

## Case Report

# Metachronous Malignancy, 27 Years After Teflon Cordal Injection

Marco Bottazzoli MD<sup>1</sup>, Alessandra Marcantoni MD<sup>1</sup>, Lorena Picori MD<sup>2</sup>, Cesare Grandi MD<sup>1</sup>,  
Franca Chierichetti MD<sup>2</sup>, Davide Donner MD<sup>2</sup>

<sup>1</sup>Department of Otorhinolaryngology, S. Chiara Hospital, Trento (TN), Italy

<sup>2</sup>Department of Nuclear Medicine, S. Chiara Hospital, Trento (TN), Italy

**\*Corresponding Author:** Dr. Marco Bottazzoli, Department of Otorhinolaryngology, S. Chiara Hospital, Largo Medaglie d'Oro, 38122, Trento, Italy, Tel: +390461903302; Fax: +390461903789; E-mail: [marco.bottazzoli@apss.tn.it](mailto:marco.bottazzoli@apss.tn.it)

**Received:** 23 July 2019; **Accepted:** 13 August 2019; **Published:** 14 November 2019

## Abstract

We report a rare case of a patient known for a long-time history of iatrogenic VC paralysis, with unusual PET-CT findings. Due to a bilateral paragangliomas (PGLs), 27 years before the patient underwent a left jugulo-petrosectomy. After admission for contralateral sudden hearing loss, MRI and PET-CT scans were acquired. We tried to critically analyze the clinical relevance of multimodal imaging in an unusual condition of comorbidities. Moreover, we suggested a physiopathological interpretation of collecting imagings and clinical otorhinolaryngological aspects. We could determine that high SUV in paralyzed left VC was related to a foreign-body reaction after laryngeal injection by polytetrafluoroethylene fluoropolymer resin (Teflon) performed 27 years before. Moreover, an asymptomatic pT1c mixed lung adenocarcinoma was serendipitously detected in the left lung. The SUVs of these two lesions were both compatible with neoplasms. A further possible lesion in the right lung highlighted by MRI was not confirmed by PET-CT imaging (MRI artifact). Although Teflon is no longer in use for laryngeal injection, clinicians should be aware of the potential misinterpretation laryngeal findings in patients with such a clinical history, even long time after the procedure.

**Keywords:** Teflon; Teflonoma; Laryngeal injection; PET-CT, False-positive; Oncology; Tumor

## 1. Introduction

Positron Emission Tomography (PET) has been increasingly used in the diagnostic investigation of patient with neoplasms, with more accuracy by fusing images with CT scan. On the other hand, a plethora of benign and

inflammatory lesions are more and more detected due to their increased 18-fluorodeoxyglucose (FDG) uptake and can be misinterpreted as malignancies. We present a case where PET showed an increased FDG uptake in an iatrogenic paralyzed vocal cord (VC), because of a left jugulo-petrosectomy performed decades before for a tympano-jugular paraganglioma (PGL): during the investigation, two serendipitously found pulmonary and laryngeal lesions suggested two synchronous malignant lesions. By subsequent analysis, we were able to determine that the high glycolytic activity was related to a foreign-body reaction after a laryngeal injection by polytetrafluoroethylene fluoropolymer resin (Teflon; Du Pont, Wilmington, Delaware, USA) performed 26 years before.

## **2. Materials and Methods**

A 70-year-old male, heavy smoker (50 pack/year) and former alcoholic, in September 2016 referred to our Department for a sudden right-sided hearing loss. The patient's history was also relevant for being affected by familiar paraganglioma (PGL)-1-syndrome, a rare genetic disease that causes multiple PGLs. This syndrome is extremely common in a nearby area (Val dei Mocheni, Trento, Italy): in his family, also his mother as well as the patient's 2 daughters carried the PGL-1-syndrome.

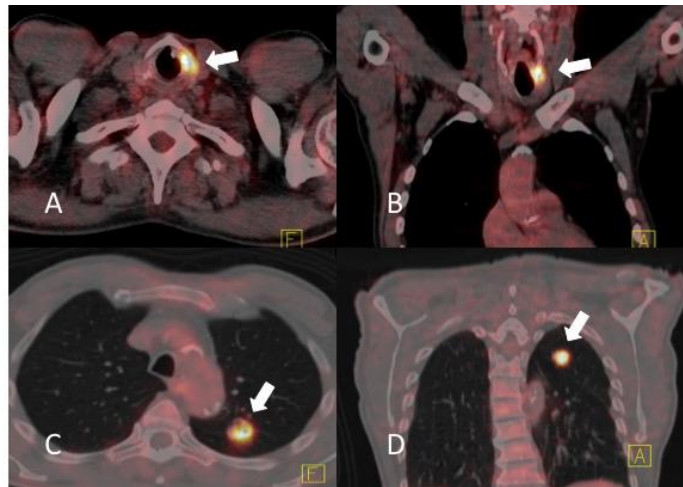
Due to multiple bilateral PGLs, the patient underwent in 1980 a left-sided radical jugulo-petrosectomy at another Institution, that caused a subsequent deficit of the left mixed nerves (8<sup>th</sup> to 12<sup>th</sup>), also consisting in complete left-sided hearing loss and left vocal cord (VC) palsy. Although a second, right-sided procedure was already scheduled for right PGL resection, it was called off in order to prevent a bilateral VC palsy. However, the patient voluntarily dropped off from follow-up for over 20 years, also because a major depressive syndrome as well as alcoholism.

