Primary lymphoepithelioma-like carcinoma of ocular adnexa: clinicopathologic features and treatment

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ABSTRACT

Background and Methods

Lymphoepithelioma-like carcinoma (LELC) is a rare malignancy in ocular adnexa.

Here, we report 4 patients with LELC and review 11 patients reported in the literature. Clinical profiles, association with Epstein–Barr virus (EBV), treatment, and outcomes are analyzed.

Results

Lacrimal glands and the lacrimal drainage system, eyelid, and conjunctiva are potential primary sites for LELC. The tumours are characterized histologically by nests of undifferentiated malignant cells surrounded by lymphoid infiltrates. Infection with EBV was confirmed in LELC of ocular adnexa, and that association seemed to be restricted to Asian populations. Results from our centre uniformly showed expression of EBV-encoded small RNAs in primary tumour, locally recurrent tumour, and metastatic lymph nodes. This disease had a tendency to relapse regionally. Postoperative radiotherapy seems to improve disease-free survival. Tumours appear to be sensitive to radiotherapy and chemotherapy based on cisplatin and 5-fluorouracil. At our centre, 3 patients were still living at 22, 33, and 76 months after surgery. One patient died of distant metastasis after a survival of 38 months.

Conclusions

Lymphoepithelioma-like carcinoma is a heterogeneous entity among ocular adnexal malignancies. Multimodality treatment provides a better chance at survival. Further investigation is required to achieve a better understanding of the biologic behavior of this entity and of its optimal treatment.

KEY WORDS

Lymphoepithelioma-like carcinoma, ocular adnexa, Epstein–Barr virus, surgery, radiotherapy

1. INTRODUCTION

Lymphoepithelioma-like carcinomas (LELCs) are malignancies that have morphologic features similar to those of undifferentiated nasopharyngeal carcinoma (UNNPC) and that occur outside the nasopharynx, such as in the salivary gland, lung, stomach, thymus, skin, urinary bladder, uterine cervix, and breast. The diagnosis of LELC depends mainly on typical histologic features: islands of malignant cells with indistinct cell boundaries and prominent nucleoli, infiltrated by dense lymphocytes. Before primary LELC can be diagnosed in other sites, UNNPC must be ruled out by nasopharyngeal imaging or biopsy.

“Ocular adnexa” refers to tissues and structures surrounding the eye, including the orbital soft tissue, lacrimal glands, lacrimal drainage system, conjunctiva, and eyelids. Lymphoepithelioma-like carcinoma of the ocular adnexa is very rare. Only 13 cases have been reported in the literature, and comprehensive descriptions of this entity’s biologic behavior and optimal treatment are lacking. To reveal some important aspects of LELC, we here report 4 cases from our cancer centre, and we review previous case reports of ocular adnexal LELC, with their clinicopathologic features, association with Epstein–Barr virus (EBV), treatment, and outcomes. To the best of our knowledge, this case series is the largest from a single institution, and the first to make an effort to review all available cases of ocular adnexal LELC.

2. METHODS

2.1 Patients

From the pathology files at Sun Yat-sen University Cancer Center, we identified 4 cases of primary LELC.
of the ocular adnexa. Nasopharyngeal imaging and biopsy were used to rule out uDNPC. Clinical data, including patient information, tumour characteristics, treatment, and outcomes, were collected. Informed consent was obtained from the patients at their first visit for the collection of clinical information. The review, analysis, and publication of these data were approved by the Research Ethics Board of Sun Yat-sen University Cancer Center. Tumour response to treatment was assessed according to the Response Evaluation Criteria in Solid Tumors. Disease-free survival (DFS) was calculated from the date of initial definitive treatment to the point of confirmed relapse or last follow-up.

