J Stomatol Oral Maxillofac Surg 126 (2025) 102307

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Original Article

Impaction of third molars and localized cancer of the oral cavity: A simple occasional finding? A retrospective case series and literature review

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ARTICLE INFO

Article History:
Received 6 January 2025
Accepted 2 March 2025
Available online 3 March 2025

Keywords:
Oral cancer
Oral inflammation
Pericoronitis
Third molar extraction

ABSTRACT

Objectives: The aim of this study is to analyze, through a literature review and the description of four clinical cases, whether prolonged tooth impaction may represent a trigger for the onset of oral carcinoma.
Materials e methods: In this report, four cases of patients needing the extraction of third molars in complete mucosal or bone impaction are described, which, due to the presence of an unusual radiographic and/or clinical aspect, were found to represent cases of oral carcinomas on histologic analysis. Patients were then referred to the ENT department for further care. A review of the literature has been performed as well.
Results: Literature analysis revealed the presence of only few case reports on the topic, suggesting therefore a lack of evidence on the correlation between tooth impaction and the onset of oral carcinomas.
Conclusions: Further studies are needed in order to give valid hypotheses. The concept of inflammation, that is at the base of oral carcinogenesis mechanism and tooth-related pathologies, such as pericoronitis, may be a common substrate to link these two phenomena.
Clinical relevance: A thorough analysis of the radiographic and clinical signs is strongly recommended prior and during surgical procedures, such as tooth extraction.

1. Introduction

Oral cancer is a widespread malignancy that represents the 13th most common malignancy and has a 5-year survival rate of 64 %, according to the International Agency for Research on Cancer [1]. Oral cancer may have different clinical presentations, and the primary site may be located at different positions in the mouth. According to the literature, some risk factors are well known, such as alcohol consumption, smoking habit, or viral infections [2,3].

Oral carcinogenesis is a highly complex multifocal process, that is based on multi-local and mutational expression of tumor suppressor genes, that may be due to the long-term exposure o various environmental and exogenous factors, such as the one previously described. These phenomena are based on chronic inflammation, that is induced by the prolonged exposure to risk factors. In this perspective, it is possible to link chronic inflammation to a common process that involves tooth impaction, the so called pericoronitis. According to Kwon et al., pericoronitis is defined as an intraoral inflammatory process due to the infection of the gingival tissue surrounding or overlying an erupting or partially erupted tooth [4]. It is well known that pericoronitis may induce a variety of symptoms, with the most recognized being pain, swelling, pus discharge, trismus, fever, and infection. It is still under debate the correct management of pericoronitis; often, it is manageable through painkillers or antibiotic therapy, frequently followed by tooth extraction [5]. A heavy delay of the extraction may induce a chronic inflammatory process since the trigger is conserved.

Pericoronitis may have a radiographic aspect, often a lightly radiotransparent lesion surrounded by a sclerotic rim, frequently restricted to the tooth crown, similarly to a follicular cyst.

The presence of an osteolytic area surrounding a third molar represents an indication for the extraction and, according to the literature, many benign and malign tumors may present a cystic or erosive aspect [6].

The aim of this article is, through the description of four clinical cases, to investigate whether prolonged third molar impaction may represent a trigger for oral cancer development.

2. Case description

Four patients came to the attention of the S.C. Clinica di Chirurgia Maxillofacciale e Odontostomatologia, Ospedale Maggiore, in Trieste, Italy, needing the extraction of a third molar, due to different indications. These cases showed different clinical and radiographical aspects which will be now described. Unluckily, being a retrospective evaluation, only radiographical images are available, except for one single case, which is documented with a clinical image.

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https://doi.org/10.1016/j.jormas.2025.102307