To treat his recent sudden hearing loss, he underwent an effective steroid therapy that restored the hearing on the right side. As changing though time in size or extension of the right PGL could have caused the right sudden hearing loss, a head and neck MRI scan was also scheduled. No changing was detected, but an irregular swelling in left VC and a serendipitous, synchronous lesion of the right pulmonary apex, both suspicious for malignancies, were highlighted.

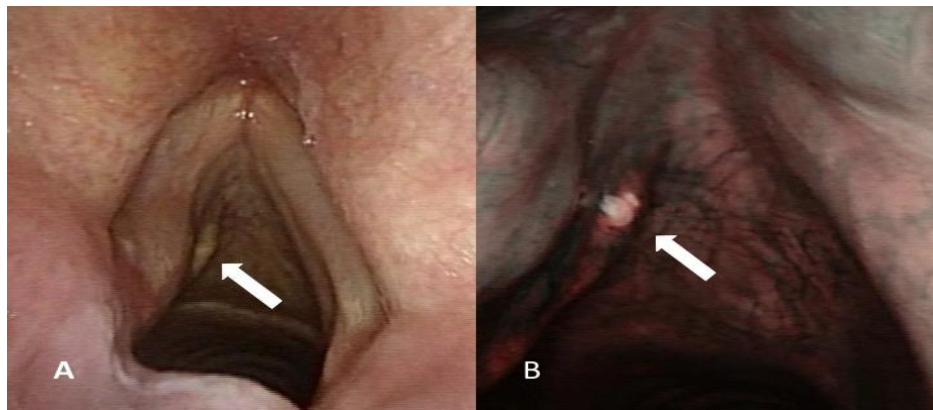
Therefore, the patient underwent a staging 18-fluorodeoxyglucose (18F-FDG) PET-CT which confirmed a suspicious lesion in the left VC, but also retrieved a further one in the superior lobe of the left lung. Their standardized uptake values (SUVs) were 9.52 and 11.76, respectively (Fig 1). On the other hand, the lesion in the right superior lobe detected by MRI was no longer confirmed at the PET-CT. No pathologic nodes nor distant metastases were found.

A subsequent office-based flexible direct laryngoscopy confirmed the palsy of the left VC, with a typical loose appearance. Moreover, a swelling of the subglottic region on the left side was noted, with a small leucoplakia at its center (Figure 2). On narrow band imaging (Figure 2), vascular pattern of the mucosa above the swelling was

normal, while the leucoplakia showed no vascular pattern at all, resembling a highly-keratinized lesion.



**Figure 1:** Axial (Figure 1A and 1C) and coronal (Figure 1B and 1D) PET-CT scans of the neck (Figure 1A and 1B) and the chest (Figure 1C and 1D) demonstrating (white arrows) two areas of pathologic FDG uptake respectively on neck and chest. The former (Figure 1A and 1B) has an SUV of 9.52 and is clearly localized within the left vocal cord. Note the absence of unilateral ossification of the left laryngeal cartilage. Similarly, the lesion in the left superior lobe (Figure 1C and D) has an SUV of 11.76. These PET-CT images are compatible either with two synchronous primitive tumors, a laryngeal metastasis from a lung tumor, or a lung metastasis from a laryngeal tumor.



**Figure 2:** White light direct laryngoscopy (left photo) demonstrating the paralyzed left true VC with a normal mucosa, while a small submucosal mass (white arrow) is present within the left conus elasticus. Note the loose endoscopic appearance of the paretic left VC. A slightly enlarged image using NBI (right photo) shows the normal mucosa overlying the swelling, with a consistently normal vascular pattern. On the other hand, the leucoplakia at the center of the swelling shows no vascular pattern at all, resembling a highly-keratinized lesion (white arrow).

CV: vocal cord, NBI: narrow band imaging.

The remaining head and neck examination was uneventful. All these examinations were all initially consistent with a possible submucosal VC malignancy.

