Hodgkin Lymphoma of the Oral Mucosa

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Abstract In this report, we describe a rare case of relapsed nodular sclerosing Hodgkin lymphoma presenting as a lesion of the oral mucosa. Although this is an uncommon clinical scenario, health care professionals should be aware of this possibility. A brief differential diagnosis and review of Hodgkin lymphoma is discussed.

Keywords Oral mucosa · Hodgkin lymphoma · Nodular sclerosing

Introduction

Hodgkin lymphoma, whether primary or relapsed, is rare in the oral soft tissues and jaws [1–6]. Although disseminated Hodgkin lymphoma involving the oral mucosa is said to be more common, we could trace only a few reports, citing 5 cases, involving the tongue, palate and tonsil [7–10]. In most of these cases, the primary site appeared to be in Waldeyer's ring [7, 9–11] although this is also a rare site for the development of this lymphoma [10, 11]. The purpose of this manuscript is to report the rare occurrence and to alert oral health care practitioners to the possibility of Hodgkin lymphoma involving the oral cavity.

Case Report

A 71 year old white male presented with a swelling in the left mandibular buccal vestibule and buccal mucosa, lateral to his left mandible. This mass had been increasing in size over the 2 months prior to his presentation, with significant growth over the previous one and a half weeks. At presentation the lesion measured approximately 6 × 3 cm. It was indurated, non-fluctuant and fixed. The overlying mucosa and skin appeared within normal limits apart from the swelling. There was no numbness or pain. No neck nodes were palpable.

The patient had smoked approximately one and a half cigarette packs per day from his teenage years until his mid-thirties, at which point he stopped, and consumed alcohol approximately once a month. He had a history of rheumatoid arthritis and bilateral hip and knee replacements several years previously. His medications were significant for amitriptyline, warfarin (for atrial fibrillation), and an analgesic patch.

Significantly, he had a history of an axillary lump which had been detected 2 years previously, which had been diagnosed as “classical Hodgkin lymphoma, nodular sclerosis subtype”. For this, he had received chemotherapy using a cocktail of 4 drugs, Adriamycin, Bleomycin, Vinblastine, and Dacarbazine [ABVD] with complete response, documented over a period of 6 months.

Grossly, the buccal mucosa excisional biopsy specimen consisted of 2 tan and brown fragments of soft tissue, the larger measuring 9 × 8 × 6 mm.

Microscopically, the lesion consisted of a vascular connective tissue stroma containing benign inflammatory cells (eosinophils, plasma cells and small lymphocytes) admixed with neoplastic cells. The neoplastic cells had large vesicular nuclei with prominent nucleoli. Classic

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binucleated Reed-Sternberg cells were seen (Fig. 1) and collagen deposition was present. The tumor cells showed positive immunoperoxidase staining for CD15 and CD30 (Fig. 2), but were negative for CD20, CD5, CD68, CD1a, S100, CD10, CD5, ALK-1 and Epstein-Barr virus Encoded RNA [EBER]. CD5 and CD20 were positive in the benign T and B cells present in the background, respectively. The diagnosis of classical Hodgkin lymphoma, nodular sclerosis subtype was made.

Fig. 1 Benign inflammatory cells admixed with neoplastic cells. (Hematoxylin and eosin stain; original magnification $\times 200$). *Inset* Reed-Sternberg cell (original magnification $\times 400$)

The oral lesion treatment included radiotherapy, at a dosage of 3000–4500 Gy, using intensity-modulated radiation therapy in order to spare the floor of mouth and surrounding anatomical structures.

Discussion

Because of the clinical characteristics of the lesion at initial presentation, malignancies were considered at the top of a differential diagnosis. Possibilities included mucoepidermoid carcinoma, adenoid cystic carcinoma, carcinoma ex-pleomorphic adenoma, fibrosarcoma or pleomorphic sarcoma, non-Hodgkin lymphoma (NHL) and metastatic tumor. Benign lesions were unlikely given the clinical features.

Metastatic tumors of the oral soft tissues are relatively uncommon and represent about 1 % of oral malignancies. The mechanism of metastasis to this region is poorly understood. The most common sites are the gingiva (50 % of all cases) and tongue (25 %). A wide variety of tumor types may be seen, and currently in males, prostate cancer is the most common, followed by lung cancer. In females, breast cancer is the most common, followed by lung cancer [12]. In many cases the primary tumor is known; but in some cases the oral lesion is the initial manifestation of malignancy. In the current case, disseminated and metastatic cancers could not be dismissed from a clinical differential diagnosis.

Fig. 2 The tumor cells showed positive immunoperoxidase staining for CD15 and CD30. (Original magnification $\times 200$)

Hodgkin lymphoma, whether primary or relapsed, is rare in the oral soft tissues and jaws. We could trace only 12 reports of primary Hodgkin lymphoma occurring in the oral mucosa, [8, 9, 13–21] and only a few occurring in the jaws [1–6]. Disseminated Hodgkin lymphoma involving the oral mucosa is said to be more common than primary lesions, however, we could trace only a few reports, citing 5 cases, involving the tongue, palate and tonsil [7–10]. In most of these cases, the primary site appeared to be in Waldeyer's ring, [7, 9–11] although Waldeyer's ring itself is a rare site for the occurrence of Hodgkin lymphoma [10, 11]. Locations in Waldeyer's ring include the nasopharynx, followed by the tonsil, base of tongue and posterior pharyngeal wall [10].

The classification of Hodgkin lymphoma has evolved since it was first described by Thomas Hodgkin and Samuel Wilks in the nineteenth century [22]. According to the World Health Organization, Hodgkin lymphoma is divided into nodular lymphocyte predominant Hodgkin lymphoma, and classical Hodgkin lymphoma (CHL) [22]. CHL is further divided into 4 subtypes: nodular sclerosing (NSHL), mixed cellularity, lymphocyte-rich and lymphocyte-depleted. NSHL is the most common, accounting for approximately 70 % of all cases. NSHL has a male:female ratio of about 1:1, different from the other CHL which generally have a male predominance [22].

NSHL most commonly involves the mediastinal lymph nodes (80 % of cases). In the current case, the patient initially presented with axillary lymphadenopathy. This was followed by dissemination to the oral area several months later, making this a stage IV lesion, with a graver prognosis.

Histologically, NSHL demonstrates a nodular growth pattern, with collagen bands interspersed between the nodules. The Reed-Sternberg [R-S] cells are present as classical binucleated cells, and as "lacunar" cells. The latter morphology is related to retraction of the cell membrane making the nuclei appear as if they are lying in lacunae. The neoplastic cells are surrounded by non-neoplastic small lymphocytes, eosinophils, plasma cells and sometimes neutrophils.

Classical Hodgkin lymphoma is negative for CD45, helping differentiation from other types of lymphoma, and is positive for PAX-5 at low density. R-S cells are positive for CD30, CD15 and are typically negative for transcription factors B-cell specific activator protein, Oct2 and BOB-1. CD15 may be expressed by only a minority of the neoplastic cells. In some cases, CD20 may be present, but is usually expressed by only a minority of the neoplastic cells. The Epstein-Barr virus related latent membrane protein can be seen in up to 30 % of NSHL [22].

Hodgkin lymphoma is treated with ABVD and/or radiotherapy, depending on the stage of disease. The overall cure rate is quite high, reaching 75 % of all cases.

In conclusion, we present a rare case of relapsed NSHL presenting as a lesion of the oral mucosa. Although this is an uncommon clinical scenario, health care professionals should be aware of this possibility.

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