CASE REPORT

Extranodal diffuse large B cell lymphoma of maxillary sinus presenting as a palatal ulcer

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SUMMARY

A multitude of disease processes ranging from periodontitis to malignancies can lead to formation of solitary ulcer on the palate. Hence solitary ulcers of palate can often be a challenging one to diagnose. We report an interesting case of a diffuse large B cell lymphoma of the maxillary sinus which perforated the palatal bone and presented clinically as a palatal ulcer. Initially the lesion manifested as a small ill-defined swelling in the posterior palatal slope in relation to 24 and 25 which were mobile and hence was erroneously diagnosed as chronic periodontal abscess. This paper is intended to stress the relevance of including non-Hodgkin's lymphoma in the differential diagnosis of solitary palatal ulcers as it may be often misdiagnosed as more common reactive or inflammatory lesions.

BACKGROUND

Lymphomas of oral cavity are rare entities and make up only 3%–5% of all lymphomas.¹ However, they occupy the third position as the most common malignancies affecting the oral region.² The lymphomas are broadly grouped into Hodgkin's and non-Hodgkin's based on the morphology of tumour cells. In the head and neck region, non-Hodgkin's lymphoma (NHL) occurs more frequently than Hodgkin's lymphoma, the most common subtype in the oral cavity being diffuse large B cell lymphoma.³ Diffuse large B cell lymphoma includes several forms of lymphoma with certain features like B cell phenotype, diffuse growth pattern and aggressive clinical history. It commonly affects older age group, the median age falling between sixth and

Figure 2 Cone beam CT image (coronal view) showing a hyperdense mass in the left maxillary sinus extending into the oral cavity perforating the palatal floor.

seventh decade⁴ and usually presents as a rapidly enlarging mass at a single nodal or extranodal site. Gingiva and hard palate are the most common intra-oral sites of involvement.⁵ In the early stages, oral lymphomas occurring in these sites can mimic more common inflammatory/reactive disease processes

Figure 1 An ulcerated swelling on the left posterior palatal slope in relation to 25.

Figure 3 Cone beam CT image (sagittal view) showing the lesion filling the lower anterior aspect of the left maxillary sinus causing a significant erosion of maxillary alveolus.

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Figure 4 Subepithelial connective tissue showing ectatic vessels (arrows) and perivascular distribution of lymphocytes (arrow heads) (H&E).

like periodontal abscess or pyogenic granuloma and can easily be misdiagnosed. We report an interesting case of diffuse large B cell lymphoma of maxillary sinus, which was diagnosed initially as a chronic periodontal abscess and later presented as a solitary non-healing ulcer of the palate.

CASE PRESENTATION

A 32-year-old female patient presented to the dental outpatient department with pain associated with the last tooth in the left side of the upper jaw. The pain was due to acute pulpitis of grossly decayed 28. As an incidental finding, the clinician also noticed a fluctuant swelling in the palatal gingiva in relation to 25 which showed grade 1 mobility. The swelling was diagnosed clinically as chronic periodontal abscess. Decayed 28 was extracted and the patient was put on antibiotics. Two weeks later, the patient reported back with an ulcer in the palate. On general examination, she was moderately built and nourished and was apparently healthy. No palpable lymph nodes were noted. On intraoral examination, an oval shaped ulcer, measuring 2 cm × 2 cm was noticed on the left posterior palatal slope in relation

Figure 5 Sheets of large to medium sized atypical round cells with moderate to abundant cytoplasm (arrows) in the deeper connective tissue (H&E).

Figure 6 Angiocentric pattern of distribution of tumour cells. Note the vessel wall destruction and vascular invasion of tumour cells (arrows) (H&E).

to 25 (figure 1). The ulcer was covered by a necrotic slough and showed irregular borders. The area surrounding the ulcer was erythematous. On palpation it was non-tender, soft in consistency and there was no associated bleeding or pus discharge.

