The PET-CT Radiological Appearance of Facial Cosmetic Injections: A Pitfall in the Evaluation of the Oncological Patient

Tima Davidson MD[1,3], Amit Druyan MD[2], Elinor Goshen MD[1,3] and Merav Lidar MD[2,3]

[1]Department of Nuclear Medicine and [2]Rheumatology Unit, Sheba Medical Center, Tel Hashomer, Israel
[3]Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

ABSTRACT: **Background:** Facial rejuvenation using different dermal and sub-dermal injectable compounds is a popular cosmetic procedure which may pose a diagnostic dilemma to the radiologist.
Objectives: To describe the appearance of cosmetic facial fillers on PET-CT.
Methods: All PET-CT exams performed between January 2015 and May 2017 in which findings suggestive of prior facial filler procedures was evident and where anamnestic confirmation with the patient was possible were reviewed.
Results: We describe five females who had undergone facial filler procedures leading to calcifications around the mouth and nasolabial triangle.
Conclusions: Familiarity with the appearance of such cosmetic procedures on PET-CT is of paramount importance in order to avoid misinterpretation of the findings leading to unnecessary apprehension and work-up.

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KEY WORDS: positron-emission tomography and computed tomography (PET-CT), cosmetics, facial fillers

Facial rejuvenation using various dermal and sub-dermal injectable compounds is a popular cosmetic procedure. Due to the seemingly "non-medical" context of these procedures as well as social prejudices and the conception that such information is not relevant, patients may fail to disclose their use. However, the aftermath of these procedures, including focal inflammation, fat necrosis, and calcifications, may pose diagnostic dilemmas when incidentally encountered by a radiologist while interpreting imaging of the face performed for unrelated reasons [1,2].

This work was presented at a radiology–rheumatology meeting focusing on the contribution of imaging to the understanding of the pathogenesis and treatment decisions in musculoskeletal rheumatic diseases that took place in December 2016 at the Sheba Medical Center, Tel Hashomer, Israel

The clinical use of positron-emission tomography and computed tomography (PET-CT) is constantly increasing, mostly for oncologic staging and follow-up [3], but also in the diagnosis of infectious and inflammatory diseases [4]. As more patients undergo PET-CTs and as the use of facial rejuvenation techniques surges, it is becoming increasingly more common to encounter signs of facial cosmetic injections when interpreting PET-CT images. Thus, the familiarity with the radiographic appearance of such cosmetic procedures is of paramount importance to avoid misinterpretation of the findings.

In this report we describe the PET-CT features of facial cosmetic injections in five patients, review the pertinent literature, and discuss the differential diagnoses of these findings.

PATIENTS AND METHODS

Patient #1 was a 61 year old woman who had recently been diagnosed with breast cancer. PET-CT performed for evaluation of her malignancy showed an increased uptake, standardized uptake values (SUV) max 5.3, in her breast as well as foci of increased uptake (SUV max 6.3) in the soft tissues around her mouth; the latter were attributed to cosmetic injections [Figure 1].

Patient #2 was a woman diagnosed with lymphoma at the age of 63 years. A PET-CT scan performed for follow-up 2 years after completing chemotherapy with complete remission showed foci of increased uptake (SUV max 7.3) in the cheeks and nasolabial triangles. The CT images showed rough calcifications in the corresponding areas. These findings were not described on previous nor on a subsequent PET-CT scan, performed 6 months later.

Patient #3 was a 78 year old woman diagnosed with metastatic breast cancer. A PET-CT performed for staging showed a metastatic disease and focal uptake in the subcutaneous fat of her cheeks bilaterally. The CT images showed rough calcifications in the corresponding areas. In a follow-up PET-CT scan, performed 6 months later, the findings in the cheeks had

Figure 1. Corresponding axial slices of positron-emission tomography and computed tomography **[A, B]** and fusion **[C]** showing foci of increased uptake in the soft tissues with coarse calcifications of the cheeks in patient #1 (cursers)