2.2 Pathology Analysis

Immunohistochemistry (IHC) was performed on paraffin-embedded sections using the avidin–biotin–peroxidase complex method, with antibodies for cytokeratin, cytokeratin 19, and P63 (Santa Cruz Biotechnology, Santa Cruz, CA, U.S.A.). In situ hybridization (ISH) for EBV-encoded small RNAs (EBERs) was performed on paraffin-embedded sections according to the manufacturer's instructions (Dako, Glostrup, Denmark). Briefly, sections were deparaffinized, rehydrated, and predigested with proteinase K. A fluorescein-conjugated EBER probe was applied, and the sections were incubated at 37°C for 2 hours. Alkaline phosphatase–conjugated antibody to fluorescein was applied, followed by chromogen. Sections were then counterstained with hematoxylin. Dark brown staining of the cell nucleus was recognized as positive.

3. CASE REPORTS

3.1 Case 1

A 40-year-old Chinese man presented in February 2004 with headache and progressive visual loss in the left eye for 2 months. He had a history of primary LELC in the left orbit, which was surgically removed in October 2003. Ophthalmology examination revealed proptosis and complete loss of ocular movement and vision in the left eye, with afferent and efferent pupillary defect. Magnetic resonance imaging (MRI) of head and neck revealed a mass in the left orbit, with wide invasion of the left globe, orbital wall, paranasal sinuses, and cavernous sinus (Figure 1).

Serum titre of anti-EBV capsid antigen immunoglobulin A (VCA-IgA) and anti-EBV early antigen IgA (EA-IgA) were elevated at 1:320 and 1:20 respectively. Computed tomography (CT) imaging of nasopharynx, chest radiography, and abdominal ultrasonography were negative.

Wide resection of the lesion, including the retrobulbar mass, the globe, and part of the orbital wall was performed. Grossly, the excised retrobulbar mass measured 5×3.5×3 cm, with a defined border and grey-white cut surface that partially surrounded the optic nerve. Microscopic examination showed features typical of LELC (Figure 2(A,B)). The IHC analysis was positive for cytokeratin in tumour cells (Figure 2(C)). The ISH test for EBERs was positive (Figure 2(D)). After surgery, CT imaging of the head and neck revealed residual tumour in the left cavernous sinus and orbital apex. Conventional radiotherapy at 56 Gy was given in 28 fractions to the left orbital region, and complete remission was achieved.

In September 2004, CT imaging of head and neck revealed enlarged left retropharyngeal and bilateral cervical lymph nodes. Biopsy of the cervical lymph nodes confirmed metastatic LELC. The ISH test for EBERs was positive.

Chemotherapy [2 cycles of cisplatin–bleomycin–5-fluouracil (5FU) and 3 cycles of cisplatin–5FU–leucovorin] was followed with conventional radiotherapy at 60 Gy in 30 fractions given to the cervical and retropharyngeal region. Stable disease and partial remission were achieved after 2 and 5 cycles of chemotherapy respectively, with complete remission being achieved after radiotherapy.

In August 2005, liver metastasis was found, and the patient began to receive occasional carmustine. This patient died of distant metastasis in December 2006.

3.2 Case 2

A 43-year-old Chinese woman presented in March 2002 with a 7-day history of swelling in the left lower eyelid. She had a history of LELC in the left lower eyelid, which was surgically resected in May 2001. Ophthalmology examination revealed a palpable, fixed mass in the left inner canthus. Visual acuity and extraocular motility were normal.

Imaging by CT revealed a soft-tissue mass in left medial orbit that was not clearly separated from the eyeball (Figure 3(A)). Her EA-IgA serum titre was normal, and her VCA-IgA was slightly elevated (1:40). The CT imaging excluded uDNPC and metastasis, and the patient was diagnosed with recurrent orbital LELC.

One cycle of cisplatin–5FU was followed by three-dimensional conformal radiotherapy at 64 Gy in 32 fractions to the left orbit, with concurrent cisplatin chemotherapy. The mass showed partial remission after neoadjuvant chemotherapy and complete remission after radiotherapy. Slight hypoposia developed in the left eye after radiotherapy.

