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CASE REPORTS

Non-Hodgkin Lymphomas of Oral Cavity

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Non-Hodgkin lymphomas (NHL) often show up in an extranodal pattern, especially in the head and neck. Intraoral locations are much less frequent, particularly when they are single. This, in turn, can lead to a prolonged diagnosis and even to inadequate treatment. Different patients with initial extranodal location of NHL which were not previously diagnosed and in which it was manifested only intraoraly are presented in this paper. These cases are presented together with the additional examinations used for the early diagnosis and with the corresponding clinical pictures, as well as with the overview of other cases from the available literature.

K e y w o r d s : **mouth neoplasms; lymphoma, non-Hodgkin; diagnosis.**

Introduction

Malignant lymphomas form a heterogeneous group of neoplasms of the lymphoid tissue with different clinical courses, depending on the treatment and the prognosis (1). Non-Hodgkin lymphomas (NHL) often show up in extranodal sites of the head and neck (2), but intraoral locations are much less frequent, especially when they are the only manifestations of this disease (3). This is why the diagnosis is frequently postponed and the treatment improper (2).

Various cases of NHL that had initial extranodal intraoral presentations, not previously diagnosed, are presented in this paper. In some cases this type was the only presentation of NHL. Such patients were sent to the Dental, Oral and Maxillofacial Surgery Department of the Insular University Hospital of Las Palmas de Gran Canaria for reviewing and studing.

Case 1

A 27-year-old male, with no medical history of immediate interest, sought treatment for the left perimandibular swelling that had developed over several weeks. He had previously been treated with antibiotics, with no positive response. Upon the exploration a hyperemic mass that fluctuated slightly at touch was found. It was painful and was intra-orally adhered to the external mandibular cortex. It was near the fistulisation, and could also be felt intra-orally (Fig 1). Ultrasonographic examination hinted at the existence of an adenoma or an abscess. Since there was no defined dental cause, it was decided to perform a fine needle biopsy which confirmed the existence of a malignant tumor. A removal/biopsy of the lesion was programmed.

Fig. 1 – In Case 1 there occures a hyperemic mass with light fluctuation on palpation, painful and adhered on the external mandible cortex with the aspect of imminent fistulisation.

A diffuse infiltration of polygonal amphophilic cytoplasm cells was detected by histological analysis as well as

the large nuclei, irregular in places, multicolored, with one or several nucleoli (Fig 2), diagnosed as anaplastic large-cell Ki1 (+) NHL. Computed tomography revealed a tumor in the left mandibular region 4.1×2.6 cm thick; there was blurriness in the surrounding fat (Fig 3). The extension study was negative, thereby classifying it as a stage I E. The patient received 6 cycles of CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) chemotherapy and radiotherapy to the affected area. After 9 months of follow-up, there was no evidence of relapse.

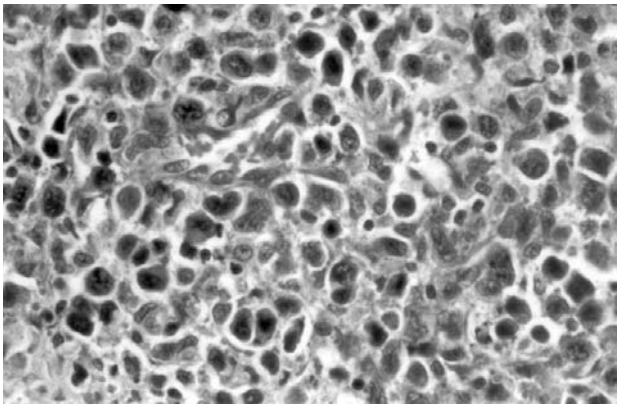

Fig. 2 – Neoplastic cells have an anaplastic occurence with ampholytic cytoplasm (HE×40)

Fig. 3 – CAT scan reveals a tumor in the left side of the mandible of 4.1×2.6 cm with enlargement and disorder of adjacent fat tissue.

Case 2

A 41-year-old male patient with no medical background of immediate interest complained of unspecific discomfort in the right perimandibular area. The x-rays did not reveal any characteristic signs, but since he was sensitive to slight discomfort upon digital pressure on the area (with no dental cause that would justify it), a CAT scan was required. The scan images revealed an expansive lesion in the right horizontal mandibular ramus, which produced the thinning and the break of the cortex with the internal areas of sclerosis, which led to the assumption of malignancy, thus a biopsy was carried out.

