Therefore, ultrasound could be used as a supplemental sign to differential diagnose.

Surgical excision is considered to be the best approach for the primary treatment of lymphangiomas, but the postsurgical recurrence rate of CLC is high.[1] Hence, a precise determination of lesion margin would be helpful to define an appropriate safety margin for surgery.[11] Ultrasound has been confirmed to have excellent correlation with the histologic thickness of malignant cutaneous tumors[12] and the present case suggests the same for CLC. The lesion showed hyperechoic characteristics combined with high vascularity and low-speed blood flow. Thanks to the precise evaluation of lesion margin by preoperative ultrasound, including color Doppler and pulse wave Doppler, repeated pre- and intraoperative biopsies were minimized. It could also prevent recurrences.

It is well known that craniofacial area is one of the most common sites of CLC.[13] At this area, the skin and subcutaneous tissue are both thin and vulnerable to stretch. So, skin tension of this area would be much more enlarged after the surgery.[14] Too much tension after surgery maybe influence local sensation and functions of nearby sensory organs such as mouth and eyes. To avoid that, we use ultrasound for precise presurgical assessment to minimize the resection area. We think this is also the value of ultrasound assessment for craniofacial CLC preoperational.

In conclusion, ultrasound (especially color Doppler and pulse wave Doppler ultrasound) is a versatile non-invasive tool that can help the in diagnosis of CLC. It could help determine the exact depth of the lesion and may help prevent recurrences, but this will have to be determined in future studies.

REFERENCES

1. Patel GA, Schwartz RA. Cutaneous lymphangioma circumscriptum: frog spawn on the skin. *Int J Dermatol* 2009;48:1290–1295
2. Wortsman X, Wortsman J. Clinical usefulness of variable-frequency ultrasound in localized lesions of the skin. *J Am Acad Dermatol* 2010;62:247–256
3. Massa AF, Menezes N, Baptista A, et al. Cutaneous Lymphangioma circumscriptum - dermoscopic features. *An Bras Dermatol* 2015;90:262–264
4. Sen I, Agarwal S. Cutaneous lesions from lymphangioma circumscriptum. *ANZ J Surg* 2017;87:E20–E21
5. Wolf IH. Dermoscopic diagnosis of vascular lesions. *Clin Dermatol* 2002;20:273–275
6. Wortsman X. Sonography of facial cutaneous basal cell carcinoma: a first-line imaging technique. *J Ultrasound Med* 2013;32:567–572
7. Lassau N, Spatz A, Avril MF, et al. Value of high-frequency US for preoperative assessment of skin tumors. *Radiographics* 1997;17:1559–1565
8. Oiso N, Itoh T, Miyake M, et al. Cutaneous lymphangioma circumscriptum with marked blood presence: histopathologic evaluation of the endothelial cells. *Eur J Dermatol* 2014;24: 127–128
9. Jha AK, Lallas A, Sonthalia S. Dermoscopy of cutaneous lymphangioma circumscriptum. *Dermatol Pract Concept* 2017;7:37–38
10. Bhat V, Salins PC, Bhat V. Imaging spectrum of hemangioma and vascular malformations of the head and neck in children and adolescents. *J Clin Imaging Sci* 2014;4:31–61
11. Martinez-Menchon T, et al. Lymphangioma circumscriptum: an example of Whimster's hypothesis. *Pediatr Dermatol* 2004;21:652–654
12. Hayashi K, Uhara H, Okuyama R. Detection of the tumor margin of basal-cell carcinoma using dermoscopy and high-frequency ultrasound with narrow pieces of surgical tape as skin markers. *Dermatol Surg* 2014;40:704–706
13. Wiegand S, Eivazi B, Barth PJ, et al. Pathogenesis of lymphangiomas. *Virchows Arch* 2008;453:1–8
14. Nasca MR, Shih AT, West DP, et al. Intermittent pressure decreases human keratinocyte proliferation in vitro. *Skin Pharmacol Physiol* 2007;20:305–312

Metastasis of Prostate Adenocarcinoma in the Mandible: Rare Occurrence in Maxillary Bones

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Objective: This article describes the case report of a prostate adenocarcinoma in the mandible.

