Nasolacrimal duct obstruction caused by lymphoproliferative infiltration in the course of chronic lymphocytic leukemia

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ABSTRACT

Background: *Endoscopic dacryocystorhinostomy (DCR) is the standard treatment of nasolacrimal duct obstruction. Only in rare cases, blockage may be caused by malignant tumors and even more exceptionally by lymphatic neoplasms so that biopsies are not routinely taken for diagnostic purposes.*

Methods: *A computerized retrieval system was used for this retrospective study to identify all patients with histologically documented lymphoproliferative infiltration in the lacrimal drainage system from 2001 to 2009.*

Results: *In four of 191 patients (2.1%), infiltration of the nasolacrimal sac mucosa with a small lymphocytic lymphoma (SLL)/chronic lymphatic leukemia (CLL) was found. Patients who develop symptoms like epiphora within the course of known CLL are highly suspicious for lymphoproliferative infiltration of the lacrimal drainage associated lymphoid tissue.*

Conclusion: *A proactive approach with ophthalmologic consultation and DCR should be followed in these patients to avoid dacryocystitis.*

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Nasolacrimal duct obstructions are classified either as primary acquired nasolacrimal duct obstruction or secondary acquired lacrimal drainage obstruction.

Primary acquired nasolacrimal duct obstruction is due to idiopathic inflammation and consecutive stenosis. Secondary acquired lacrimal drainage obstruction can be caused by infections, traumatic damage, mechanical obstruction, or neoplastic infiltration. The typical symptoms are epiphora, mucoid discharge, recurrent dacryocystitis, and painful swelling over the lacrimal sac.

The etiology indicates that malignant tumors of the lacrimal drainage system are rarely an underlying cause of secondary acquired lacrimal drainage obstruction. However, 90% of obstructive neoplasms are of epithelial origin, whereas lymphomas are very rare. Thus, there are <70 cases of primary lymphoma that originate from the lacrimal sac described in the literature over the past 30 years.[1] Most of the cases are lymphomas of the mucosa-associated lymphatic tissue. In a larger series, of 353 cases of ocular adnex lymphoma, the researchers reported only ~9 cases (2.5%) with lacrimal sac involvement.[2] The majority of lymphomas described within the lacrimal drainage system were interpreted as secondary infiltrations in the course to systemic lymphoproliferative disease.[3] Due to the rareness of lymphoma manifestation at this specific location, there are only case reports and small series studies documented in the literature.[4]

We observed a total of three patients who received dacryocystorhinostomy (DCR), with infiltration of the nasolacrimal sac mucosa by small lymphocytic lymphoma (SLL)/chronic lymphatic leukemia (CLL) and decided to review our charts and find out how many of our patients with DCR had lymphocytic neoplasm.

METHODS

A computerized retrieval system was used to identify four patients with histologically documented infiltration of the lacrimal drainage system by SLL/CLL from 2001 to 2009. After obtaining informed consent and approval by the Cantonal Ethics Commission, St. Gallen, the medical records of these four patients were reviewed. All the patients were interviewed for recurrence of nasolacrimal duct obstruction symptoms.

RESULTS

At the Department of Otorhinolaryngology, Cantonal Hospital, St. Gallen, a total of 261 endoscopic DCRs were performed on 191 patients from May 2001 to December 2009. Biopsy specimens were inconsistently taken, mainly in patients with clinical, anamnestic, or intraoperative suspicion for a malignant lesion. In four patients (2.1%), infiltration of the nasolacrimal

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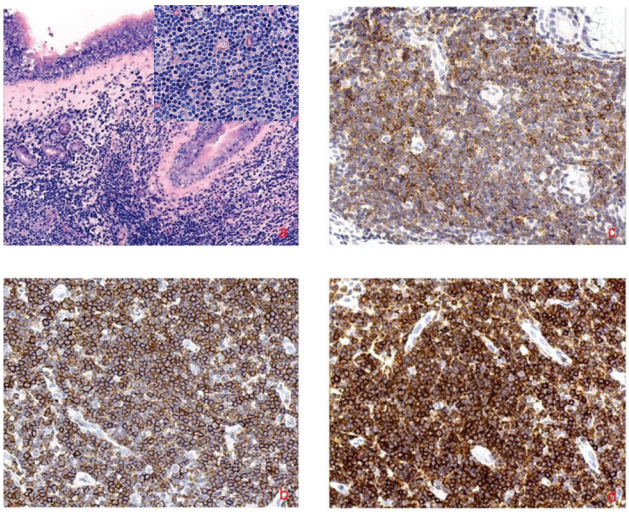