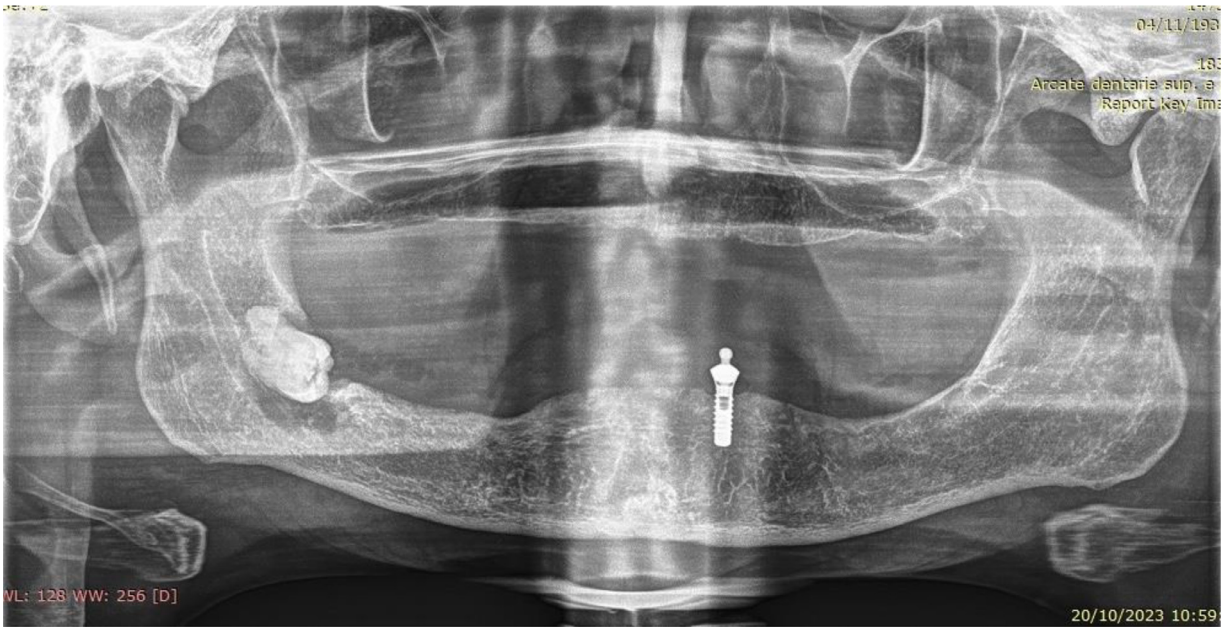

Fig. 1. Orthopanoramic. A pericoronal radiotransparent lesion involving tooth 4.8 is visible.

2.1. Case 1

M.S., a 90-year-old diabetic female, came to our attention in 2022 due to a referred pain on the right hemi-mandibular side, that set few days before. She was fully edentulous, except for a single implant placed at the level of the former tooth 3.3, that presented a ball attachment, previously used as a support for a removable prosthesis. No signs of mucosal inflammation were detected. The pain was described as strong, and slightly responsive to anti-inflammatory therapy. An orthopanoramic X-ray was performed, that revealed the presence of an impacted horizontal tooth 4.8, that showed an osteolytic area mainly associated with the crown of the tooth [Fig. 1]. Therefore, tooth extraction was scheduled, and a CBCT exam was performed, due to the proximity to the inferior alveolar nerve [Fig. 2].

During tooth surgical tooth extraction, the tissue surrounding the element was sent for histological analysis, as this, according to our Clinics, represents normal practice for the cases of suspicious radiographic lesions. Following the surgical act, the patient suffered severe pain, that was not responsive to painkillers nor antibiotics.

The histological analysis revealed the presence of tissue flaps that were strongly infiltrated by meanly differentiated and keratinized squamous carcinoma [Fig. 3].

According to the hospital protocols, the patient was referred to the ENT department where she kept on with the necessary care.

2.2. Case 2

P.D., a 78-year-old male, was sent by his dentist in 2015 due to the presence of pain and swelling of the left hemi-mandibular side, scarcely responsive to anti-inflammatory and antibiotic therapy. From a systemic point of view, he presented type 2 diabetes and had a previous diagnosis of Warthin tumor of the left parotid gland. The radiographic analyses revealed the presence of an impacted 3.8, accompanied by an osteolytic and semi-cystic lesion, surrounding most of the tooth [Figs. 4 and 5]. Similarly to the previous case, no mucosal alteration was detectable, and the extraction of the tooth was scheduled. In this specific case, the tooth 3.7 was extracted as well, due to its periodontal compromission caused by the entity of the osteolytic lesion. The histological analysis revealed a squamous-patterned carcinoma arisen inside a cystic structure and was defined as a primary intra-osseous carcinoma, according to the classification from the 5th Edition of the World Health Organization [7] [Fig. 6]. Similarly to the previous case, the patient was sent to the ENT department.