Histologically, the tumor cells diffusely infiltrated the soft tissue areas; they were made of small lymphocytes with hyperchromatic nuclei, slightly irregular, with extensively isolated figures of mitosis. Immunohistochemically, neoplastic cells were monoclonal and they expressed lymphocyte B markers, which led to the diagnosis of small NHL cell of low degree malignity. The rest of the stage study results were strictly normal. The patient received 8 cycles of CHOP chemotherapy. He remained in remission during 30 months of follow-up.

Case 3

A 40-year-old male patient entered the Emergency Unit due to an episode of retromolar pericoronitis of the lower left wisdom tooth (Fig 4), that was accompanied by intense pain and fever of 38.5 – 40°C, not responding to the antibiotic/anti-inflammatory ambulatory treatment. HIV+ and Hepatitis B, diagnosed six years earlier, were in his pertinent medical history. The patient was not receiving antiviral treatment at a time. He had left peripheral facial paralysis for months earlier, treated with vitamin complexes. The analyses detected a CD 4 count of 37. Because of his medical history a biopsy was ordered. Histologically, there was a diffuse infiltration of poorly defined eosinophile cytoplasm cells, though clear in some areas. The nuclei were vesiculous and of the irregular morphology, with nucleoli. There were many mitotic figures. Immunohistochemically the tumor cells were lymphocytes B, which led to the diagnosis of diffuse large cell immunophenotype B NHL. The patient was sent to his country of origin to undergo treatment.

Fig. 4 – Behind the third molar there is an ulcerous lesion, which may be confused as a stage of pericoronitis.

Case 4

A 22-year-old male patient with right hemimandibular pain and a post-extraction wound that would not heal where several molars were removed in order to allow tooth movement. This patient came to our department complaining of persistent pain and the movement of other molars, swelling and hemimandibular ipsilateral numbness. The patient re-

ported that he had been on sick leave due to the intense lower back pain that radiated to his lower limbs. Upon the exploration, multiple painful bilateral lymphadenopaties were found, the largest one being located in the right submandibular area. Histologically a diffuse infiltration was identified, made of medium-sized cells mixed with macrophages that gave it a starry sky appearance. Tumor cells had regular nuclei and hardly any cytoplasm, with one or several unimpressive nucleoli. Abundant mitotic figures were identified. Immunohistochemically the tumor cells were lymphocytes B, which lead to the diagnosis of diffuse small cells NHL, immunophenotype B, Burkitt type. The CAT scan revealed an adenopathic mass located in the area of the mandibular angle, along with multiple cervical lymphadenopathy. The bone marrow biopsy of the iliac crest revealed severe lymphoblastic leukemia of B cells (Burkitt type), morphology L3 of the FAB, stage IV E. In the treatment the CODOX-M protocol was used and the leukemia entered in complete remission, consolidated with IVA C. After that the patient was without recurrence.

Discussion

Although the predominant sites of lymphoma occurence are lymph nodes, where it shows progressive enlargement, it also occurs in other organs, as an exclusive manifestation (1). NHL in 24% were of extra lymph node localization and 25% of these occured in the head and neck region (4). In his study of 1 467 cases of extra lymph node NHL, Freeman et al (5) found that 28% affected the head and neck area and 2% were located in the oral cavity. Takahashi et al (6) obtained the results demonstrating that 8% of extra lymph node NHL was in the oral cavity. This could be considered a low incidence of NHL oral manifestation, even more so if focused only on its intraosseous occurrence. In this paper four Caucasian males 22, 27, 40 and 41 years of age were presented, in which NHL was diagnosed only through its oral symptoms, although one of them was with a complete clinical picture in the final two months and the other was HIV positive. Primary lymphoma located in the mandible was not frequent. Current literature described about 100 cases of mandible NHL (7). In addition, there are various publications on isolated NHL occurence (4, 8–12). Some authors reported two cases of NHL in the same article (14, 15). Larson et al (2) in their review of 100 patients with extra lymph node lymphoma of the head and neck reported no mandible localization, while in the study of Conley et al (16) there was only one case with the oral manifestation. Econopoulos´ review (17) of 116 cases of head and neck NHL treated between 1977 and 1997 reported 9 cases (7.8%) with mandible and/or gingival involvement. Eisnbound et al (18) analyzed 31 case of oral cavity NHL and found 14 patients with bone invasion, 5 of them in the mandible. In their retrospective analysis of 31 cases of Burkitt´s lymphoma in young adolescents between 12 and 17 years of age, Anavi et al (19) reported 2 cases of mandible involvement. In this paper 3 cases of primary localization and diagnostic of NHL of the mandible are presented (one of the cases not considered as primary NHL of mandible); one was located in the left retromolar triangle and two others were on the right side of mandible body. Two of the patients were classified as being in stage IE, while the third patient was in stage IV. Eisenbud et al (18) presented 31 case in four stages of NHL, respectively. Evaluating only the cases with mandible involvement, the patients were pressented as 1 at stage I, 2 at stage III and 1 at stage IV.