Figure 1. *(A) Giemsa stain: overview with diffuse small lymphocytic mucosal infiltration without lymphoepithelial lesions. Inlet: Lymphoproliferation dominated by small lymphocytes, intermingled with prolymphocytes and paraimmunoblasts. (B) Dim positivity for CD20. (C) and (D) Strong positivity for CD5 and CD23.*

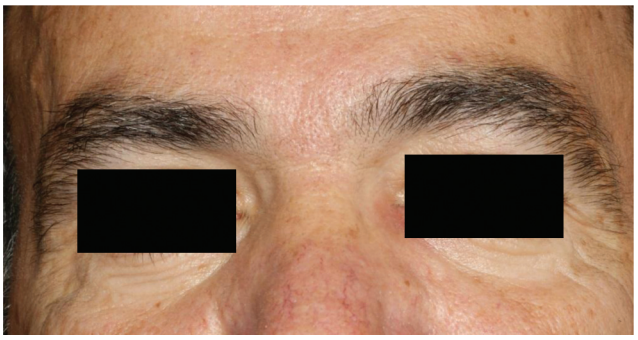

Figure 2. *Swelling, redness and left canthal mass in patient 4.*

sac mucosa by SLL/CLL was found by histologic examination (Fig. 1).

The mean age at the time of surgery was 62.75 years (range, 62–68 years). All the patients were men. Three of four patients had a history of known chronic lymphocytic lymphoma before surgery. However, one patient without known CLL revealed primary localized involvement first of the left side and, consequently, 2 years later, of the right lacrimal drainage system followed by dacryocystitis. Bilateral lacrimal drainage system involvement was histologic proven in two more patients.

The interval between the primary diagnosis of CLL and the first DCR surgery in the remaining three patients averaged 46.66 months (range, 14–98 months). All four patients presented with epiphora and recurring dacryocystitis (Fig. 2). Routine canalicular intubation was used for all the patients according to the method of Hatt.[5] None of the patients required revision surgery, chemotherapy, or radiotherapy for local disease control. The mean follow-up until December 2013 was 48 months (range, 3–76 months).

The first patient, a 64-year-old man, underwent left DCR in 2001, 14 months after the initial diagnosis of CLL, due to epiphora and recurrent dacryocystitis. He had received chemotherapy with chlorambucil and prednisone up to 9 months before surgery. After successful left DCR, the patient developed right-sided dacryocystitis, and DCR on the right side was performed 3 months after the first surgery. Biopsy specimens were taken during both surgeries, and histologic examination showed infiltration by SLL/CLL in the lacrimal sac as well as in the surrounding nasal and/or ethmoidal mucosa. The patient died in 2004 without having any symptoms of nasolacrimal duct obstruction.

The second patient, a 62-year-old man, had bilateral epiphora for 4 months and recurrent left-sided dacryocystitis. CLL had been diagnosed more than 2 years before surgery but did not require any medical treatment. We performed endoscopic DCR on the left side and a canaliculonasal intubation on the right side. Biopsy specimens taken from the left lacrimal sac and nasal and/or ethmoidal mucosa showed infiltration by SLL/CLL.

The third patient, a 68-year-old man, presented with a lacrimal sac abscess and was admitted to surgery. He had recurrent left-sided dacryocystitis in the past 6 months and no history of CLL. Biopsy specimens taken during DCR showed infiltration of the lacrimal sac and the adjacent ethmoidal mucosa by SLL/CLL. The patient was sent for an oncologic consultation, and the diagnosis of CLL was established. Five months after successful left-sided DCR, the patient developed right-sided epiphora. Right-sided DCR was performed 20 months after his first symptoms when he developed a painful medial canthal mass. Histology showed infiltration by SLL/CLL of the lacrimal sac and of the adjacent nasal and/or ethmoidal mucosa. Because the blood count was normal, the patient did not receive more chemotherapy and recovered without event from surgery.

The fourth patient had the longest history of CLL before nasolacrimal duct involvement. He was diagnosed with Rai stage 0 CLL in July 2001, upstaged to Rai stage II in 2006, and received an initial chemotherapy with chlorambucil in 2008. He had his first left-sided dacryocystitis in August 2009. As in all other cases, the histology showed an infiltration by SLL/CLL of the lacrimal sac and of the adjacent nasal and/or ethmoidal mucosa. The patient did not have any lacrimal drainage obstruction after surgery but received further chemotherapy due to systemic disease. Five years later, he developed right-sided dacryocystitis and underwent successful DCR (Table 1).