2.3. Case 3

The third case, D.B., a 61-year-old male heavy smoker (20+ cigarettes per day), was the only one presenting a clinical visible

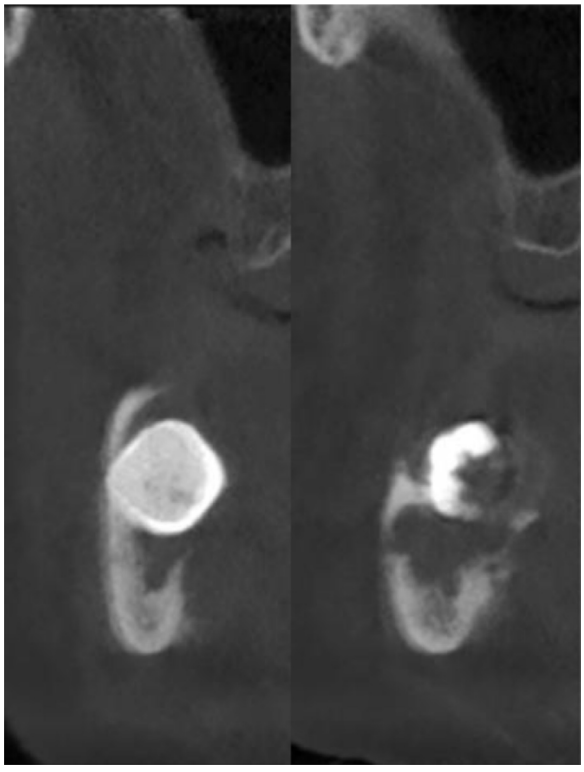

Fig. 2. CBCT scans. An osteolytic aspect is observable.

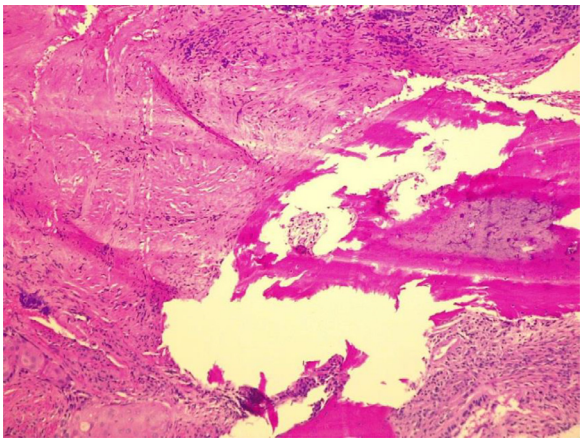

Fig. 3. Histologic image.

alteration of the mucosa. The patient, visited in 2023, described pain in the right hemi-maxilla, that was not responding to anti-inflammatories. On the intraoral examination, a vegetative and ulcerated lesion was detected, in correspondence of the impacted tooth 1.8 [Fig. 7]. The orthopanoramic revealed the presence of the impacted 1.8 [Fig. 8]. Tooth extraction was performed, together with an incisional biopsy. The histological analysis revealed an oral mucosa infiltrated by meanly differentiated squamous-cell carcinoma, that presented a necrobiotic component as well [Fig. 9]. Also in this case, the patient was referred to the ENT department.

2.4. Case 4

The last case is by far considered the strangest one by our research group. This patient, G.Z., a 54-year-old male, light smoker (4 cigarettes per day), was sent to our attention by his own dentist to evaluate the extraction of symptomatic tooth 3.8, that radiographically presented an associated cystic lesion and was purposed to be approached under general anesthesia. The patient referred also some previous multiple episodes of pain in the right hemi-mandibular region, where the orthopanoramic showed the presence of the impacted 4.8 without any radiographic alterations of the surrounding bone, and therefore, according with the patient, the extraction of this element was scheduled as well, in the same session with the tooth 3.8 [Fig. 10]. Also in this case, no alterations of the mucosa were detected.