Regarding the form of NHL presentation, two of the cases were with a painful fast-growing mass simulating an abscess, which coincided with the cases reported in the literature (12–14, 20), although our cases were of Ki1 NHL, a condition rarely described in the literature. One of the cases of Macintyre et al review (14) and a case of other authors (4, 9, 11) coincided with our fourth case. In fact, a dentist even extracted one or more teeth initially, believing the lesion to be an inflammatory process. In our fourth case, the clinical picture looked like an osteomyelitic process, presenting numbness of lower hemilip as well as teeth motility. These symptoms matched the symptoms from the literature (4, 8, 9, 11), though in older patients than ours (32, 53, 60 and 80 years of age), who also underwent teeth extractions earlier, the proper diagnosis was made. Anavi et al (19) also found that more frequent symptoms present in mandible NHL were teeth motility and teeth pain, with preserved dental vitality. Due to that, NHL should be considered in differential diagnosis of any process that presents teeth motility and any periapical radiolucency that is not related to other facts from the clinical history (traumatism, periodontal disease, deep caries, etc.). Bearing this in mind, in our second case we presented a case that was clinically and radiologically invisible, and only exhibited via CAT scan vestibular mandible cortex destruction. Heng et al (10) published one paper on a case where a periapical radiolucency treated endodonticaly proved resistant to that treatment and was accompanied with hemimandible paresthesis, after which NHL was diagnosed. In the case presented by Wright et al (21) neither endodontic therapy nor extraction was performed. Instead, antibiotherapy was given, followed by the curettage of the lesion 10 days later because a periodontal process was suspected. In patients with immunodepression (e.g. immunodeficiencies, autoimmune diseases or after recent transplantation), there was a greater frequency of NHL. Characteristically, these were classified as strain B NHL with very high levels of malignancy, rapid clinical progression, and frequent extra lymph node affectation. Therefore, it was not strange that there was a major incidence of lymphomas in the patients affected with HIV (21). In 1985 The Center for Disease Control (CDC) included the high grade malignant and primary cerebral NHL within the criteria for the diagnosis of AIDS. This criteria were accompanied by intermediate grade malignant NHL in the CDC study done in 1987 (23). The current classification of AIDS (24) proposed in 1992 did not consider any change regarding NHL,

but there were indications that other types of lymphoma or lymphoproliferative disease could be incorporated into the current definition of AIDS. In the study of Ioachim et al (25) 111 cases of AIDS-associated lymphomas were evaluated, only 3 of them localized in the oral cavity. Stolarski et al (26) published one case of NHL where the patient was not aware of being HIV positive. In the third case of this article it was known that the patient was HIV positive, but until that moment there was not sufficient proof to consider it as AIDS.

Conclusion

NHL of the head and neck region, particularly of the mandible, are rare and may be confused with other neoplasms or periapical or periodontal inflammatory processes. There is usually a mass or swelling, showing rapid growth and enlargement, but this is not necessarily the case. Sometimes there is only numbing or teeth motility. Considering this, it is supposed that in every doubtful case a biopsy and CAT scan are indicated.

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A p s t r a k t

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NON-HODŽKINOVI LIMFOMI USNE DUPLJE

Non-Hodžkinovi limfomi se često javljaju ekstranodalno, naročito na glavi i vratu. Intraoralna lokalizacija nije česta, naročito kad je jedina. To može da dovede do prolongirane dijagnoze i čak do neadekvatnog lečenja. U radu se prikazuju različiti slučajevi s inicijalnim ekstranodalnim lokalizacijama koji nisu prethodno dijagnostikovani, od kojih je nekima NHL manifestovan samo intraoralno. Prikazani su uz dodatna ispitivanja korišćena za ranu dijagnostiku i odgovarajuće kliničke slike i pregled drugih slučajeva iz raspoložive literature.

K lj u č n e r e č i : usta, neoplazme; limfom, nehodžkinov; dijagnoza.