Primary B-Cell Lymphoma of the Mandible

Primary lymphomas of the jaws are uncommon and only 2% of extra-nodal lymphomas arise in the oral region. A case of a primary B-cell lymphoma is reported that was associated with an impacted third molar in the mandible. A dentigerous cyst was associated with the impacted tooth. The neoplastic tissue was removed together with the molar tooth and diagnosed immunocytologically as a B-cell lymphoma. The patient was treated with radiotherapy and followed up for 17 years with no signs of recurrence.

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Abstract

Primäre Lymphome der Kiefer sind sehr selten und nur 2 % der Lymphome außerhalb von Lymphknoten treten in der Mundhöhle auf. Die Autoren berichten über einen Fall eines primären B-Zellen Lymphoms, welches vergesellschaftet war mit einem retinierten Weisheitszahn des Unterkiefers.

Eine „follikuläre Zyste" umgab den retinierten Weisheitszahn. Das neoplastische Gewebe wurde zusammen mit dem dritten Molaren entfernt und immunzytologisch als B-Zell-Lymphom diagnostiziert. Die Patientin wurde bestrahlt und über einen Zeitraum von 17 Jahren nachuntersucht. Es traten keine Zeichen eines Rezidivs auf. In der Einführung berichten die Autoren über verschiedene Systeme der Klassifikation, um danach eingehend über den Fall einer 27-jährigen Patientin zu berichten. Nachdem die Diagnose: B-Zell-Lymphom gestellt war, wurde in einem Zweiteingriff ein regionärer Lymphknoten entnommen und histologisch aufgearbeitet. Es gab keine Anzeichen einer granulomatösen Entzündung oder Malignität. Die Diagnose wurde durch eine zweite Pathologin in einer auf Lymphome spezialisierten Klinik bestätigt. Deren Onkologe empfahl eine Radiatio. Der rechte Unterkiefer im Bereich des Operationsgebietes wurde mit 36 Gy bestrahlt. Der Fall bestätigt wieder einmal die Bedeutung einer histologischen Untersuchung.

■ Lymphomas are malignant lesions of cells derived from lymphoid tissue.[1] Lymphoid proliferation is divided into Hodgkin's disease in which Reed Sternberg giant cells are present and non-Hodgkin's lymphoma that account for all other neoplastic lymphoid proliferations.[1] It has been determined that only 2 % of extra nodal lymphomas arise primarily in the jaws or the oral cavity.[1,2] Most lymphomas are exclusively of B-cell lineage (98 %), with 58 % of these sub-typed as diffuse large B-cell lymphomas.[1]

Classification systems have been modified and changed throughout the years. In the 1990's the Working Formation of non Hodgkin's lymphomas was used for clinical evaluation and treatment (Tab.1).[6] Prior to this the Kiel classification, updated in 1992, was used extensively especially in Europe.[5] This was supplemented by the Anne-Arbor staging system (Tab. 2) which is currently used in clinics in Cape Town.[6] The WHO Real Classification of non Hodgkin's lymphomas according to the clinical aggressiveness is also used (Tab. 3).[1,2,8] Non Hodgkin's lymphomas have been reported in the oral soft tissues, but there have been few reported cases of primary lymphoma in the jaws.[1,7,9] A case of a primary B-cell lymphoma of the mandible is reported in an adult female with a 17 year non-recurrence follow up.

Case Report

A 27-year-old female was referred to a maxillofacial and oral surgeon in April 1992 for the removal of her wisdom teeth. She had no systemic symptoms; however, she reported a numb feeling over the whole of her mouth in the recent past which had recovered. Her past medical history indicated that she had a heart murmur which was insignificant and she did not take prophylactic antibiotics. Her general health was good. She had past operations with no general anaesthetic problems. She did have low blood pressure and was anaemic. Extra-oral

Low Grade
Small lymphocytic
Follicular, predominantly small cleaved cell
Follicular, mixed small cleaved and large cell
Intermediate Grade
Follicular, predominantly large cell
Diffuse, small cleaved cell
Diffuse, mixed small and large cell
Diffuse, large cells
High-Grade
Large cell immunoblastic
Lymphoblastic
Small non-cleaved cell
Miscellaneous