Background: Prostate adenocarcinoma is a malignant tumor common in men from the fourth decade of life. The occurrence of oral metastatic lesions is rare.

Case Report: A 78-year-old male patient was referred to the oral and maxillofacial surgery service of the Pontifical Catholic University of Rio Grande do Sul for complaints of painless volume increase in the mandible. The diagnosis through the association of clinical, radiographic, and histopathological examination with the patient's health history determined that the lesion was prostatic adenocarcinoma metastasis.

Conclusion: Despite the rare occurrence of metastases in the oral region, the dental surgeon should be aware of the possibility for correct diagnostic conduction and, subsequently, the institution of treatment in the early stages of disease.

Key Words: Mandibular metastases, oral lesions, prostate cancer

The malignant lesions that affect the oral cavity correspond to 5% to 6% of all that occur in the other regions of the human body. Of the malignant lesions of the oral cavity, only 1% are metastatic lesions. Metastases consist of the migration of malignant neoplastic cells from a primary tumor site to a distant tissue. This event is due to the loss of intercellular adhesion, increased motility, and proliferative index of neoplastic cells. Such cells may travel via blood or lymphatic pathways to distant organs.[1]

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Metastatic lesions in the oral cavity are more common in bone tissue than in soft tissue. The mandible is usually the most affected region. The primary sites of the most common metastatic lesions are breast (25%), lung (13%), prostate (10%), colon (7%), kidney (3%), and thyroid.[2]

Prostate adenocarcinoma is a slow-growing malignant tumor more common in men from the fourth decade of life. Clinically, it is characterized by local prostate enlargement. Microscopically, we observe columnar cells arranged in acinar-like patterns of nest without secretory function. It is a tumor with high metastatic potential in advanced stages.[3]

The diagnosis of the metastases in the oral cavity is a challenge for the dentists since such lesions assume clinical and radiographic characteristics similar to other oral lesions. In general, the behavior and histopathology of metastases are similar to those of the primary tumor. In this context, a careful and multidisciplinary clinical evaluation is necessary to define a correct diagnosis and establish the ideal treatment.[4]

The objective of this study is to report a case of prostate adenocarcinoma metastasis in the mandible.

CLINICAL REPORT

A 78-year-old male patient came to the oral and maxillofacial surgery service of the PUCRS complaining of painless volume increase with a 30-day evolution in the mandibular region on the left side in March 2017. According to the patient, the event started after a posterior tooth exodontia in the region of the referred complaint.

The patient had arterial hypertension, Chagas disease, hypothyroidism, and a history of prostate adenocarcinoma diagnosed in January 2001. The patient underwent radiotherapy for a month that kept him in control. Seven years after radiotherapy, the patient presented recurrence of the disease and started multiple interventions: hormonal therapy with goserelin acetate from 2008 to 2014 and bicalutamide from 2010 to 2011, total orchiectomy in 2014 and from November 2015 to February 2016 underwent through chemotherapy with docetaxel.

At the extraoral clinical examination, facial asymmetry was observed due to an increase in volume in the mandibular region of the left side. Intraorally, swelling was observed in the posterior region of the alveolar ridge covered by a firm and erythematous mucosa (Fig. 1A and B).

The cone beam tomography revealed a diffuse radiolucent image of osteolytic aspect in the mandibular region of the left side (Fig. 1C–F). Associating clinical characteristics and medical history, the diagnostic hypotheses considered were: metastatic lesion, osteomyelitis or fibro-osseous lesion. An incisional biopsy was performed under local anesthesia and the surgical specimens were submitted to histopathological examination (Fig. 1G and H).

Microscopically, under routine staining of hematoxylin and eosin, there were proliferations of undifferentiated neoplastic cells that had pleomorphism and atypical mitosis figures. The proliferations formed nodules that infiltrated the adjacent stroma. Some tumor islands had ductile structures. These characteristics determined the diagnosis of undifferentiated carcinoma (Fig. 2A–D).

Due to the inconclusive histopathological diagnosis, an immunohistochemical panel with cell markers (antibodies) selected according to the patient's health history was established in an attempt to establish the tissue origin of the mandible lesion (Supplemental Digital Content, Table 1, http://links.lww.com/SCS/A920).