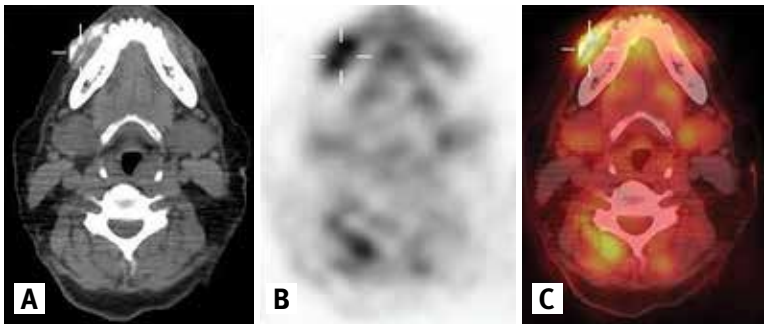
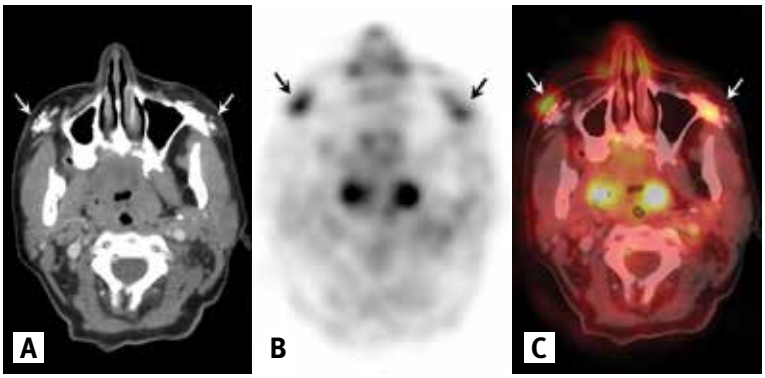


Figure 2. [A] Corresponding axial slices showing microcalcifications on computed tomography (CT), **[B]** increased fludeoxyglucose ^{18}F-FDG uptake on positron-emission tomography (PET), and **[C]** superimposition of both findings on fusion in patient #5



resolved; however, PET-CT performed after 24 more months again demonstrated increased uptake (SUV max 8.5) in the subcutaneous fat of the lower jaw and bilaterally in the cheeks. CT images showed that the corresponding areas were hyperdense and calcified.

Patient #4 was a 74 year old woman. She had a history of bone marrow transplantation due to multiple myeloma, a cutaneous lymphoma, and lung cancer. Three consecutive PET-CT exams performed 6 months apart showed foci of increased uptake (SUV max 6.1) in the subcutaneous facial fat of her jaws and cheeks (bilaterally but more on the left side). In the corresponding areas the CT images showed foci of calcification.

Patient #5 was a 53 year old woman with locally advanced breast cancer. A PET-CT performed for evaluation of her disease status showed an incidental finding of increased uptake (SUV max 6.4) in the soft tissues of the cheeks, with corresponding hyperdense findings typical of coarse calcifications, on CT [Figure 2].

DISCUSSION

PET-CT is a highly sensitive imaging modality for oncologic and inflammatory processes [4]. Incidental findings of increased uptake in the PET-CT may pose diagnostic dilemmas and lead to unnecessary apprehension and unwarranted workup. In this report we provide, to the best of our knowledge, the first description of PET-CT characteristics of facial fillers in female patients undergoing evaluation for metastatic disease.

Subcutaneous injections of various drugs have been reported to cause increased uptake in PET-CT images [5,6,7], attributed mostly to local inflammation at the site of the injection. Similarly, injection of silicone particles around the vocal cords has been shown to cause increased uptake on PET-CT, which has been attributed to a local inflammatory process [8]. Calcium hydroxylapatite has been associated with hypermetabolism, which may be a source of false-positive findings on PET-CT [9,10]. Hypermetabolism associated with other fillers has also been noted [11], which has been attributed to a subclinical inflammatory response.

Ginat and Schatz [1] reviewed the imaging features of a number of midface injectable fillers. They focused mainly on magnetic resonance imaging (MRI) and CT scans, with only limited attention to PET-CT imaging. Ho et al. [2] described four cases of cosmetic-related changes on PET-CT, but only one of them was of a cosmetic facial injection. Here we describe the PET-CT findings in five women who had undergone cosmetic procedures with facial fillers. We show increased fludeoxyglucose (^{18}F-FDG FDG) uptake in the acute phase that may decrease and even disappear with time, leaving evidence of permanent microcalcifications on CT scans.