Tab. 1: A working formulation of non-Hodgkin's lymphomas for clinical usage.[1]

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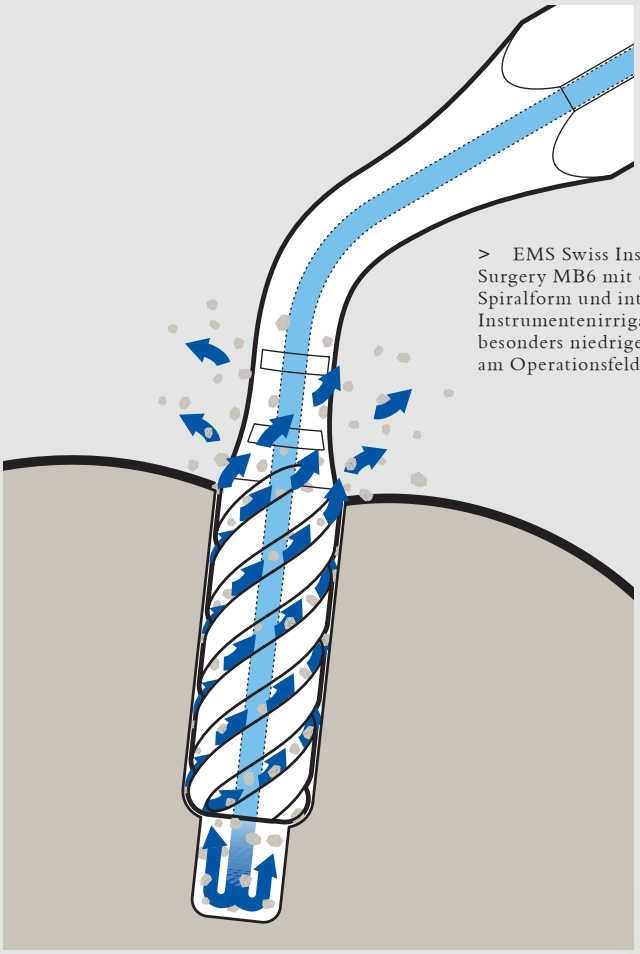

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Stage	Defining System
Stage I	Restricted to single lymph node region (1) or a single extranodal site (I-E)
Stage II	Two or more areas of nodal involvement on same side of the diaphragm (II) or one or more lymph nodes regions with an extranodal site (II-E)
Stage III	Lymphatic involvement on both sides of the diaphragm (III), possibly with an extranodal site (III-E), the spleen (III-S) or both (III-SE)
Stage IV	Liver, marrow, or other extensive extranodal disease
Sub stages	
Substage E	Localised, extranodal disease
Substage A	Absence of systemic signs
Substage B	Presence of unexplained weight loss (≥10% in 6 months) and or unexplained fever, and or night sweats
The spleen is considered nodal.	

Tab. 2: Ann-Arbour staging system.[6]

examination of the head and neck revealed that there was lymphadenopathy of the submandibular group of lymph nodes on the right side. Her temporo-mandibular joint functioned well and there were no cranial nerve problems. Intra-oral examination showed limited space for the wisdom teeth. Apart from slight crowding, she was in Class 1 bite on both sides. Her tongue function was normal, her glossopharyngeal and vagal nerve function were normal and the mucosae intact. The orthopantomograph showed that the 38 tooth had a mesio-angular inclination and was close to the inferior alveolar nerve (Fig. 1). The 48 tooth had a disto-angular inclination in the ramus of the mandible and showed some radiolucency around its crown in the distal aspect (Fig. 2). Its root was also near the inferior alveolar nerve. It was decided that both lower wisdom teeth should be removed under general anaesthetic. The intra-bony soft tissue distal to the crown of the 48 was removed and placed in 10 % formalin solution and sent for histological examination. The patient was given the normal post operation regime of antibiotics, analgesics and a mouth rinse. She was examined again one week later at which time the pathology report was discussed with her.

