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Progressive Eyelid and Facial Swelling Due to Follicular Lymphoma

Periorbital swelling is a cardinal manifestation of Melkersson-Rosenthal syndrome and may occur in many other diseases, including severe acne, vasculitis, sarcoidosis, or impaired venous or lymphatic drainage complicating neoplasia or radiotherapy of the neck. Rarely has it been reported as the sole manifesting sign of lymphoma.13

Figure 1. Clinical photograph, computed tomographic scans, and positron emission tomographic scans. A, Right eyelid and facial swelling. Coronal (B) and axial (C) computed tomographic scans show erosion of maxilla (arrowheads) and mucosal and soft tissue thickening (arrows). Fluorine 18 (18F)-labeled fluorodeoxyglucose positron emission tomographic scans show widespread lymphoma before (D) and complete response after (E) chemotherapy. R indicates right.
Report of a Case. A 43-year-old man developed right eyelid swelling in April 2007. He had no history of trauma, infection, or constitutional symptoms. Physical examination revealed right-sided facial edema, most pronounced in the eyelid and cheek soft tissues (Figure 1A). A right cervical lymph node, palpable by the patient for 6 months, measured 1 cm. Computed tomography revealed diffuse infiltration of right facial soft tissues including the masticator and parapharyngeal spaces, nasopharynx, and maxillary sinus mucosa (Figure 1B and C). Ocular examination showed only right upper eyelid swelling that prompted biopsy, which revealed perivascular inflammatory infiltrates composed predominantly of lymphocytes, plasma cells, occasional eosinophils, and rare tingible-body macrophages. The clinical and histological findings were interpreted as suspicious for Melkersson-Rosenthal syndrome.

Additional right cheek skin and sublabial mucosa biopsy results also were consistent with cheilitis granulomatosis of Melkersson-Rosenthal syndrome. However, the marked density of the lymphoid infiltrates raised the possibility of lymphoma (Figure 2A and B). Four months after the onset of facial edema, the patient developed right maxillary tooth hypersensitivity. Reexamination of the computed tomographic scan bone windows revealed bone resorption along the lateral wall of the maxillary sinus, raising suspicion of a malignant neoplasm (Figure 1). Biopsies of the right cervical lymph node, maxillary sinus mucosa, cheek skin, and sublabial mucosa revealed diffuse follicle center cell lymphoma (Figure 2C), a morphologic variant of follicular lymphoma that lacks the usual nodular architecture and instead exhibits diffuse lymphocytic infiltrates composed of centrocytes, with fewer centroblasts. Immunohistochemistry for CD20, CD10, and BCL6 (Figure 2D-F) confirmed the diagnosis.

At staging 8 months after initial symptoms, computed tomographic and fluorine 18 (18F)–labeled fluoro-deoxyglucose positron emission tomographic scans showed extensive systemic involvement, the latter showing enhancement in the right maxillary sinus, right temporalis muscle, skull base, mediastinum, retroperitoneum, mesenteric lymph nodes, bones of the thorax and pelvis, both femurs, abdominal soft tissue, and right periformis muscle (Figure 1D). Bone marrow biopsy revealed paratrabecular lymphomatous infiltrates, composing 10% to 20% of the marrow. Final staging was of stage IVE follicular lymphoma. The patient began receiving cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, and prednisone chemotherapy that resulted in resolution of infiltrates on 18F-fluorodeoxyglucose positron emission tomographic scanning 14 months after symptom onset (Figure 1E). However, repeated bone marrow biopsy showed residual disease. He then received tositumomab (BEXXAR), an iodine I 131–labeled anti-CD20 monoclonal antibody, to target and kill the malignant B lymphocytes, resulting in negative marrow biopsy results 2 months later.

Comment. Periocular facial swelling as the manifesting sign of lymphoma is rare. To our knowledge, there are only 3 cases reported in the literature.1-3 Moreover, follicular lymphoma of the nose and paranasal sinuses is extremely rare. In a series of 70 patients at the M. D. Anderson Cancer Center over 46 years, Logsdon et al4 reported no cases of follicular lymphoma. In contrast, orbital involvement by follicular lymphoma ranges from 10% to 30% of cases.5 Follicular lymphomas arise from germinal center B cells, where antigen exposure occurs, whereas lymphomas of mucosa-associated lymphoid tissue are believed to develop from post–germinal center B cells. Both entities are low-grade lymphomas, but follicular lymphomas have an 8-year survival of 60% to 65% with a failure-free survival of approximately 35%, whereas lymphomas of mucosa-associated lymphoid tissue have an 8-year survival of approximately 80% and a failure-free survival of 65%.6 Our case demonstrates a very unusual manifestation of follicular lymphoma, with extensive facial swelling and sinus involvement, that clinically mim-

Figure 2. Dense perivascular lymphocytic infiltrates (hematoxylin-eosin, original magnification ×100) (A), with most having positive immunoreactivity for CD20 (original magnification ×200) (B), in sublabial mucosa. Maxillary mucosa shows a diffuse infiltrate of malignant B lymphocytes (hematoxylin-eosin) (C) with cell membrane CD20 (D) and CD10 (E) immunopositivity and BCL6 nuclear immunoreactivity (F) (original magnification ×400).

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icked Melkersson-Rosenthal syndrome and was the only initial indicator of widespread systemic disease.

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Financial Disclosure: None reported.

Funding/Support: This work was supported by core grant EY07003 and grant EY09441 (Dr Elner) from the National Institutes of Health. Dr Elner is a recipient of the Lew R. Wasserman Merit Award from Research to Prevent Blindness.


Primary Peripheral T-Cell Lymphoma of the Orbit

A 34-year-old woman had a progressively protruding and painful mass of the right orbit for 1 month. On examination, the soft-tissue mass was about 5 cm in diameter and firmly fixed to the right orbit with resultant protrusion of the lower eyelid and proptosis (Figure 1A and B). Visual acuity was no light perception, coupled with limited eyeball motility. There was neither hepatosplenomegaly nor lymphadenopathy. Her family history was noncontributory. Computed tomography of the orbits revealed a large mass measuring 7.1 × 4.9 × 4.8 cm and completely occupying the expanded right orbit without bony destruction (Figure 1C). Magnetic resonance imaging of the orbits showed a large, heterogeneously enhancing soft-tissue mass compressing and pushing the eyeball anteriorly and extending posteriorly to the optic canal (Figure 1D). A small incision was made through the superotemporal conjunctiva and Tenon capsule, where tumor cell invasion with a cicatrizing nature was identified and incised. Histopathological analysis of orbital biopsy specimens demonstrated atypical lymphoid cell infiltration with positive immunoreactivities for CD3 and CD2 (Figure 2). The neoplastic cells were negative for CD56, CD15, CD30, and latent membrane protein 1 (Figure 3). Evaluation of T-cell receptor gene rearrangement using polymerase chain reaction showed monoclonality over the T-Cell re-

Figure 1. Clinical photographs, computed tomographic scan, and magnetic resonance image. A. The right eye, showing obvious protrusion of the eyelid and proptosis. B. Lateral view of the right eye. C. Contrast-enhanced computed tomography of the brain revealed a huge mass occupying the right orbit with no bony destruction. D. Magnetic resonance imaging of the brain showed a heterogeneously enhancing soft-tissue mass extending from the eyeball to the optic canal.