In July 2005, left supraclavicular lymph node metastasis was confirmed by biopsy. Two cycles of cisplatin–5FU, followed by conventional radiotherapy at 60 Gy in 30 fractions were given to the left supraclavicular region. In May 2006, CT imaging revealed enlarged left parotid lymph nodes, which were removed. Metastatic LELC was confirmed by pathology.
LYMPHOEPITHELIOMA-LIKE CARCINOMA OF OCULAR ADNEXA

**Figure 1** For patient 1, magnetic resonance imaging revealed a mass of soft tissue occupying the left orbit, with isointensity on (A) T1- and (B) T2-weighted scans, and (C,D) obvious enhancement. The mass invades the left globe, orbital wall, paranasal sinuses, and cavernous sinus.

...analysis [Figure 3(B,C)]. The IHC analysis showed positive staining for cytokeratin and P63. The ISH test for EBERs was positive [Figure 3(D)]. Conventional radiotherapy was given at 68 Gy in 34 fractions to the left parotid region and the left cervix, followed by chemotherapy (1 cycle of paclitaxel-cisplatin and 1 cycle of paclitaxel-carboplatin).

In September 2007, the patient presented with back pain, numbness, and weakness of the lower limbs. Imaging by CT revealed multiple metastasis to thoracic vertebrae and liver. Paraplegia occurred a few days later, and this patient was lost to follow-up.

### 3.3 Case 3

A 20-year-old Chinese woman presented in July 2010 with epiphora for 5 months. Ophthalmology examination revealed a hard, fixed mass in the right inner canthus. Imaging of the orbit by CT revealed a homogenous, well-defined soft-tissue mass in the region of the right lacrimal sac, without adjacent invasion. Complete excision of the mass and the right lacrimal sac was performed.

The excised mass was dark red, unencapsulated, irregular, firm, and 2.5×1.5 cm in size. Histology examination showed features typical of lelc [Figure 4(B,C)]. The IHC analysis showed positive staining for cytokeratin, cytokeratin 19, and P63. The ISH test for EBERs was positive [Figure 4(D)]. Biopsy and MRI excluded UDNPC.

In April 2011, the patient developed right proptosis. Magnetic resonance imaging of the orbit supported recurrent tumour in the right inferomedial orbit, with no invasion to the globe or orbital wall. Workup excluded regional or distal metastasis. The mass was completely excised, and recurrent lelc...
was confirmed by pathology analysis. The ISH test for EBERs was positive.

In July 2011, MRI of the head and neck revealed recurrent tumour in the right inferomedial orbit, growing along the right nasolacrimal duct [Figure 4(A)]. Chemotherapy with 4 cycles of docetaxel–cisplatin–5FU, followed by intensity-modulated radiotherapy at 68 Gy in 34 fractions was given to the right orbit. The mass showed partial remission after neoadjuvant chemotherapy and complete remission after radiotherapy.

### 3.4 Case 4

A 53-year-old Chinese woman presented in March 1999 with epiphora for 1 month. Ophthalmology examination revealed a palpable hard fixed mass on the right inferomedial orbit. Irrigation into the lower canaliculus resulted in backflow from the upper canaliculus. Extraocular motility of the right eye was limited in the medial and inferomedial direction.

Imaging of the orbit by CT revealed a heterogeneous soft-tissue mass in the right lacrimal sac region, 3×3×2 cm in size. The mass extended along the orbital wall into the retrobulbar space, with no invasion to the orbital wall, globe, or optic nerve. Imaging by CT of the nasopharynx, chest, and abdomen was normal.

Subtotal excision of the mass was performed. Grossly, it was dark red, unencapsulated, and ill-defined. Histology examination showed features typical of LELC. The IHC analysis showed positive staining for keratin. The ISH test for EBERs was positive.

The patient was diagnosed with LELC of lacrimal sac. She refused postoperative radiotherapy.