Other than soft tissue infections of the cheeks and nasolabial folds, findings showed that post-facial filler procedures should be differentiated form Merkel cell carcinoma, a highly aggressive primary neuroendocrine carcinoma of the skin that typically involves the sun-exposed areas of the head, face, and neck. Importantly, skin metastases in patients with malignant melanoma, which frequently undergo PET-CT for staging of their disease, may present similarly on PET-CT.

CONCLUSIONS

The recognition of the radiologic PET-CT appearance of facial cosmetic injections as presented in the current report is essential for the interpreting radiologist to avoid unnecessary investigations. Otherwise, increased uptake on PET-CT together with local calcifications may be falsely interpreted as infection, malignancy, or metastatic disease.

Correspondence
Dr. T Davidson
Dept. of Nuclear Medicine, Sheba Medical Center, Tel Hashomer 5265601, Israel
Fax: 03-5302075
email: tima.davidson@sheba.health.gov.il

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Capsule

Metformin alters the gut microbiome of individuals with treatment-naive type 2 diabetes, contributing to the therapeutic effects of the drug

Metformin is widely used in the treatment of type 2 diabetes (T2D), but its mechanism of action is poorly defined. Recent evidence implicates the gut microbiota as a site of metformin action. In a double-blind study, Wu and collaborators randomized individuals with treatment-naive T2D to placebo or metformin for 4 months and showed that metformin had strong effects on the gut microbiome. These results were verified in a subset of the placebo group that switched to metformin 6 months after the start of the trial. Transfer of fecal samples (obtained before and 4 months after treatment) from metformin-treated donors to germ-free mice showed that glucose tolerance was improved in mice that received metformin-altered microbiota. By directly investigating metformin–microbiota interactions in a gut simulator, the authors showed that metformin affected pathways with common biological functions in species from two different phyla, and many of the metformin-regulated genes in these species encoded metalloproteins or metal transporters. These findings provide support for the notion that altered gut microbiota mediates some of metformin's antidiabetic.

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Eitan Israeli

Capsule

Citrullination of NF-κB p65 promotes its nuclear localization and TLR-induced expression of IL-1β and TNFα

Many citrullinated proteins are known autoantigens in rheumatoid arthritis, which is a disease mediated by inflammatory cytokines, such as tumor necrosis factor–α (TNFα). Citrullinated proteins are generated by converting peptidylarginine to peptidylcitrulline, a process catalyzed by the peptidylarginine deiminase (PAD), including PAD1 to PAD4 and PAD6. Several major risk factors for rheumatoid arthritis are associated with heightened citrullination. However, the physiological role of citrullination in immune cells is poorly understood. Sun and co-authors reported that suppression of PAD activity attenuates toll-like receptor-induced expression of interleukin-1β (IL-1β) and TNFα by neutrophils in vivo and in vitro but not their global transcription activity. Mechanistically, PAD4 directly citrullinates nuclear factor κB (NF-κB) p65 and enhances the interaction of p65 with importin α3, which brings p65 into the nucleus. The citrullination-enhanced interaction of p65 with importin α3 and its nuclear translocation and transcriptional activity can be attributed to citrullination of four arginine residues located in the Rel homology domain of p65. Furthermore, a rheumatoid arthritis-prone variant of PAD4, carrying three missense mutations, is more efficient in interacting with p65 and enhancing NF-κB activity. Together, these data not only demonstrate a critical role of citrullination in an NF-κB–dependent expression of IL-1β and TNFα but also provide a molecular mechanism by which heightened citrullination propagates inflammation in rheumatoid arthritis. Accordingly, attenuating p65-mediated production of IL-1β and TNFα by blocking the citrullination of p65 has great therapeutic potential in rheumatoid arthritis.

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Eitan Israeli

"Neither genius, fame, nor love show the greatness of the soul. Only kindness can do that"

Jean Baptiste Henri Lacordaire, (1802–1861), preacher, journalist, and activist