Primary T cell lymphoma of salivary gland: a report of a case and review of the literature

W S R Hew, F A Carey, N M Kernohan, A D Heppleston, R Jackson, R F Jarrett

Lymphoma of the salivary gland accounts for 5% of cases of extranodal lymphoma and 10% of malignant salivary gland tumours. Most primary salivary gland lymphomas are B marginal zone lymphomas arising on a background of sialadenitis associated with autoimmune disorders such as Sjögren’s syndrome. Primary T cell lymphoma of the salivary gland is rare. This report describes a case of primary T cell lymphoma arising in the parotid gland of an elderly white man, which was notable for its striking resemblance to a B cell extranodal marginal zone lymphoma. Immunohistochemistry and gene rearrangement studies confirmed the clonal T cell nature of the tumour. There was no molecular evidence of Epstein-Barr virus (EBV) infection of neoplastic or surroundings cells. Only 14 cases of primary T cell lymphoma of the salivary glands have been recorded in the literature, most being from the Orient and having extremely variable prognosis. Those with a T/natural killer cell phenotype are associated with EBV infection. This case highlights the fact that T cell lymphoma in the salivary gland can mimic closely the morphological features of B cell extranodal marginal zone lymphoma.

**CASE REPORT**

A 69 year old white man presented with an apparently isolated swelling on the left side of his neck that had become progressively more prominent over a period of several months. He was otherwise well. Clinical examination revealed a large mass that appeared to arise within the left parotid gland. There was no clinical or laboratory evidence of pre-existing autoimmune disease, enteropathy, or more extensive disease of the lymphoreticular system. The patient progressed to an incisional biopsy of the mass.

We received multiple pale fragments of tissue admixed with some adipose tissue measuring altogether 20 × 8 × 8 mm. Macroscopic examination revealed no specific features. Microscopy revealed salivary and adipose tissue widely infiltrated by a monotonous population of medium sized cells with cleaved nuclei and inconspicuous nucleoli. Frequent mitotic activity and apoptotic bodies were evident (fig 1A). Occasional groups of malignant cells were identified infiltrating ductal epithelium, the appearances being reminiscent of lymphoepithelial lesions of a low grade extranodal marginal zone non-Hodgkin’s lymphoma (NHL) (fig 1B). However, immunohistochemical staining revealed that the neoplastic cells were positive for markers indicative of T cell lineage (CD3, CD5, CD43, and UCHL 1) (fig 1C,D) and negative for the B cell markers CD20 and CD79a (fig 1E). Sections stained for the natural killer (NK) cell marker CD56, CD30, ALK1 (anaplastic lymphoma kinase antibody), CD21, granzyme B, and TdT (terminal deoxynucleotidyl transferase) were negative. The features of the infiltrate were those of a T cell NHL, which also showed involvement of the surgical resection margins. There was no evidence that the lymphoma had arisen within an intraparotid lymph node and staging investigations did not identify disease at any other site.

Epstein-Barr virus (EBV) has been associated with the development of salivary gland T cell NHL, but in this case in situ hybridisation for Epstein-Barr virus (EBV) encoded early nuclear RNA (EBER) was negative in the neoplastic cells. DNA extracted from paraffin wax embedded sections was submitted for polymerase chain reaction (PCR) analysis to detect clonal rearrangements of the immunoglobulin heavy chain (Igh) gene and of the T cell receptor γ (TCRγ) using the strategy described by McCarthy et al. Clonal rearrangement of the Igh gene was not identified but reactions to detect rearrangement of the TCRγ gene disclosed a single monoclonal fragment (fig 2). The PCR products were cloned and the nucleotide sequence of seven independent clones was determined in both directions; five clones were found to have identical sequences. Comparison with the corresponding germ line sequences revealed that this consensus rearrangement was “out of frame” and therefore non-functional. This result provided indirect evidence that the neoplastic T cell population expresses TCRββ and not the TCRγβ.

Further staging investigations including clinical, haematological, and radiological examinations revealed no evidence of widespread disease.

The patient was treated initially with local radiotherapy to reduce the size of the parotid tumour, followed by systemic chemotherapy (CHOP regimen—cyclophosphamide, hydroxydaunorubicin (adriamycin), oncovin (vincristine), and prednisolone).