INVESTIGATIONS

Cone beam CT (CBCT) was performed using CS9300 scanner (Rochester, NY14608ma, USA) with acquisition protocol as follows: 90 kVp, 5 mA, 11.3 s and field of view of 17×13.5. The coronal view showed a hyperdense mass in the left maxillary sinus extending into the oral cavity perforating the palatal floor (figure 2). In the sagittal view, the lesion was found to be filling the lower anterior aspect of the left maxillary sinus and a significant erosion of maxillary alveolus was noticed (figure 3).

DIFFERENTIAL DIAGNOSIS

Based on the clinical presentation, the following lesions were considered as differential diagnosis.

1. Necrotising sialometaplasia.
2. Infections (tuberculosis, histoplasmosis).
3. Salivary gland malignancies (mucoepidermoid carcinoma, adenoid cystic carcinoma).
4. Squamous cell carcinoma.
5. Connective tissue malignancies.

TREATMENT AND FOLLOW-UP

Incisional biopsy of the lesion was carried out. The histopathological examination of the tissue sections showed superficial hyperplastic, hyperparakeratinised stratified squamous epithelium showing areas of ulceration. The connective tissue stroma was highly cellular and the subepithelial connective tissue showed dense infiltrate of chronic inflammatory cells predominantly lymphocytes suggesting the inflammatory nature of the lesion. Ectatic vessels and perivascular distribution of lymphocytes were also noticed in the superficial connective tissue (figure 4). But the deeper connective tissue showed sheets of large to medium sized atypical round cells with moderate to abundant cytoplasm (figure 5). The nuclei were folded or convoluted and had irregular outline. Angiocentric pattern of distribution of tumour cells was noted with one large vessel showing vessel wall destruction and vascular invasion (figure 6). The sections

Figure 7 Immunohistochemical expressions of the tumour cells. (A) Showing strong positivity for CD45. (B) Strongly positive for CD20 suggesting B cell origin of tumour. (C) Positive expression for MUM-1.

also showed areas of necrosis. The microscopic features were suggestive of haematolymphoid malignancy. Though angiocentric distribution of atypical round cells favoured the possibility of angiocentric T cell lymphoma, other (NHLs), embryonal rhabdomyosarcoma, monophasic synovial sarcoma and poorly differentiated squamous cell carcinomas were considered as differential diagnosis. On immunohistochemical staining (IHC), the tumour cells stained positive for CD45 (figure 7A) and CD20 (figure 7B). CK, EMA, vimentin, CD31, SMA, desmin CD three and CD138 were negative. Ki 67 positivity was noticed in 60% of the cells. Thus, based on the microscopic findings and IHC, a final diagnosis of diffuse large B cell lymphoma was made. Following the diagnosis, a set of prognostic markers were used to subtype the tumour in order to decide on the chemotherapeutic regimen. The tumour cells were negative for CD10, but showed positivity for BCL6 and MUM1 (figure 7C). The markers for double expressor lymphomas, MYC and BCL2 were negative. Hence the lesion was subtyped as diffuse large B cell lymphoma, activated B cell subtype.

OUTCOME AND FOLLOW-UP

The patient was put on chemotherapy and regression in the size of the tumour was noticed over a period of 3 months.

DISCUSSION

Non-NHLs are a heterogeneous group of lymphoproliferative malignancies which can involve lymph nodes and lymphoid organs as well as extranodal organs and tissues.⁶ 20%–30% of NHLs arise from the extranodal sites.⁷ The most common sites for extranodal NHL are the gastrointestinal tract followed by head and neck region.⁸ Oral lymphoma and paraoral lymphoma represent about 2.5% of the total cases of lymphoma.⁹ Lymphomas of palate can occur either as a lesion arising from palatal mucosa or as a palatal extension of a lesion which originates in the maxillary sinus. Their diagnosis at times can be extremely challenging as the clinical manifestations often mimic a wide range of pathologies affecting palatal region. The case discussed here, initially presented as an asymptomatic fluctuant swelling in the palate associated with the roots of left maxillary second premolar which was mobile and hence it was mistaken for chronic periodontal abscess. The lesion persisted even after a course of antibiotics was completed and underwent ulceration over a period of 2 weeks. The clinical presentation at this stage mimicked necrotising sialometaplasia, a reactive lesion of minor salivary gland which begins as a swelling and then progresses as a rapidly growing ulcer before it heals completely. Ulcers due to infections like tuberculosis and histoplasmosis which are known to present as solitary palatal ulcers were also considered as differential diagnosis. However, rapidity in the growth of the tumour, mobility of the adjacent teeth and imaging studies which revealed a tumour mass in the left maxillary sinus perforating the palatal floor suggested that the lesion most likely could be a malignant neoplasm arising from the maxillary sinus. Microscopically,

