratio of 1:1 [1].

A known but rare complication of this syndrome is squamous cell carcinoma of the skin. Although squamous cell carcinoma in KID patients has been described in several reports [2,3], there are no statistics about the incidence currently available. However, the cause for the development of squamous cell carcinoma has been discussed in previous studies; chronic infections and dysplastic histologic changes of the skin, as well as genetic defects in combination or alone are high risk factors and play a role in the carcinogenesis of skin cancer [2,4]. Recent molecular studies [4,5] revealed autosomal dominant mutations in the GJB2 gene encoding the gap junction protein connexin-26 (Cx26) as well as de novo mutations. These mutations can impair the development of gap junction systems at the cell membranes or disturb the function of existing gap junction channels. The increased susceptibility to squamous cell carcinoma in KID patients illustrates how important intact intercellular gap junction communication is for epithelial homeostasis and for development of ectodermally derived tissues. Self-examination, clinical history and radiological staging procedures will be the most important ways to evaluate for the potential development of new squamous cell carcinomas.

Several studies, including both adult and pediatric patients with solid primary tumors have shown, that patients benefit from the use of integrated 18F-FDG PET/CT because of its superior diagnostic accuracy over 18F-FDG PET or CT alone [6,7]. The most commonly radiopharmaceutical used for PET/CT examinations in oncology is 2-[18F] Fluor-2-deoxyglucose (18F-FDG). Of note, 18F-FDG is not a very tumor-specific radionuclide and will accumulate in organs with physiologically

high glucose metabolism (brain, heart), as well as in regions with active local inflammatory disease (arthritis, infection, etc.) or in sites with hyperactivity (muscular, nervous). This can be a potential pitfall and impair the diagnostic accuracy of 18F-FDG PET/CT imaging.

In our patient, an increased 18F-FDG uptake was noticed in the subcutaneous tissue above the scalp which was worrisome for metastatic disease. However, local suppuration which is produced during inflammatory responses was most likely the cause for the high SUV value in these regions. This finding is in agreement with other previous reports of inflammations that may mimic neoplasm on PET/CT imaging [8].

To our knowledge, this is the first case report that illustrates 18F-FDG PET/CT findings in a patient with KID syndrome. Our data show, that 18F-FDG PET/CT can be misleading in these patients, since both neoplastic and inflammatory lesions, which may occur in these patients, may show a marked 18F-FDG uptake. Therefore, as the standard of reference, histopathology of the scalp lesions was required to definitely rule out metastatic disease.

In summary, patients with KID syndrome have a well known increased susceptibility to skin infections and the development of squamous cell carcinomas. Both, these inflammatory lesions and carcinomas have a high glucose metabolism leading to an increased 18F-FDG uptake and, therefore, high SUV value on 18F-FDG PET/CT. Thus, the value of this exam has to be evaluated for every individual patient. If an 18F-FDG PET is performed in these patients for staging purposes, findings on 18F-FDG PET/CT must be correlated with clinical findings and, eventually, additional biopsy.

References Gill Sans MT 10

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Multiple Scalp Lesions w KID Syndrome Mimicking Metastatic Squamous Cell Carcinoma on 18F-FDG PET/CT

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