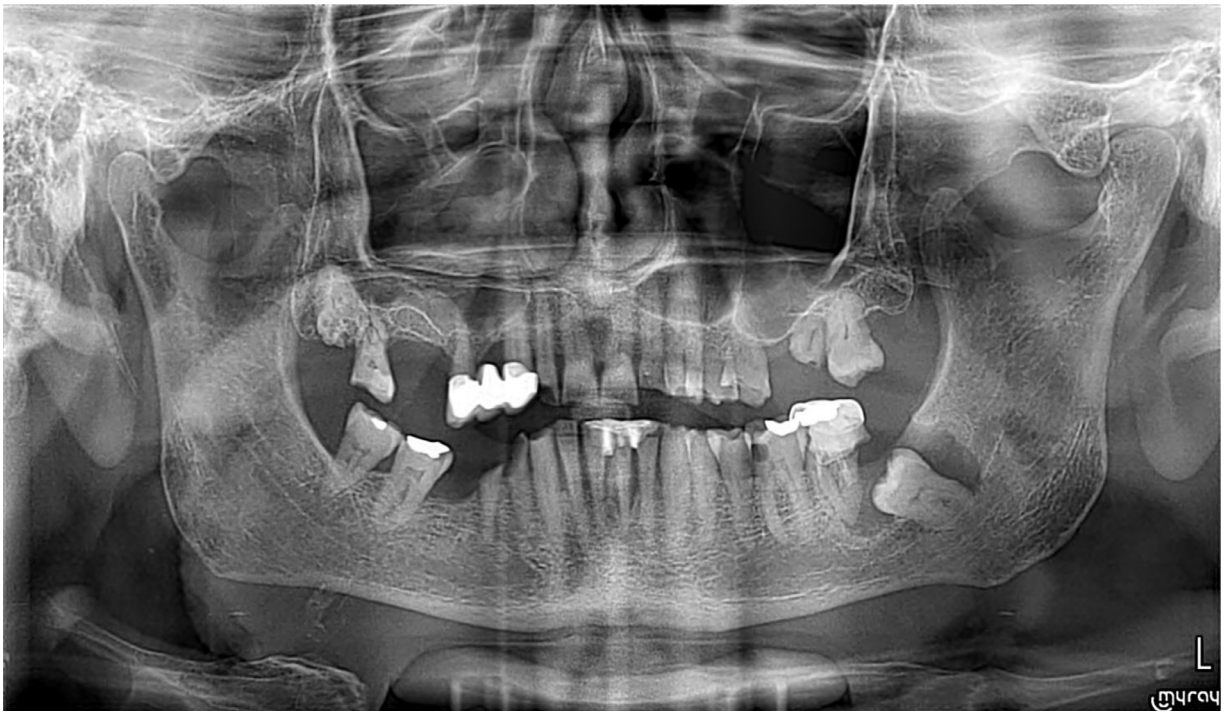

Fig. 4. Orthopanoramic. A peri-coronal radiotrasparency surrounding the tooth 3.8 is observable.

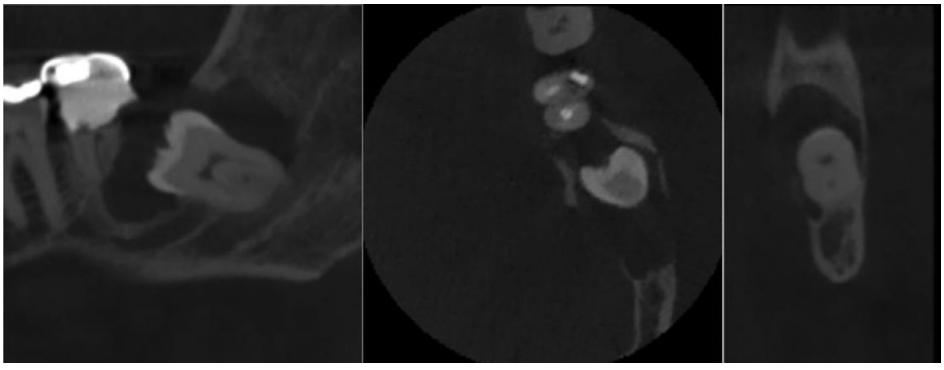

Fig. 5. CBCT scans. Periodontal compromission of the element 3.7 is visible.

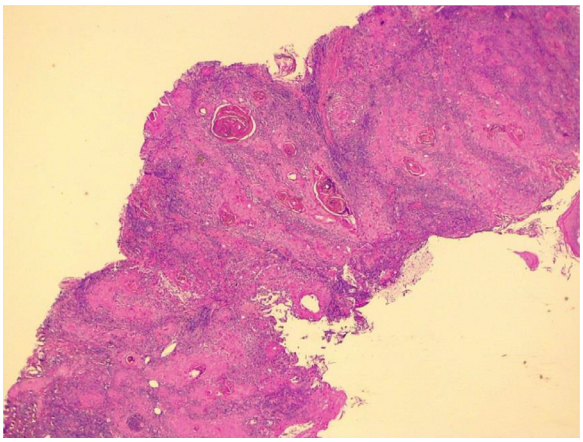

Fig. 6. Histologic image.

Fig. 8. Vegetative lesion in correspondence of impacted 1.8.