### **3. Results**

A direct laryngoscopy with biopsy under general anesthesia was scheduled, in order to confirm the diagnosis of malignancy. Final histopathologic report showed no evidence of neoplasm, but a marked inflammation with granulomatous reaction, including foreign-body giant cells and reactive fibrosis. The granulomatous reaction was induced by fragments of exogenous translucent material, so a diagnosis of foreign-body-induced Teflon granuloma (teflonoma) was made. Upon further interviews, the patient reported that, few months after the jugulo-petrosectomy in 1980, he underwent a Teflon injection into the left paralyzed VC, to improve his voice quality. Initially, he experienced a good vocal result, followed by a gradual worsening of the dysphonia. Despite the deterioration, he did not express any concern on the quality of the voice, refusing any additional treatment. Furthermore, he referred of having forgotten about this procedure, due to its minimal morbidity.

In the following months, the patient also underwent an atypical resection of the superior lobe of the left lung, leading to a radical excision of the pulmonary neoplasm, subsequently defined as a pT1c pN0 cM0 mixed adenocarcinoma (papillary, micropapillary, acinic, and lepidic types). At the time of submission of the present paper, the patient was alive without evidence of disease for 35 months, while the remaining right PGL did not show any progression in the last 27 years.

### **4. Discussion**

By identifying areas of augmented glucose uptake, PET can localize malignancies, metastatic lesions, and unknown primary tumors [1]. While PET-CT has a negative predictive value up to 100% [2] there is a multiplicity of conditions that physiologically increase SUV. Infectious, autoimmune, or granulomatous diseases as well as other benign lesions may have an increased FDG uptake. These areas of high uptake can be misinterpreted as a malignancy, due to the high glucose usage by activated granulocytes, lymphocytes, and macrophages.

An asymmetrical FDG uptake in VCs is a well-known feature in patients with unilateral VC paralysis: an increased<sup>[2]</sup> or even superphysiologic [3, 4] SUV is usually found in unparalyzed VC, theoretically caused by the overactivity of healthy laryngeal muscles that compensate the paralyzed VC. Physiological asymmetrical increased FDG uptake in VCs can be also caused by muscular activation during speech, entailing that the patient should refrain from talking during FDG administration and PET scanning [4].

An effective surgical procedure to correct a unilateral paralyzed VC is the medialization by injection of the paralyzed one, to improve vocal quality. This procedure was once performed by external puncture, while nowadays is done by endoscopy. To the best of our knowledge, the first report of cord medialization dates back to 1911, by Brunings, who used paraffin to successfully treat patients with VC paralysis [5]. However, paraffin was prone to dislocate itself and cause inflammation of the surrounding tissues, with a specific, foreign-body reaction defined as paraffinoma [5].

In the last century, a variety of materials were tested in the search of the ideal one to inject: it should be stable through time, atoxic, and without risk of extrusion or dislocation. Medializations were performed by: cartilage graft, bovine bone paste, tantalum powder, silicone, hydroxyapatite, Teflon, and autologous fat [6]. Only the latter proved not to cause a local inflammation, but its clinical effectiveness on vocal improvement may be unstable through time due to physiological reabsorption.

Use of Teflon was first described in 1962 by Arnold [7] and become mostly popular throughout the 1980s for laryngeal medialization after unilateral paralysis. Its use is also reported in microvascular decompression for hemifacial spasm [8], velopharyngeal augmentation [9], and even for urologic purposes, such as periurethral bulking for male incontinence [10-12]. Teflon was considered an ideal material because it was thought to be biologically stable and not be able to migrate, or cause significant postoperative modifications in tissue thickness. When the proper quantity of Teflon was injected in the correct site, the procedure proved to be effective in relieving dysphonia due to unilateral recurrent laryngeal nerve paralysis. In the short term after its use, few major clinical complications were described [13], although even significant cases of acute airway obstruction have been reported [13].

An inflammatory response to Teflon always occurs. Differently from what believed in the past [14], the phagocytosis of Teflon immediately evokes inflammation, that leads to a local giant-cells foreign-body reaction. Within 3 to 6 months, a collagenous capsule around Teflon can be demonstrated [6]. The granulomatous inflammatory response is known to persist through time, but its duration is still undetermined [15]; in a minority of cases, it can evolve in the so-called teflonoma. Duband et al believed that teflonomas could occur only in badly performed injections, due to overspill or wrong site and depth of injection [6]. However, badly performed injections should theoretically become symptomatic almost immediately, while teflonomas are usually developed after a variable time span characterized by an improved vocal quality, that suggests an evolution through the years. Moreover, they are typically serendipitously detected. Initially, these granulomas are not always recognized both because of their slow progression and that their onset may be delayed for many years. Therefore, it is reasonable to hypothesize that granulomas should relate to Teflon progressive dislocation or to inflammatory overreaction, rather than badly performed injections.