The positive reaction with the following immunomarkers determined a diagnosis compatible with metastatic lesion originating from the primary prostate site (Fig. 3A–G): CK AE1/AE3, epithelial membrane antigen (EMA), p63, prostate-specific antigen (PSA) 28/4A, androgen receptor, CDX2 (AMT 28) CK 20 (kS20.8), prostate specific acid phosphatase antibody (PASE/4LJ), thyroid transcription factor (TTF-1 SPT24), CD 57 (natural killer-1).

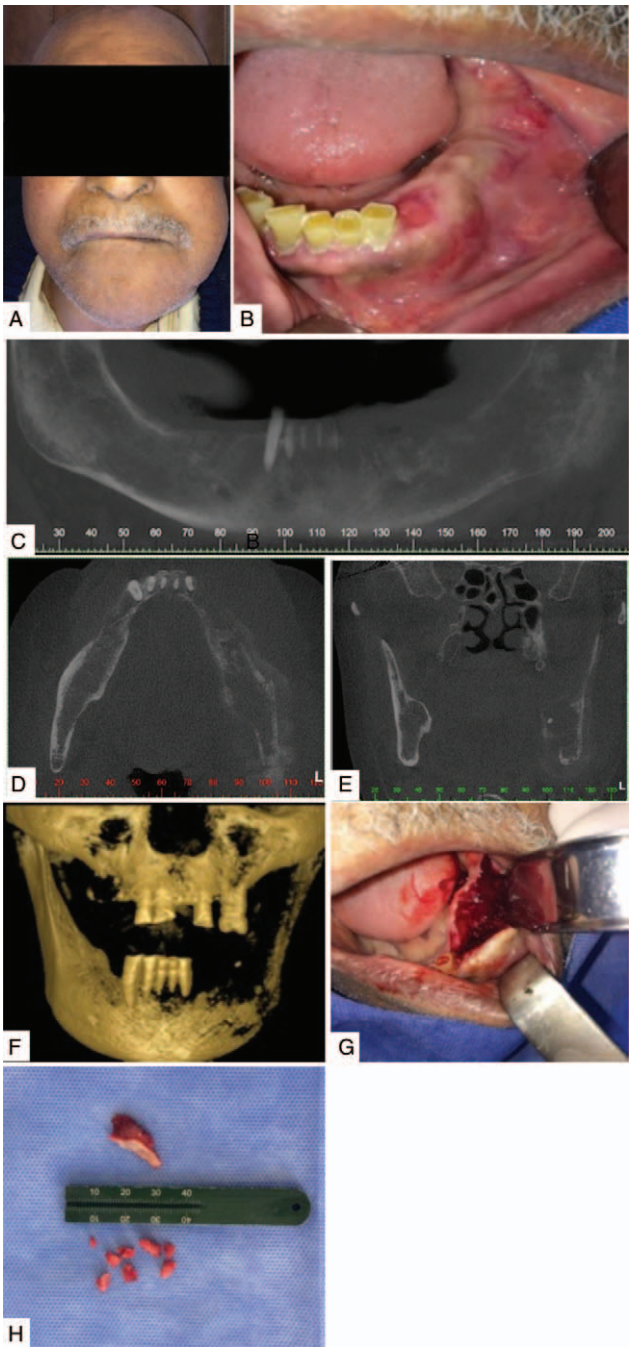

FIGURE 1. Clinical evaluation, radiographic images, and incisional biopsy. (A) Extraoral clinical examination: facial asymmetry and volume increase in the mandible on the left side. (B) Intraoral clinical examination: evident swelling in the alveolar ridge of the left side covered by firm and erythematous mucosa. (C) Panoramic reconstruction of the computed tomography showing diffuse radiolucent image in the mandibular region of the left side. (D) Computed tomography: axial section demonstrating the region of bone destruction on the left side. (E) Computed tomography: coronal section demonstrating the region of bone destruction on the left side. (F) Three-dimensional tomographic reconstruction. (G) Transoperative aspect of the lesional site during incisional biopsy. (H) Surgical specimens (above the ruler, soft tissue portion; below, bone tissue).