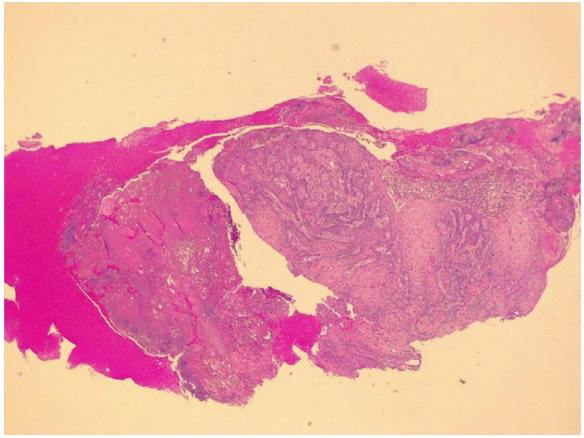

Fig. 9. Histologic image.

Intraoperatively, following the extraction of the tooth 3.8 and the removal of the cystic lesion, that was sent for histological analysis, the tooth 4.8 was extracted and, following the preparation of the surgical flap, an area of dysplastic mucosa was detected and was sent for histological analysis as well.

The histological analysis confirmed the diagnostic hypothesis of cystic lesion for the left hemi-mandibular region, and specifically was a keratin cyst. The other specimen, associated with the element 4.8, surprised the clinicians, as it showed the presence of squamous cell carcinoma [Fig. 11]. Similarly to the other three cases, the patient was referred to the ENT department.

3. Discussion

The indications for third molars' extraction are widely described in literature [6,7]. The presence of a radiographic alteration, mainly expressed as a radiolucency in the case of osteolytic or cystic lesions, represents one of these. Commonly, cystic lesions are associated with the crown of the impacted tooth, and are defined as follicular cysts, that present a well-known histologic aspect. Often, the radiographic aspect is suggestive for a cystic lesion, but the histologic analysis is always diagnostic. In this case series, two of the four cases presented a radiographic alteration, that was suggestive for a cystic (case 2) and erosive (case 1) lesion. On the other hand, the other two cases did not

Fig. 7. Orthopanoramic. No alteration of the bone structures is observable.