Pathology Report

The tissue received from the right mandibular third molar region (tooth 48) was reviewed by an Oral Pathologist. The specimen consisted of a molar tooth with soft tissue attached to the amelo-cemental junction. There was also a separate mass of soft rubbery tissue measuring 25 x 20 x 15 mm in size. The soft tissues were sectioned and those associated with the crown of the tooth were processed separately from the other soft tissue mass. Microscopic examination of the tissues from around the crown of the tooth showed features in keeping with that of a dentigerous cyst. The histological picture of the other mass of soft tissue showed a mass of lymphoid tissue containing numerous diffuse areas of lymphocytes with no germinal centre formation. The lymphocytic population showed numerous immunoblasts with prominent nucleoli (Fig. 3). Numerous mitotic figures were also evident in the lymphoid tissue.

The immunocytochemistry staining of these tissues at this stage consisted of B-cell and T-cell markers: L26-positive, UCHL1-positive, MB2-positive, CD21-negative and CD3-negative. This therefore indicated that the lymphoid tissue was reactive; containing both B- and T-cells, and a

Indolent lymphomas
B-cell neoplasms
Small lymphocytic lymphoma B-cell chronic lymphocytic leukaemia
Lymphoplasmocytic lymphoma (± Waldenstroms macroglobulinaemia)
Plasma cell myeloma/plasmacytoma
Hairy cell leukaemia
Follicular lymphoma (grades 1 and 11)
Marginal zone B-cell lymphoma
Mantle cell lymphoma
T-cell neoplasms
T-cell large granular lymphocytic leukaemia
Mycosis fungoides
T-cell prolymphocytic leukaemia
Natural killer cell neoplasms
Natural killer cell large granular lymphocytic leukaemia
Aggressive lymphomas
Follicular lymphoma (grade III)
Diffuse large B-cell lymphomas
Peripheral T-cell lymphomas
Anaplastic large cell lymphoma
T-null cells
Highly aggressive lymphomas
Burkitt's lymphoma
Precursor B lymphoblastic leukaemia/lymphoma
Adult T-cell lymphoma/leukaemia
Precursor T lymphoblastic leukaemia/lymphoma
Special group of localised indolent lymphomas
Extranodal marginal zone B-cell lymphoma of MALT type*
Primary cutaneous anaplastic large cell lymphoma
* MALT = mucosa-associated lymphoid tissue

Tab. 3: WHO REAL classification of non-Hodgkin's lymphomas according to clinical aggressiveness.[7]

