

## ABSTRACT

cancers was performed with intra-operative exam of resection margins; definitive histological exam to assess HPP. Follow-up performed with clinical exam and ultrasonographical evaluation of neck's nodes, in order to perform lymphadenectomy only on pathological ones. Medical records were collected for each patient, focusing on risk factor, clinical presentation, site and W.H.O.'s sub-site classifications, and HPP used (grading, TT, TD, histological structures invaded by cancer, like muscles, vessels, nerves, salivary ducts). HPP's correlation with occurrence of nodal metastasis was assessed with  $\chi^2$ -test (1 g.l. and  $\alpha < 0,05$ ), then compared to select the more reliable ones.

**RESULTS:** The database gathered 85 cases of oral tongue cancer occurred from 2005 to 2015. The early tongue cancer affects more males (58,82%), during the seventh decade of life (31,74%), occurring on tongue's lateral margins more frequently (77,64%) than other tongue's sub-sites, in form of ulcer (54,11%) or of exophytic mass (31,76%). The early tongue cancers are often of stage one (56,47%) and rarely of stage zero (2,35%), according to cTNM stadiation. The most frequent histological form is invasive (98,83%) well-differentiated (52,94%) carcinoma, with a large nest invasion pattern (75,29%) extended to the extrinsic muscles of tongue (72,94%) and rarely extended to vessels (7,06%), nerves (17,65%) or salivary ducts (15,29%). Few lymphadenectomies were performed (10,58%), with only two cases of occult metastasis in nodes that needed a pTNM re-stadiation to third stage (2%). The 98,73% of patients involved in this study is still alive, documented by a follow up period lasting from 2 to 12 years. Only one died because of multiple carcinomas and 6 because of other reasons. Our statistical analysis allowed to correlate all HPP to occurrence of nodal metastasis (except TT) with statistical significance. The HPP more predictable are: grading, TD, invasion of intrinsic muscles of tongue, invasion pattern, vascular invasion.

**CONCLUSIONS:** This study about the early tongue cancer proves the efficacy of the management used in Odontostomatology's Unit of University of Bari revealing a 98,73% of patients without carcinomas in a period from 2 to 12 years. The main Histological Prognostic Parameters useful to evaluate the risk of nodal metastasis are: grading, TD, invasion pattern (proper of OSCC), vascular invasion and invasion of the intrinsic muscles of tongue (exclusive of early tongue cancers). TT can't be considered as a HPP useful for early tongue cancer.

### Cost of illness of oral lichen planus: preliminary report of a multicentric study

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**BACKGROUND:** To estimate the economic costs of oral lichen planus (OLP) through an out-patient multicentric study conducted in Finland and in Italy.

**METHODS:** A multicentric retrospective study was conducted, retrieving clinical records of patients affected by OLP and

followed at Kuopio University Hospital (Kuopio, Finland) and at Oral Pathology Departments of Catholic University (Rome, Italy), to evaluate the economic burden of OLP. Direct costs concerning diagnostic procedures (i.e., biopsies, swabs, blood exams), therapeutic management (either local and/or systemic) and follow-up visits were obtained from clinical records. **RESULTS:** One hundred and eight patients with confirmed diagnosis of OLP (81 females and 27 male), 50 Finnish and 58 Italians, with a mean age of 60.8, were enrolled in this study. Buccal mucosa (81%) and gingiva (48%) were the most involved sites, followed by the tongue (37%). Considering clinical presentation, 59 patients (54.6%) had mixed form, 32 the red (29.6%) and 17 white form (15.7%). The mean follow-up was 24.58 months with a mean of 8.6 visits per patient (4.2 times per year). The study population was divided into two subgroups according to need of therapy: 73 subjects received therapy (Group 1) and 35 did not (Group 2). Group 1 had a mean follow-up time of 30 months, receiving a mean of 10.4 visits (range 2-36; 4.2 per year), 1.4 biopsies (range 1-3; 0.57 per year) and 1.9 swabs (range 0-17; 0.7 per year) with a mean of 395 applications of immunosuppressive topical therapy (range 24-2610; 132 administrations per year) and 273 administrations of topical anti-mycotic (range 21-2264; 96 administrations per year); Group 2 had a mean follow-up time of 14 months, receiving a mean of 5.1 visits (range 1-17; 4.4 per year), 1.2 biopsies (range 1-3; 1.0 per year) and 0.5 swabs (0.4 per year). Within each group, it was possible to compare costs between Finnish and Italian patients: in Group 1 (treated patients) the mean cost was 1249 euros per Finnish patient, whereas 398 euros per Italian patient; in Group 2 (untreated patients) the mean cost was 805 euros per Finnish patient, whereas 352 euros per Italian patient.

**CONCLUSIONS:** This multicentric study provides a preliminary estimate of OLP patients management cost: the most interesting aspect was the different economic burden between Finnish and Italian Health Care Systems, being the Finnish one more expensive. Moreover, in both health care systems, to undergo therapy for OLP highly increased the economic impact. Some difficulties were encountered during the study, in fact many different pharmacological regimens were adopted, due to variable clinical response to therapy. Since OLP is considered a potentially malignant disorder, future studies should address the impact of neoplastic transformation on the economic burden of this disease.

### Stomatitis and VR-TKI: a review of current literature in 4369 patients

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**BACKGROUND:** Traditional treatment of malignancies with chemotherapeutic agents often cause the damage of normal healthy cells. Oral toxicities are a common cause of dose delays and interruption of cancer therapy. In the last decades, new targeted agents have been developed aiming to decrease the rate of side effects on healthy cells. Multitargeted tyrosine kinase inhibitors (TKI) represent a class of target specific anti-neoplastic agents. Even this kind of targeted therapy based

on VR-TKI shown some class specific adverse events that include fatigue/asthenia, anorexia/loss of appetite, hand-foot reactions, dysgeusia, diarrhea/abdominal pain, hypothyroidism, hypertension, myelosuppression and stomatitis. Literature reports that one quarter of patients treated with multitargeted angiogenesis kinase inhibitors develop an oral adverse event within 2 months of therapy.

