

## **Botox Injections to the Face: A Mimic of Richter's Transformation**

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### **ABSTRACT**

Chronic Lymphocytic Lymphoma (CLL) may transform into an aggressive high grade variant in approximately 4-6% of cases known as Richter's Transformation (RT). Cutaneous lymphoma as well as other high-grade lymphomas may be a rare presentation of RT. As minimally invasive cosmetic procedures increase in popularity, we present an important mimicker of cutaneous uptake of the lower face simulating RT in a patient with CLL, after the injection of collagen fillers and botulinum toxin A (Botox) to the lower face. To our knowledge there are no previous studies on this important observation. Reading physicians should be cognisant of this masquerade to prevent misdiagnosis.

*Keywords:* Botox, mimicker, PET/CT, Richter's Transformation

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### **INTRODUCTION**

Minimally invasive cosmetic procedures that include injection of Botox and soft tissue fillers (including collagen based fillers and Hyaluronic acid) for rejuvenation of the face are increasing in popularity.

The PET/CT scan remains the most sensitive method for detecting high-grade transformation of chronic low-grade lymphoma. We present a unique case of uptake within the face on PET/CT in a 58 year old woman with a one-year history of Chronic Lymphocytic Leukaemia (CLL) who recently underwent cosmetic injections into the face mimicking Richter's Transformation (RT). To our knowledge this is the first case of facial cosmetic injections mimicking high-

grade transformation of lymphoma. This study describes the findings and presents features to aid readers to differentiate between inflammatory changes related to cosmetic injections and those related to true high-grade transformation of lymphoma to prevent misdiagnosis that may result in inappropriate treatments.

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## CASE REPORT

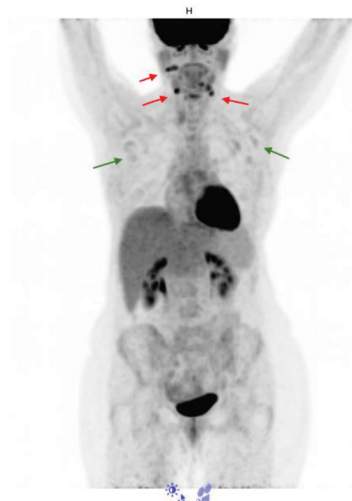
A 58-year old woman with a one-year history of CLL was referred as an outpatient to our institution for PET/CT. Significant past history voluntarily disclosed by the patient included coronary bypass 10 years prior to presentation and L4-L5 disc prolapse treated conservatively, nil else. The request for PET/CT scan was to investigate a recent onset of unexplained fatigue and specifically exclude high-grade transformation of CLL. Clinical examination of the patient revealed prominent lymph nodes in the left posterior triangle of the neck, which the patient self-reported as remaining unchanged over the last 12 months. No new lymphadenopathy was identified. Fasting blood sugar level was 3.8 mmol/L. The patient was injected with 305 MBq of F-18 FDG and underwent imaging after 81 minutes of uptake. Imaging was obtained on a Siemens Biograph PET/CT over 5 bed positions, with 3-minute acquisitions per position. Interrogation of the images demonstrated moderate to intense (SUV Max 7.00) symmetrical uptake within the soft tissue and skin of the face at the infra-orbital ridges, and symmetric uptake within the soft tissues along the mandible bilaterally extending to the soft tissues anterior to the symphysis mentis. These findings were on a background of low-grade uptake (average SUV Max 2.4) within bilateral deep cervical lymph nodes, bilateral axillary, mediastinal, subcarinal, and bilateral inguinal lymph node stations. Remaining visceral and osseous uptake was within physiologic limits. Due to the isolated symmetric nature of the uptake within the face and in light of the previous cosmetic surgery (breast implantation evidenced by CT images), the patient was subsequently questioned regarding any recent cosmetic procedures or instrumentation to the face. The patient then disclosed having had injections of soft tissue fillers and Botox seven days earlier in the exact distribution as seen on the metabolic images. This was discussed with the referring physician who also confirmed the patient's surgical history.

Table 1  
*Features Common to RT and Mimic (Surgical Inflammation)*

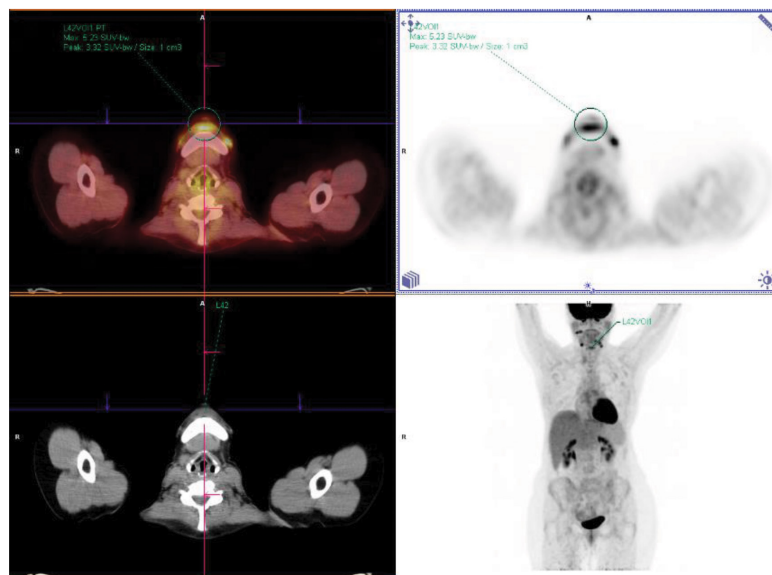
Features common to both RT and Mimic (Surgical Inflammation)
SUV Max > 5.0
Involve extra-nodal soft tissues