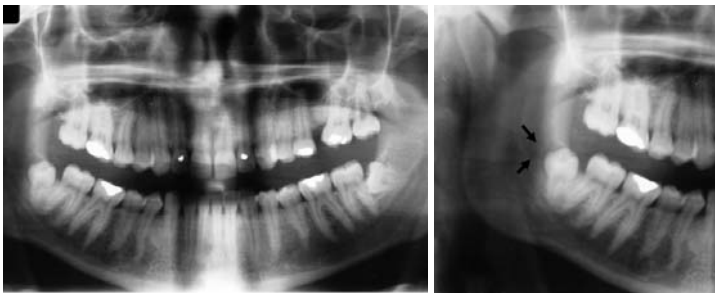
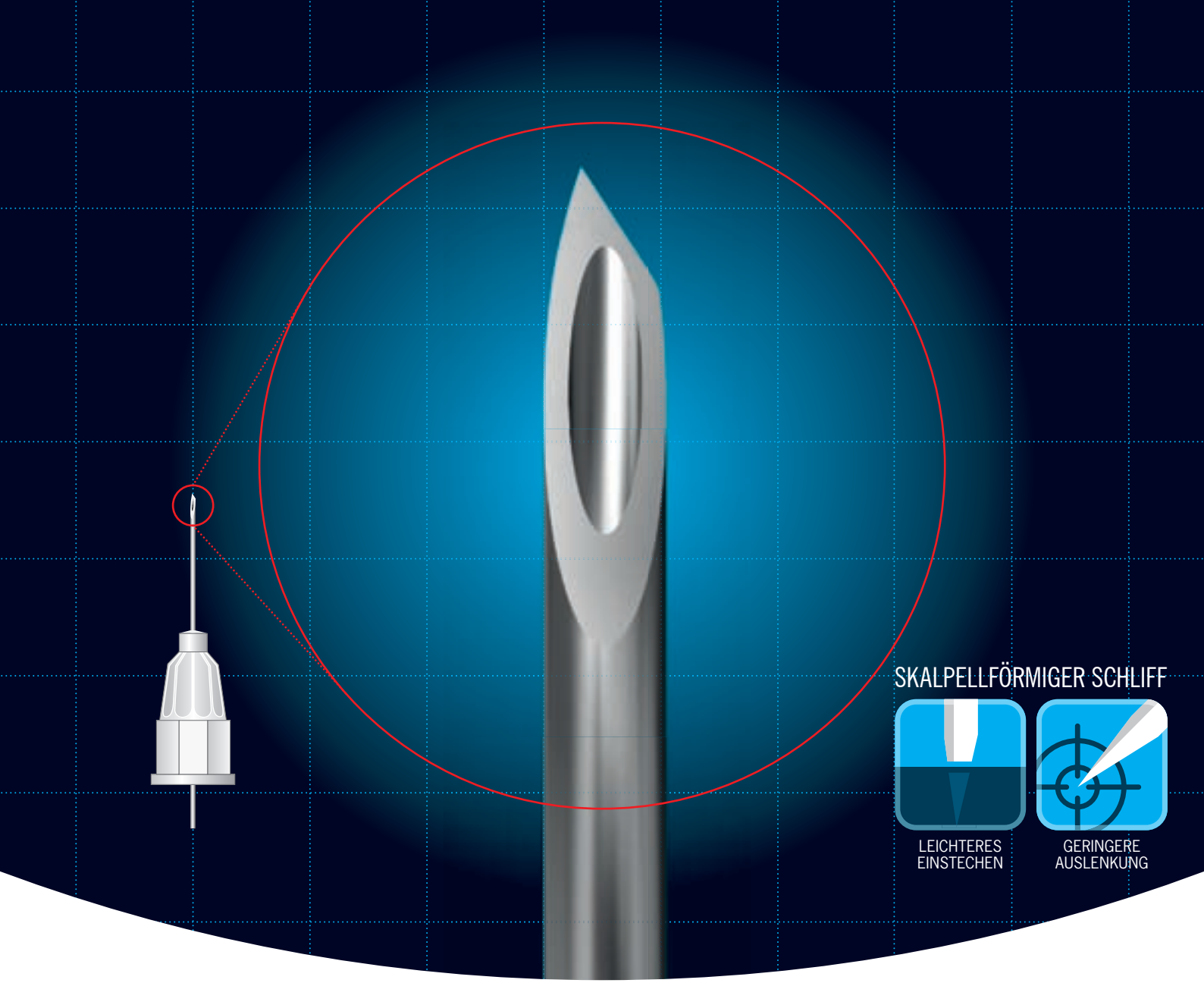


Fig. 1: Pre-operative Panthomographic radiograph showing the impacted mandibular 3rd molars 38 and 48. – **Fig. 2:** The right Mandibular 3rd molar (48) with a radiolucent area distal to the crown (arrow).



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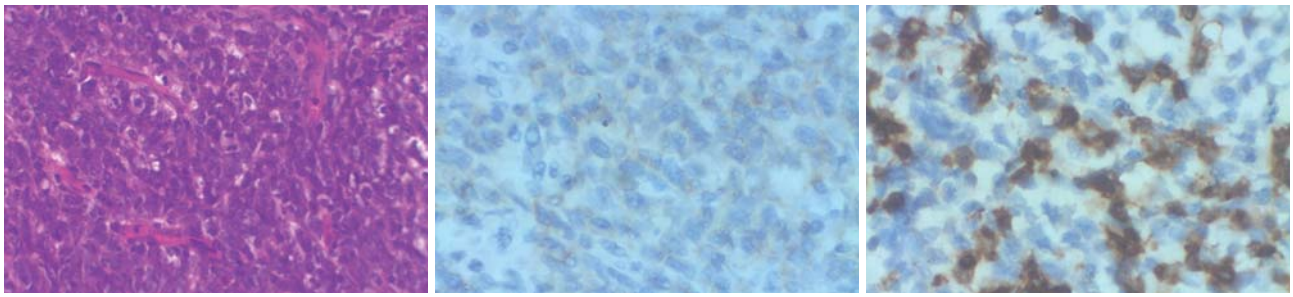