Teflonomas usually occur at site of treatment, mostly in the subglottic region when considering laryngeal injections [16]. However, some papers report Teflon granulomas at distant sites: cervical lymphnodes after laryngeal injection in animals [17] as well as distant localizations (lung, brain, kidney, and spleen) after periurethral injections for urinary incontinence in animals [12] and in a single human case report [11]. Teflon granulomas are a known complication of a VC medialisation, eventually occurring in approximately 2-3% of patients [18]. When a teflonoma becomes clinically significant, it usually causes a deterioration in the quality of the voice [19]. The tendency to induce granulomas, even long after a technically correct injection, was actually one of the major problems that led to abandon the use of Teflon, fostering the development of other, safer types of injectable materials, such as autologous fat.

A possible, not well known non-neoplastic cause of increased FDG uptake is a granulomatous reaction to previous cordal injections, included those performed with Teflon. According to the literature, Teflon-related PET-CT findings were reported after a period of time from the laryngeal injection that ranged from months [20] to almost 20 years [21]. Moreover, a single article demonstrated pathological SUVs in 2 cases of nasopharyngeal Teflon injection after 25 and 27 years respectively [9] clearly confuting the belief that inflammation is temporary [14]. The duration of Teflon-related FDG avidity is unknown [15]; therefore, it can be foreseen that the inflammatory response to Teflon injection can last indefinitely. 18F-FDG high uptake is also described after use of silicone elastomers [22, 23], with chronic foreign-body granulomatous reactions analogous to those caused by Teflon injections. However, silicone elastomers are believed to be related to less side effects [22]. Accordingly, only 2 cases of silicone-related foreign-body reactions were reported in the scientific literature, to the best of our knowledge.

Differently from Teflon and silicone elastomers, injection of calcium hydroxyapatite and/or methylcellulose proved that injected and non-injected cords had no statistical difference in SUVs [20]. Grant et al also demonstrated the absence of significant relation between SUV and time from injection as well as the extreme variability of SUVs in VCs, either treated or untreated [20]. However, beside the very short time span between injection and the PET-CT scan (range 0.1-8.0 months, median 3.2 months) [20], this paper seems to be hardly comparable to the case we report mainly because of the different injected materials.

Appearance at CT or MR imaging of laryngeal teflonomas is advocated by some authors to be diriment [9, 15, 24]. In particular, it is expected to have a low-to-intermediate intensity on T2-weighted MRI scans [9, 24] while on CT imaging it should appear as not well defined, high-density, amorphous material with high density [15, 24]. However, CT and MRI may be misleading, as sometimes long-lasting granulomas may no longer have a regular shape, but may resemble a malignancy by presenting as spiculated, possibly due to the fibroblastic reaction that leads to retracting scars. Moreover, SUVs of teflonomas can be extremely high (up to 15.0) [15] further mimicking a tumour.

Beside the rarity of the coexistence of unusual clinical conditions (PGL-1-syndrome, bilateral PGLs, sudden hearing loss, and serendipitous finding of pulmonary neoplasm), in the case we report, correct diagnosis was jeopardized by the fact that Teflon injection was not initially reported by the patient, as he considered it as a procedure of minor relevance. At the same time, gadolinium-enhanced MRI was not diriment, while such an intense SUV (9.52) was unexpected after 27 years without previous symptoms, including pain, dysphonia, dysphagia, or any other sign related to the inflammatory process of the VC.

## **5. Conclusions**

PET shows areas with increased glycolytic activity, with a variety of benign lesions that may produce high FDG uptake that may be misinterpreted as malignancies. It is therefore mandatory to critically interpretate SUVs: they



quantify a metabolic process. VC medializations performed with laryngeal injection of eterologous substances produce an FDG-avid lesion which may show a high SUV. Among them, Teflon injection may have significant foreign-body granulomatous reaction, with long-lasting inflammation and fibrosis. Teflon granulomas should be considered in differential diagnosis of patients with history of VC paralysis treated with injection laryngoplasty. Inflammatory reaction to Teflon can persist indefinitely and its clinical relevance may therefore be underestimate. Although Teflon is no longer in use for laryngeal injection, nuclear medicine physicians, radiologists, and head and neck surgeons should be aware of the potential misinterpretation laryngeal findings in patients with such a clinical history, even decades after the procedure.

Beyond literature evidences, our case highlights the arduous clinical assessment in a patient with uncommon synchronous pathologies (PGL-1-syndrome, bilateral PGLs, sudden hearing loss, and serendipitous finding of pulmonary tumor). Moreover, to the best of our knowledge, no other laryngeal teflonoma was ever reported after such a long spawn of time.

### **Acknowledgments**

None of the authors have any potential conflicts of interest to disclose. No source of support and no funds were received for this paper.

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**Citation:** Bottazzoli M, Marcantoni A, Picori L, Grandi C, Chierichetti F, Donner D. Metachronous Malignancy, 27 Years After Teflon Cordal Injection *Archives of Clinical and Medical Case Reports* 3 (2019): 442-450.



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