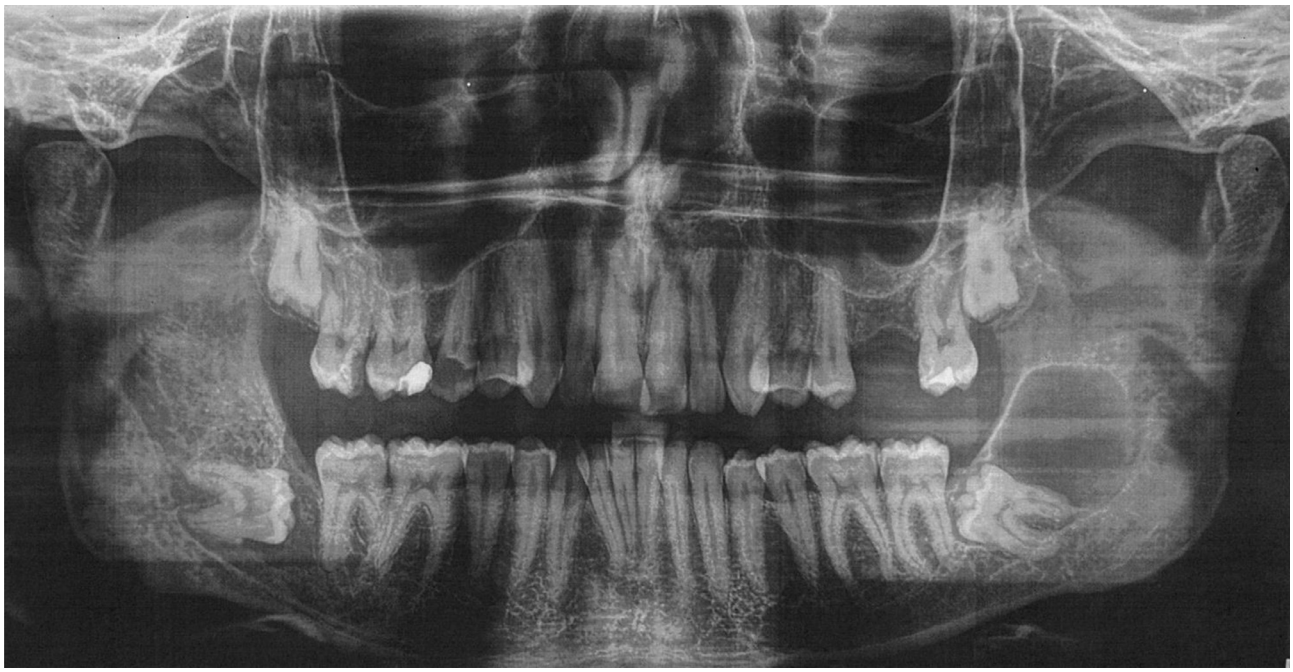

Fig. 10. Orthopanoramic. A simil-cystic lesion is observable in the left hemi-mandibular region. On the right hemi-mandibular region, the orthopanoramic is not suggestive for any preliminary diagnosis.

show any radiographic sign, but the indication for extraction was due to the presence of a visible mucosal alteration (case 3) and to an intra-operatory tissue alteration evaluated clinically (case 4).

The etiologic factors for oral carcinoma are well described in the scientific literature, and are mainly related to voluptuary (e.g. smoking, alcohol addiction) and infective factors (HPV). These factors act by promoting and enhancing an inflammatory process that may lead to an often-visible mucosal alteration in the oral cavity. In this sense, a protracted tooth impaction may enhance a chronic inflammatory process, which is known to be at the base of the phenomenon of local carcinogenesis [8]. Few studies focused on the link between oral inflammation and carcinogenesis, suggesting that persistent inflammation promotes cell proliferation and may induce a DNA damage [9]. In fact, inflammation could be a part in the distruction of cancer cells through immune surveillance, and could also facilitate cancer invasion by generating growth signals and modifying the microenvironment [10–12]. Furthermore, a study conducted by Kavarthapu suggested a link between periodontitis and oral cancer, considering chronic inflammation as a trigger for oral carcinogenesis [13].

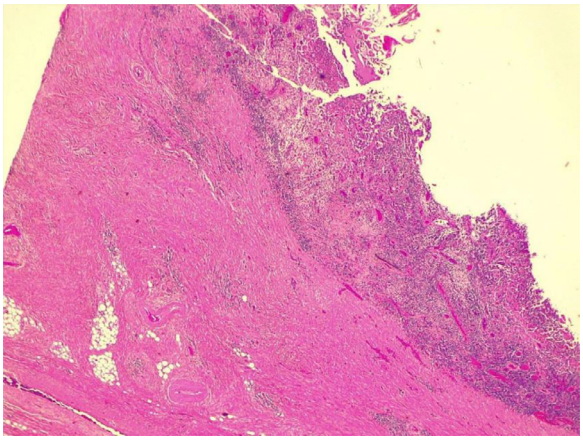

Fig. 11. Histologic image

This concept could be easily assessed in case 1, in which the only presence of an inflammatory focus in the oral cavity, due to the prolonged presence of an impacted tooth, lead to the onset of a tumoral lesion in correspondence to that specific site, without any other mucosal alteration in the mouth.

All the four cases, according to our opinion, presented two common findings. The first is the absence of a response to any first line antalgic therapy, even after the surgical acts. The other aspect is the profuse intra-operatory bleeding. This could be related to the high vascularization of this kind of lesions, also enhanced by the underlying inflammatory process.

The presence of tumoral lesions, specifically carcinomas, associated with impacted third molars, is not a common finding in literature [14–19].

The four patients were soon referred to the ENT department, according to the protocols of our hospital, and underwent surgical and radio-chemical treatment basing on the final histological grading of the lesion.

4. Conclusions

The aim of this case series was to describe four unusual cases of carcinoma arising in correspondence of an impacted third molar, that happened in the same Department in a 5-year time frame. It is still controversial whether tooth impaction represents a triggering factor for the onset of oral carcinoma, but it is authors' opinion that, in the case of middle- or advanced-age patient presenting an impacted wisdom tooth, a thorough clinical and radiological valutation should be performed. In this case series, not all the patients presented clear dental symptoms associated with the impaction, such as the common phenomenon of pericoronitis. In these cases, the absence of clinical images, except for case 3, is suggestive for an initial mucosal health, without any visible alteration, therefore not requiring the acquisition of a photographic documentation.

The presence of an unusual tissue, together with a profuse intra-operatory bleeding, should lead the clinician to perform a histologic analysis.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Matteo Zotti: Writing – original draft, Methodology, Data curation. **Rossana Bussani:** Validation, Supervision, Data curation. **Michele Maglione:** Writing – review & editing, Supervision, Resources.

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