Fig. 3: The photomicrograph of the soft tissue adjacent to the right mandibular 3rd molar. The atypical lymphoid cells extend into blood vessel walls; numerous mitotic figures are visible. (Haematoxylin & Eosin x 400). – **Fig. 4:** Immunocytochemical staining for T (UCHL) 1 (T-cells) is negative (x 400). – **Fig. 5:** Immunocytochemical staining for L26 (B-cells) is positive (x 400).

mixed cell lymphoma was present. An initial diagnosis of dentigerous cyst and mixed cell lymphoma was made.
Due to the nature of the lymphoid tissue and the extra nodal location of the tissue within the bone, it was decided that a lymph node from the submandibular area be removed to establish whether there was a neoplastic change in other lymph nodes.
A right submandibular lymph node was subsequently removed and measured 12 mm in cross section. The surgeon reported that there was no sign of lymphadenopathy in the area of the operation, either in the submandibular or of the deep cervical group of lymph nodes. The histological picture of the submandibular node showed scattered germinal centres with reactive follicles in the cortical area and sinus histiocytosis of the medulla. There were no signs of any granulomatous inflammation and no evidence of malignancy. The lymph node therefore showed reactive changes probably as a result of the recent wisdom tooth removal.
The histological sections together with the processed tissue was referred and reviewed by another pathologist in the lymphoma clinic. She reported that the atypical lymphoid follicles had poorly formed mantles, showed no polarization and contained predominantly large non-cleaved cells which spilled out from the follicles into the inter-follicular areas where they infiltrated the fat and blood vessel walls. There was no evidence of epithelial structures associated with these lymphoid aggregates and the infiltrating cells were predominantly intermediate to large in size and showed plasmacytoid differentiation. The immunophenotypic staining profile of the large cells was interpreted as follows: L26-positive; LCA-positive; L26-positive; MB2-positive; T (UCHL)1-negative; CD21-negative; BerH2-negative; CD3-negative; CAM 5,2-negative. This profile was in keeping with a B-cell lineage. Immunohistochemical staining for immunoglobulins showed Lambda light chain restriction with expression of IgM heavy chain. In view of the morphological features and the demonstration of light chain restriction a diagnosis of Non-Hodgkin's malignant lymphoma was made with centroblastic and centrocytic features consisting of follicular large cells which were becoming diffuse and of intermediate grade (Category D of the Working Formulation).
The opinion of the oncologist at the lymphoma clinic was that the patient should be treated with radical radiotherapy in the area of the neoplasm to reduce possible mobility from the original lymphoma. She received 36Gy to the right mandible in the area of the lesion. Treatment was completed in 1992 and she was discharged from the lymphoma clinic in 2000. The patient returned at regular intervals to the original maxillofacial surgeon for monitoring. Clinical examinations and orthopathamographic radiographs up to 2009 showed no sign of recurrent disease.

Discussion

Lymphoma is the second most common neoplasm after carcinoma in the head and neck areas, but occurrence within the oral cavity is uncommon and within the jaws rare. This reported case, firstly diagnosed in 1992, was diagnosed and classified using the original Working Formulation (Table 1).[6] This stated that it was a non-Hodgkin malignant lymphoma with a centroblastic and centrocytic growth pattern consisting of a follicular large cell lymphoma going onto intermediate grade. The lymphoma was placed into category D of the Working Formulation. Today, using the Anne-Arbor staging system, this would be classified as stage IE.
The early diagnosis of this primary B-cell lymphoma and the subsequent radiotherapy was successful in eradicating this neoplasm. The long term follow up of this patient over 17 years was undertaken with subsequent orthopantomographs. There has been no recurrence of the neoplasm. It is stressed that all tissue removed at operation by the Oral and Maxillofacial Surgeons should not be discarded, but sent for histological investigation by an Oral Pathologist. If the surgeon in this case discarded the tissue from the third molar area, thinking that it was probably hyperplastic follicular tissue, the diagnosis of a primary lymphoma would have been lost and possibly resulted in serious complications for the patient at a later stage. ■

Literaturliste

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