Table 2  
*Differences between RT and Mimic (Surgical Inflammation)*

High-grade Transformation	Mimic (Surgical Inflammation)
<b>Asymmetric Uptake</b>	Symmetric uptake within the face
<b>High grade uptake within high-volume nodal tissue</b>	Predictable distribution within the soft tissues of the face in low volume nodal areas.
<b>Possible visceral or osseous extra-nodal uptake</b>	No visceral or extra nodal uptake (uptake isolated to the face)



*Figure 1.* Antero-posterior and lateral whole Body Maximum Intensity Projection (MIP) images of a 56 year old women with CLL, being investigated for RT. MIP image demonstrate multiple foci of moderate to intense FDG avidity identified at the infra-orbital ridges, right greater than left (red arrows) and along the mandible and symphysis mentis (pre-jowl distribution)<sup>1</sup>. Low grade FDG uptake is seen within the deep cervical and axillary nodal stations in keeping with the patient's CLL (green arrows)



*Figure 2.* Fused PET/CT images of the lower face. Further symmetrical focal moderate to intense uptake within the soft tissue anterior to the ramus and body of the mandible. Focal uptake is also seen anterior to the symphysis mentis. This region is also a target for injectable therapy to counteract the pre-jowl sag which contributes to aging of the face<sup>1-5</sup>. The area demonstrates similar moderate to intense FDG avidity to the infra-orbital ridges, again exceeding an SUV max of 5.0. All areas were confirmed to be the result of injections performed seven days prior to the study after obtaining a thorough history of the patient.

## DISCUSSION

The number of minimally invasive cosmetic procedures are increasing worldwide. In the United States Botox and soft tissue filler injections (STFI) are the two most common procedures for facial rejuvenation with approximately 9 million procedures performed by board-certified plastic surgeons in 2014 (Plastics Surgery Statistics, 2015). In light of this trend, radiologists and nuclear medicine physicians need to be aware and remain cognisant of the potential for misdiagnosis to prevent inappropriate treatments. The PET/CT scan remains the most accurate method of diagnosing transformation of lymphoma from indolent, low-grade subtypes to high-grade malignancies<sup>2</sup>. The RT is seen in 4-6% of all patients with CLL (Robak et al., 2005; Bruzzi et al., 2006; Yilmaz et al., 2014). Using PET/CT images alone, RT is diagnosed when intense metabolic activity is seen within nodal or extra-nodal tissue, with an SUV Max of greater than 5 relatively specific for high grade transformation (Bruzzi et al., 2006). The diagnosis of RT has important implications for patient management in that more aggressive chemotherapy regimens are needed. Biopsy is generally mandatory for diagnosis when it is highly suspect on PET/CT images (Bruzzi et al., 2006). In our specific case, biopsy (a follow-up of PET/CT) was deemed unethical once the patient disclosed a clear surgical history and the uptake following a distribution consistent with the procedure (Kane, 2005; Wise and Greco, 2006; Fattabi, 2007; Niamtu, 2009; Schierle and Casas, 2011). Nodal and extra nodal uptake in cases of RT can be highly varied in terms of distribution. Typically, intense uptake is seen within pre-existing low grade nodal or extra nodal disease (Robak et al., 2005; Bruzzi et al., 2006; Yilmaz et al., 2014). As seen in our case however, a symmetric pattern of isolated uptake, especially in areas with low volume lymphoid tissue such as the soft tissues anterior to the inferior and supra-orbital ridge, forehead, lateral canthus of the eyes and along the jaw-line, generally point to inflammatory changes typical of the procedure which should prompt the reporting physician or radiologist of this important mimicker and prevent misdiagnosis.

## REFERENCES

- ASPS. (2015). Plastics Surgery Statistics. *American Society of Plastic Surgeons*. Retrieved November, 2015, from <http://www.plasticsurgery.org/news/plastic-surgery-statistics/2014-statistics.html>
- Bruzzi, J. F., Macapinlac, H., Tsimberidou, A. M., Truong, M. T., Keating, M. J., Marom, E. M. & Munden, R. F. (2006). Detection of Richter's Transformation of Chronic Lymphocytic Leukemia by PET/CT. *Journal of Nuclear Medicine*, 47(8), 1267-1273.
- Fattahi, T. (2008). The Prejowl Sulcus: An Important Consideration in Lower Face Rejuvenation. *Journal Oral of Maxillofacial Surgery*, 66(2), 355-358.
- Kane, M. A. (2005). Botox injections for lower facial rejuvenation. *Oral and Maxillofacial Surgery Clinics of North America*, 17(1), 41-49.
- Niamtu, J. (2009). Complications in fillers and Botox. *Oral and Maxillofacial Surgery Clinics of North America*, 21(1), 13-21.
- Robak, E., Tybor, J. G., Kordek, R., Wawrzyniak, E., Bartkowiak, J., Bednarek, A., ... Robak, T. (2005). Richter syndrome first manifesting as cutaneous B-cell lymphoma clonally distinct from primary B-cell chronic lymphocytic leukaemia. *British Journal of Dermatology*, 153(4), 833-7.

- Schierle, C. F., & Casas, L. A. (2011). Non-surgical rejuvenation of the ageing face with injectable Poly-L-Lactic acid for restoration of soft tissue volume. *Aesthetic Surgery Journal*, 31(1), 95-109.
- Wise, J. B., & Greco, T. (2006). Injectable treatments for the ageing face. *Facial Plastic Surgery*, 22(2), 140 – 146.
- Yılmaz, S., Ozhan, M., Asa, S., Sağer, M. S., Biricik, F. S., Halaç, M., & Sonmezoğlu, K. (2014). Detection of Hodgkin's Transformation in a case of Chronic Lymphocytic Leukemia by PET/CT. *Molecular Imaging & Radionuclide Therapy*, 23(2), 67-69.