**METHODS:** The following review was performed to answer to the question "What is the rate of incidence of oral stomatitis in patients treated with VEGF TKIs?". A systematic search was performed on the PubMed online database using a combination of MESH terms and free text words: "sunitinib" (free text) OR "sorafenib" (free text) OR "axitinib" (free text) OR "cabozantinib" (free text) OR "pazopanib" (free text) OR "regorafenib" (free text) OR "nintedanib" (free text) OR "vatalanib" (free text) combined through the use of Boolean operator AND with the key words "stomatitis" (MESH) OR "mucositis" (MESH). (i) performed on human subjects, (ii) reporting about the use of an mTOR inhibitor, (iii) written in the English language, and (iv) reporting about the incidence of stomatitis or oral mucositis. Case reports and studies on animal model were excluded from this study. No restrictions were applied to the year of publication.

**RESULTS:** The incidence of stomatitis of any grade according to the agent was 35.2% for sunitinib, 20.52% for sorafenib, 20.63% for axitinib and 34.21% for cabozantinib. All the agents showed high rates of low grade stomatitis (G1-G2) while the onset of severe stomatitis (G3-G4) was low.

**CONCLUSIONS:** Analysis of the reports with patients treated with sunitinib, sorafenib, axitinib and cabozantinib showed a clear prevalence of stomatitis grade 1 or 2. These data differ from that of patients treated with conventional chemotherapy in which mucositis is predominantly of grade 3 or 4.

## Celiac disease and clinical manifestations in the oral cavity in the pediatric patient

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**BACKGROUND:** Celiac Disease (CD) is extremely variable: it may arise with the typical gastrointestinal symptoms, but also with extra-intestinal signs and/or symptoms such as those of the oral cavity. Therefore, it is often detected lately or not diagnosed at all: approximately 70-80% of cases still escape diagnosis. The aim of this study is to observe the presence of alterations in the oral cavity of the celiac children and, in particular, the enamel hypoplasia, at variable degree (see Aine classification), and Recurrent Aphthous Stomatitis (RAS) in order to assess whether these have statistical significance such as to consider the dental visit useful to intercept the atypical forms of CD.

**METHODS:** We performed an accurate objective examination of the oral cavity in 38 celiac patients from 4 to 16 years (27 F - 71%, 11 M - 29%; average age 9.7, range 4-16), diagnosed according to the ESPGHAN criteria by a team of dentists at the dental clinic of the University of Foggia. The team searched changes in the enamel and the RAS. The parents were asked to complete a survey in order to bring out data concerning the manifestations of RAS and to evaluate some other

statistical and clinical aspects of Celiac Disease. Hypoplasia from Grade 0 to Grade IV were observed, according to Aine classification based on the symmetry and the bilateralism of the lesions and on the chronological coherence.

**RESULTS:** After objective examinations, 10.5% of patients did not show any defect of the enamel, while in 89.5% these alterations appear with a variable frequency, with a total of 221 affected teeth. Grade I lesions occur with a frequency of 68%, Grade II lesions in 15%, Grade III lesions in 12%, grade IV lesions in 5%. The most affected teeth were the incisors (frequency of 41%) followed by molars (frequency of 28%). The third incisor is the most involved dental portion (48% frequency). The manifestation of RAS occurred in 61% of cases and, after a gluten-free diet, ulcers disappeared or decreased in 77% of cases.

**CONCLUSIONS:** The results obtained with this study represent a significant statistical value that supports the possibility to use such clinical manifestations as markers of CD in those forms that manifest themselves in a non-specific way and to consider them equal to all other atypical clinical manifestations related to it. Starting from an objective examination of the oral cavity, the doctor may consider necessary to investigate about the familiarity with CD and any other signs and symptoms related to it and, therefore, decide whether and what exams require to make an early diagnosis.

## Oral amelanotic melanoma of the hard palate: a case report

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**BACKGROUND:** Oral melanoma is an uncommon malignant neoplasm which arises from melanocytes; the amelanotic one is extremely rare in oral cavity. Oral melanomas have unknown etiology because the affected sites are not exposed to solar radiations, however some studies have underlined a possible role of ill-fitting dentures, tobacco, amalgam tattoo, nevus and racial pigmentation as risk factors. This malignant neoplasm is really aggressive therefore an early diagnosis is mandatory to improve patient prognosis. Since an early diagnosis is difficult, amelanotic melanoma has a poorer prognosis than the pigmented one. Immunohistochemical staining is crucial for the histological diagnosis. The aim of this work is to describe a case of oral amelanotic melanoma occurred in a 50-years-old male patient.

**CASE REPORT:** In november 2017 a 50-years-old male patient, 10 cigarettes/day smoker since 20 years old, referred to Complex Operating Unit of Oral Pathology and Surgery, University of Bari, with a wide bleeding and painless lesion on the anterior and left hard palate. Clinical oral examination revealed a swelled, ulcerated, reddish and multi-lobular lesion with a firm-elastic consistency. Ortopantomography (OPT) and Computed Tomography (CT) with 3D reconstruction showed the presence of a wide and expansive osteolytic lesion involving the anterior part of the hard palate and extending on the left hard palate and the left nasal floor. Fine Needle Aspiration Cytology (FNAC), Fine Needle Aspiration Biopsy (FNAB) and incisional biopsy were performed to obtain a certain pre-surgical histopathological diagnosis. Hystological features revealed a low differentiated malignant neoplasia with high replication index ( Ki67 > 90% )