**DISCUSSION**

We report a case of primary T cell NHL of the parotid gland in an elderly white man, which was particularly notable for its close morphological resemblance to a low grade extranodal marginal zone NHL of salivary gland mucosa associated lymphoid tissue. Primary T cell NHL of the salivary glands is rare in Western populations, the present case being only the third such case described. NHL of the salivary glands is an uncommon form of malignancy, accounting for 5% of cases of extranodal lymphoma, and 10% of malignant diseases of the salivary glands. Most cases that are bone fide primary lesions of the salivary glands are B cell extranodal marginal zone NHL, usually arising on a background of myoepithelial sialadenitis. This case demonstrates that primary T cell lymphoma of...
The salivary gland can mimic closely a low grade extranodal marginal zone B cell lymphoma. However, the lack of evidence of pre-existing sialadenitis or evidence of underlying autoimmune disease may prompt consideration of an alternative diagnosis, and recourse to immunohistochemistry and gene rearrangement studies should readily distinguish this lesion from primary B cell marginal zone lymphomas, which are more commonly encountered in the salivary glands. There was no evidence to suggest that the tumour in this case was nodally based, either arising in an intrasalivary lymph node or representing extensive nodal or extranodal disease secondarily involving the salivary gland.

"Primary T cell non-Hodgkin’s lymphoma of the salivary glands is rare in Western populations, the present case being only the third such case described"

The histological features of cases described in the literature are variable (table 1). A review of the literature discloses that primary T cell lymphoma of the salivary glands is rare, with only 14 cases described, all but two of which have been from Oriental countries. The parotid and submandibular glands are the most frequently involved salivary tissues, although occasional cases are described in the sublingual glands. The most frequent histological type of this condition is a peripheral T cell lymphoma, often of low grade morphology, although occasionally pleomorphic. Staining for markers indicative of NK cell differentiation further identifies a few cases of angiocentric T/NK lymphomas and a similar number of cases of T anaplastic large cell lymphoma are also described. Of the 11 cases where data have been recorded, in seven cases...
The experience of Chan et al. suggests a variable outcome, with survival after diagnosis ranging from six weeks to more than four years. The two patients who had the longest survival were EBV and CD56 negative, although one apparently similar patient survived for only six months. To date, the patient described in our report remains disease free more than 30 months after diagnosis.

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**Take home message**

- T cell lymphoma in the salivary gland can closely mimic the morphological features of B cell extranodal marginal zone lymphoma

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**Table 1** Histological features of cases of primary T cell lymphoma of the salivary glands described in the literature (including our case)

<table>
<thead>
<tr>
<th>Refs</th>
<th>Sex</th>
<th>Age</th>
<th>Ethnic origin</th>
<th>Family history</th>
<th>Site of disease</th>
<th>Histology</th>
<th>EBV status (ISH or IHC)</th>
<th>Treatment</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>M</td>
<td>46</td>
<td>Chinese</td>
<td>N/A</td>
<td>Submandibular</td>
<td>T NHL</td>
<td>Negative (N/A)</td>
<td>Chemotherapy MACOP</td>
<td>&gt;48 months</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>48</td>
<td>N/A</td>
<td>Parotid</td>
<td>T NHL</td>
<td>T-naplastic large cell</td>
<td>Positive</td>
<td>Multimodality treatment not otherwise specified</td>
<td>&gt;18 months</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>79</td>
<td>N/A</td>
<td>Submandibular</td>
<td>T NHL</td>
<td>T-naplastic large cell</td>
<td>Negative</td>
<td>Multimodality treatment not otherwise specified</td>
<td>&gt;18 months</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>69</td>
<td>White</td>
<td>Nil</td>
<td>Parotid</td>
<td>T NHL</td>
<td>Negative (N/A)</td>
<td>Multimodality treatment not otherwise specified</td>
<td>&gt;30 months</td>
</tr>
</tbody>
</table>

EBV, Epstein-Barr virus; ICH, immunohistochemistry; ISH, in situ hybridisation; MACOB, methotrexate, adriamycin (doxorubicin), cyclophosphamide, oncovin (vincristine), and prednisolone; N/A, data not available/commented on in the original literature; NHL, non-Hodgkin’s lymphoma; NK, natural killer cell.

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**REFERENCES**

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