though dense infiltrate of lymphocytes in the superficial connective tissue was a bit misleading, the presence of sheets of large atypical round cells in the deeper connective showing perivascular distribution and vascular invasion helped us in narrowing down our diagnosis to haematolymphoid pathology. Angiocentric T cell lymphoma, other (NHLs), embryonal rhabdomyosarcoma, monophasic synovial sarcoma and poorly differentiated squamous cell carcinoma were considered as histopathological differential diagnosis. Angiocentric T cell lymphoma topped the list as the most likely diagnosis in this case, as it presented clinically as a destructive lesion of the palate and microscopically, round atypical lymphocyte like tumour cells showed the typical angiocentric pattern of distribution with vessel wall destruction and vascular invasion. However, a final diagnosis of large B cell lymphoma was made on further evaluation using a panel of IHC markers which showed that the tumour cells were B cell in origin (CD45 positive, CD20 positive and CD3 negative) and lacked plasmacytoid differentiation (CD138 negative).

Diffuse large B cell lymphoma (DLBCL) is a malignant proliferation of large B cells with very heterogeneous morphology, phenotype and molecular and clinical findings.¹⁰ DLBCL includes several subtypes with different clinical course. Identification of these subtypes has prognostic and therapeutic significance. The importance of classifying DLBCL based on cell of origin as activated B cell (ABC) or germinal centre B cell (GCB) is widely accepted based on differences in clinical outcome, gene expression, chromosomal alterations and somatic mutations^{11 12} and it has been found that ABC exhibits poorer prognosis than GCB.¹³ A recent classification of diffuse large B cell lymphomas has a recommendation that routine practice should recognise tumours belonging to the GCB and ABC subsets using either immunohistochemical surrogates or other means, as they may become available.¹⁴ Gene expression studies using DNA microarrays which formed the basis for this subcategorisation is not still applicable to routine clinical practice. Immunophenotyping of the tumour cells by Han's classifier using the IHC markers CD 10, BCL6 (germinal centre markers) and MUM-1 is widely used for all practical purpose. DLBCs are subclassified as GCB subgroup if CD10 and/or BCL6 are positive and MUM-1 is negative and as non-GCB subgroup if CD10 is negative and MUM-1 is positive.¹³ Certain high grade B cell lymphomas which show BCL2/BCL6 along with MYC expression, termed as 'double expressor lymphomas' had been found to behave very aggressively.¹⁵ In our case, the tumour cells were negative for both BCL2 and MYC. The proliferative marker, Ki 67 was used as a prognostic marker and 60% of the tumour cells were found to be positive. The Ki 67 expression in DLBC usually varies between 30% and 100%¹⁶ and an expression of >80% are termed as 'highly proliferative' or aggressive tumours.¹⁷

DLBCL are aggressive tumours that can be rapidly fatal if left untreated. Complete remission can be achieved in a significant number of the patients with intensive combination chemotherapy. Hence early diagnosis plays an important role in the management. As it often present as palatal ulcers, DLBCLs should always be considered as a differential diagnosis for rapidly progressing solitary ulcers of palate. Microscopic diagnosis, can be challenging as inflammation is a common occurrence in oral biopsies and at times it might be difficult to differentiate reactive lymphocytic proliferation from neoplastic proliferation. Immunomarkers might be of great help in such situations and stratification of DLBCL by IHC is an effective method of delineating the subtypes.

Learning points

- ▶ A wide range of disease processes can manifest as solitary ulcers of palate.
- ▶ Non-Hodgkin's lymphoma presenting as solitary palatal ulcer may be easily misdiagnosed as more common inflammatory or reactive diseases.
- ▶ Diffuse large B cell lymphomas should always be considered as a differential diagnosis for rapidly progressing solitary ulcers of palate.

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