Table 1 **Summary of the patients with CLL involvement in the lacrimal drainage system**

Sex	Age (y)	Interval Between Diagnosis Primary Disease and Surgery, L/R (mo)	Site, L/R	Symptoms	Histology/ Diagnosis	Chemotherapy
M	64	14/17	L/R	Dacryocystitis/epiphora	SLL/CLL Rai stage II	Chlorambucil/prednisone
M	62	28	L/R	Dacryocystitis/epiphora	SLL/CLL Rai stage I	None
M	68	0/25	L/R	Dacryocystitis/epiphora	SLL/CLL Rai stage I	Chlorambucil
M	57	98/158	L/R	Dacryocystitis/epiphora	SLL/CLL Rai stage II	Chlorambucil/prednisone

L = left; R = right.

DISCUSSION

Lacrimal drainage–associated lymphoid tissue is an extranodal lymphoid tissue compartment in the lacrimal drainage system, mainly in the lacrimal sac and duct. Lacrimal drainage–associated lymphoid tissue is part of the mucosa-associated lymphatic tissue, but little is known about its function, and it is believed to play an important role in ocular surface integrity by forming a functional unit with the cornea, the lacrimal gland, and the nasal mucosa through lymphocyte recirculation.[6] This theory might be supported by our findings of concomitant infiltration of the adjacent nasal and/or ethmoidal mucosa, and lacrimal sac mucosa by lymphoma. However, there are only a few case reports and small series studies that report about the involvement of the lacrimal drainage system by non-Hodgkin lymphoma, *e.g.,* SLL/CLL.

A larger retrospective study from Denmark, which included 643 biopsy specimens of the lacrimal drainage system from 1910 to 1999 revealed only six cases (0.9%) with B-cell lymphoma.[7] At the Mayo Clinic, Salour *et al.*[8] found, in 471 lacrimal sac biopsy specimens, just two lymphoma (0.4%). Yip *et al.*[4] reviewed the cases of patients with leukemia or lymphoma that showed infiltration of the lacrimal drainage system. During a time frame of 8.5 years, they found 10 of 381 patients (2%) who had CLL infiltration. Four of these patients had bilateral involvement.

Biologically, SLL and CLL are identical. Whereas SLL is a solid tumor mainly in the lymph node, CLL stands for leukemic disease documented by lymphocytosis in the peripheral blood and bone marrow infiltration. In our study there were three histologically proven and one clinically suspected bilateral infiltration by SLL/CLL of four patients.

Heindl *et al.*[9] reviewed 19 biopsy specimens of 500 external DCRs taken at their institution and reported three cases of non-Hodgkin B-cell lymphoma. Biopsies were only taken if the mucosa appeared suspicious during surgery. It is very controversial if one should routinely biopsy during DCR surgery. Merkonidis *et al.*[10] prospectively studied this topic and concluded that routine biopsy is not indicated if there is no clinical suspicion. In their 193 specimens, there was no malignancy, and, in the literature review, they found just a 0.08% incidence of malignancy.[10] The same recommendation is given by Altan-Yaycioglu *et al.*,[11] who prospectively evaluated 205 consecutive cases; in their population, there was just one manifestation of CLL. In our study, there was a 2.3% incidence of CLL in the lacrimal drainage system. Three of our four patients had histologically proven bilateral involvement, and the remaining patient had a suspected involvement. There was no patient with DCR and with CLL and a negative biopsy result.

CONCLUSION

In patients with known systemic lymphoproliferative disorders, there should be a high suspicion for involvement of the lacrimal drainage–associated lymphoid tissue if they present with epiphora or dacryocystitis. A bilateral involvement of the lacrimal drainage system should be expected, and the patient should be monitored and routinely questioned for symptoms of epiphora. If symptoms of nasolacrimal duct obstruction are present, then a proactive approach with ophthalmologic consultation and DCR can avoid dacryocystitis, which might have a more complicated course during chemotherapy due to immunosuppression.

DCR surgery and stenting of the nasolacrimal drainage system, in our experience, are well-tolerated treatments with a very low complication rate. Biopsies performed during surgery would confirm the leukemic or lymphomatous infiltration and can help in targeting an

adjuvant therapy, such as radiotherapy or chemotherapy. Although, in our patients, surgery was sufficient for local treatment because none developed a recurrence within the 48-month mean follow-up period. As mentioned, the surrounding nasal mucosa forms a functional unit with the lacrimal drainage system; thus extended biopsy will prove the involvement of the adjacent sinus and nasal mucosa.

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