The patient was referred to the Oncology Service of the São Lucas Hospital of PUCRS in April 2017. The treatment was

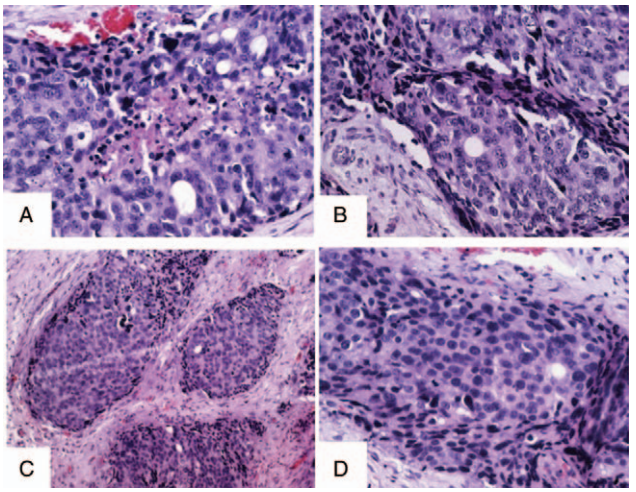

FIGURE 2. Microscopic images on hematoxylin and eosin. (A) Evidence of central area of necrosis, hyperchromatic cells, and ductiform structures (200× magnification). (B) Ductiform structures, nuclear hyperchromatism, and cellular atypia (100× magnification). (C) Proliferations of undifferentiated neoplastic cells in the form of tumoral islands (200× magnification). (D) Areas of nuclear hyperchromatism and atypical mitosis (200× magnification).

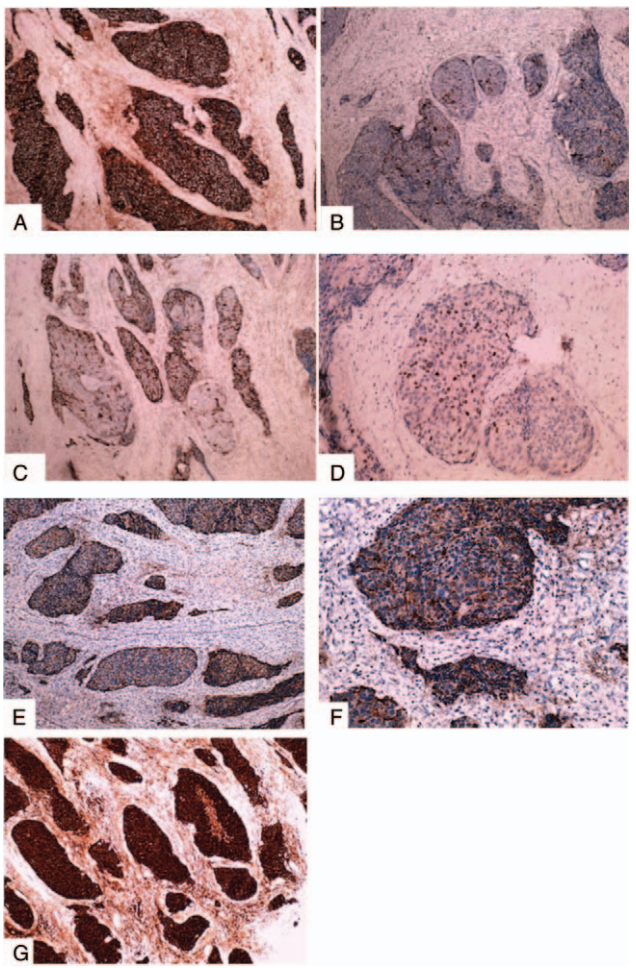

FIGURE 3. Photomicrographs with positive immunohistochemical reaction for the antibodies (100× magnification). (A) AE1 AE2; (B) CD 57; (C) epithelial membrane antigen (EMA); (D) P63; (E) PSA I; (F) PSA II; and (G) androgen receptor.

radiotherapy in the regions of metastases: mandible (left side) and lumbar spine at doses of 4200 cGy and 1200 cGy, respectively. In May of the same year, the patient presented clinical worsening and died.

DISCUSSION

Prostate adenocarcinoma is a malignant prostate tumor common in men over 40 years of age. The occurrence of symptomatology in advanced stages of disease justifies the need for clinical evaluation as routine for early diagnosis. One of the most commonly used routine tests in asymptomatic patients for diagnosis is the PSA examination. It is a marker that, as a rule, is present at high levels in patients with suspected prostate cancer. The patient in this case report presented high levels of PSA.[5]

The prognosis of prostate cancer is obscure since, when discovered, it is already assuming clinical characteristics of great proportions with risk of occurrence of metastases.[6–8]

Radiotherapy, chemotherapy, and endocrine therapy are the main therapeutic options for prostate carcinoma. Transurethral resection and radical prostatectomy are the most used. The association of radiotherapy as a previous adjuvant treatment is aimed at controlling the dimensions of the tumor.[4] In the patient in this report, the procedure was the total orchiectomy procedure and subsequently docetaxel chemotherapy.

Metastases of prostate carcinoma are common in surrounding lymph nodes (hypogastric, iliac, presacral, and para-aortic obturator) and also in bones such as thoracic vertebrae, lumbar vertebrae, and pelvis. The metastases in orofacial regions are extremely rare, but when they occur they preferentially affect the posterior mandible region as presented.[8–10]

The diagnosis of metastatic lesions in the orofacial region is still a dilemma for dentists because they present nonspecific aspects that mimic other oral lesions. Clinically, these metastases can cause pain, paresthesia, edema, ulcers, and pathological fractures, symptoms that can easily be mistaken for other oral lesions. Diagnosis should include imaging, histopathological examination and prior investigation of the patient's cancer history. In addition, diagnostic resources such as scintigraphy and immunohistochemical panel may be determinant for the definitive diagnosis.[11,12]

The first choice of treatment is hormonal therapy when bone metastases related to prostate cancer occur. This therapeutic conduct consists in administration of estrogenic compounds or luteinizing hormone–releasing hormone analogs, either alone or in combination with anti-androgens (androgen receptor blockers). The hormonal therapy can be associated or not with the surgical procedure.[13] The patient in this report underwent hormonal blockade therapy with goserelin acetate and bicalutamide, but did not obtain significant improvement.

In situations of failure of hormonal therapy, chemotherapy and radiotherapy may be instituted.[4] The patient underwent radiotherapy with a dose of 4200 cGy on mandible metastasis and 1200 cGy for lumbar spine metastasis. When metastases occur in bone regions, the prognosis worsens. In this situation it is demanded the establishment of methods to enable comfort, well-being, and systemic control. Even with the recommended therapeutic conduction, the referred patient presented clinical worsening in his evolution and subsequent death.

CONCLUSIONS

The rare occurrence of metastases in the oral region complicates the diagnosis by the dentist. In addition, such lesions present clinical, radiographic, and histological features that mimic other lesions. Although the occurrence of oral metastases is uncommon, dental surgeons should be alert to establish an early diagnosis for the

institution of therapy in the early stages of the disease and increase the chances of survival.

REFERENCES

1. Baldawa P, Shirol P, Alur J, Kulkarni VV. Metastasis: to and fro. *J Oral Maxillofac Pathol* 2017;21:463–464
2. Zandi M, Jafari M, Isapour M, Jafari AA. Mandibular metastasis in a patient with undiscovered synchronous thyroid and prostate cancer: a diagnostic dilemma. *J Oral Maxillofac Pathol* 2014;18:449–452
3. Albers DD. Adenocarcinoma of the prostate, metastatic to the mandible: report of case. *J Am Dent Assoc* 1970;81:883–886
4. Menezes JD, Cappellari PF, Capelari MM, et al. Mandibular metastasis of adenocarcinoma from prostate cancer: case report according to epidemiology and current therapeutical trends of the advanced prostate cancer. *J Appl Oral Sci* 2013;21:490–495
5. Pezaro C, Woo HH, Davis ID. Prostate cancer: measuring PSA. *Intern Med J* 2014;44:433–440
6. Gleason DF, Mellinger GT. Prediction of prognosis for prostatic adenocarcinoma by combined histological grading and clinical staging. *J Urol* 2017;197 (2S):S134–S139
7. Braunhut BL, Punnen S, Kryvenko ON. Updates on grading and staging of prostate cancer. *Surg Pathol Clin* 2018;11:759–774
8. Soares EC, Costa FW, Rocha-Filho FD, et al. Metastatic prostate adenocarcinoma associated with numb chin syndrome. *J Craniofac Surg* 2011;22:2366–2368
9. Head CS, Hematpour K, Sercarz J, et al. Carcinoma of the prostate presenting as a painful parotid mass with mandibular invasion: a case report. *Ear Nose Throat J* 2009;88:E7–8
10. Sorbera RJ, Taylor RG. Carcinoma of the prostate metastatic to the oro-facial region and mandible. *Br J Oral Surg* 1966;4:121–126
11. Xu Y, Wang Y, Zhou R, et al. The benign mimickers of prostatic acinar adenocarcinoma. *Chin J Cancer Res* 2016;28:72–79
12. Pruckmayer M, Glaser C, Nasel C, et al. Bone metastasis with superimposed osteomyelitis in prostate cancer. *J Nucl Med* 1996;37:999–1001
13. Andriole MD, Catalona MD. Prostate carcinoma. *Annu Rev Med* 1994;45:351–359

Filler Migration and Florid Granulomatous Reaction to Hyaluronic Acid Mimicking a Buccal Tumor

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Abstract: Hyaluronic acid is among the most commonly used cosmetic fillers. Although considered biocompatible and safe, it may rarely cause a wide range of complications. The authors report a case of migration of hyaluronic acid concomitant with granulomatous inflammatory response that mimicked a buccal tumor. A 52-year-old female presented with a solid painless mass of the right buccal area. The patient denied any history of trauma and cosmetic procedures of the affected area. Skin and mucosal membrane were intact and the lesion was firm and well fixed in the deep plane. Due to worrisome clinical presentation and the patient's history of breast cancer, the lesion was excised radically. Histopathological examination revealed multiple granulomas surrounding amorphous lakes of hyaluronic acid. During repeated, thorough anamnesis the patient admitted having underwent lip augmentation and nasolabial fold correction with HA two years before, after which the filler must have migrated posteriorly. Physicians need to be aware of various complications associated with cosmetic fillers as they may mimic severe clinical conditions.

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Key Words: Granuloma, hyaluronic acid, tumor

CASE PRESENTATION

Cosmetic fillers are increasingly popular in esthetic medicine and hyaluronic acid (HA), considered biocompatible and extremely well tolerable, is among the most commonly used agents. We present a case of delayed granulomatous reaction to HA associated with its migration from the injection site that clinically mimicked a malignancy.

The 52-year old Caucasian female presented with a solid, painless mass in the right buccal area. The patient denied any cosmetic procedures in the area of the lesion and history of trauma. Several months before she had been diagnosed with breast cancer which, at the time of presentation, was in local and regional remission.

The mass was firm on palpation and fixed in the deep plane. Skin and mucosal membrane were intact and a slight tenderness was present in proximity to the parotid duct. Sensory and motor functions of the face were intact. A buccal Stark lymph node was palpable adjacent to the lesion, but no other signs of lymphadenopathy were clinically evident. Contrast CT visualized a tumor-like fibrotic lesion measuring $10 \times 25 \times 16$ mm (Fig. 1). Clinically, the patient's history of cancer and worrisome presentation raised concerns about neoplastic character of the lesion—either a primary process arising from buccal soft tissues or salivary glands, or a distant recurrence of breast malignancy.

Therefore, and to avoid possible facial nerve damage during a biopsy, a radical excision under general anesthesia was scheduled. A horizontal skin incision under the parotid duct revealed a solid tumorous mass fused with adjacent soft tissues. The lesion was excised and a typical layer-by-layer suturing with a temporary gauze compression was applied for 5 days.

Histopathological examination revealed adipose tissue and fragments of skeletal muscle with numerous foreign body-type granulomas surrounded by dense fibrosis. Pools of amorphous greyish-blue material in the center of each granuloma were surrounded by numerous multinucleated giant-cells with focal palisading and scattered mononuclear cells. Ancillary immunohistochemical reactions demonstrated that the giant cells were positive for CD68 and negative for cytokeratins. Staining with Alcian Blue at pH 2.5 produced bright-blue color of the amorphous material (Fig. 2). Overall, the diagnosis of a tumor-like granulomatous reaction to injected HA was made.