In May 1999, she re-presented with orbital tumour progression, which was completely excised. The pathology analysis confirmed LELC. Postoperative conventional radiotherapy was given at 60 Gy in 30 fractions to the right orbit.
Up to December 2001, no disease relapse was observed. The patient developed neovascular glaucoma of the right eye, which eventually caused complete visual loss.

4. OBSERVATIONS

4.1 Tumour Origin

In patients at our hospital, the primary tumour originated in orbit (case 1), eyelid (case 2), and lacrimal sac (cases 3 and 4). In case 1, the patient presented with recurrent tumour that occupied the whole orbit and invaded widely to adjacent structures. From the past history of orbital lelc resection, we presumed that the tumour originated from the orbit. The specific site of origin (lacrimal gland, lacrimal sac, or conjunctiva) was hard to determine because of inadequate past charting.

4.2 Pathology Analysis

Our 4 patients were diagnosed with lelc based on typical histologic features: nests or islands of malignant cells infiltrated by dense lymphocytes. Tumour cells showed indistinct cell boundaries, pale cytoplasm, round vesicular nuclei, and prominent nucleoli. Immunohistochemistry studies and EBV analyses were performed in all cases. The IHC showed positivity in the malignant cells for epithelial markers such as cytokeratin (cases 1–3), keratin (case 4), cytokeratin 19 (case 3), and P63 (cases 2 and 3). The ISH test for EBERs was positive in all cases. In case 1, IHC was performed for recurrent orbital tumour and metastatic lymph nodes, and the results were uniformly positive. In case 3, the ISH tests for primary and recurrent orbital tumours were uniformly positive.

4.3 Treatment and Outcomes

Table 1 summarizes treatment and outcomes in our 4 patients. All underwent surgical excision as initial treatment. Complete excision of primary tumour was achieved in 3 patients. Failures after initial treatment included regional relapse (cases 1–3) and distant metastasis (cases 1 and 2). Regional relapse developed at the primary site (case 3) and at both the primary site and the regional lymph nodes (cases 1 and 2). Distal metastasis occurred in liver (cases 1 and 2) and bone (case 2).

Salvage treatment for relapse at primary sites included reoperation (case 3), reoperation plus radiotherapy (case 1), chemotherapy plus radiotherapy (cases 2 and 3). Salvage treatment for lymph-node relapse included chemotherapy plus radiotherapy (case 1) and surgery plus chemoradiotherapy (case 2). Radiation doses to recurrent tumour ranged from 56 Gy to 68 Gy. Radiotherapy alone (case 1) or combined with chemotherapy (cases 2 and 3) achieved complete remission without relapse in the radiation fields during follow-up. Regimens using cisplatin–5FU (cases 1–3) achieved partial remission in the salvage neoadjuvant setting.

4.4 Survival

Median follow-up was 36 months for our patients (range: 22–38 months). Patients who underwent surgery as initial definitive treatment experienced disease relapse at 4–10 months after surgery, with a median DFS of 9 months. At the last follow-up, patients 3 and 4 were living and had been free of tumour for 22 and 33 months respectively after their first surgery. Patient 2 was living at 76 months after her first surgery, with bone and liver metastasis. Patient 1 died of distant metastasis, with a survival time of 38 months.

4.5 Visual Acuity After Radiotherapy

After eye-preserving surgery, 3 patients received radiotherapy to the orbital region. Patient 2 had slight hypoposia for 3 years after three-dimensional conformal radiotherapy at 64 Gy. Patient 3 showed no visual deterioration for 2 months after intensity-modulated radiation therapy at 68 Gy, but patient 4 developed neovascular glaucoma and complete visual loss 2.5 years after conventional external-beam radiotherapy at 60 Gy.

4.6 Literature Review

We searched PubMed for all English publications with the keywords “lymphoepithelioma–like carcinoma,” “lymphoepithelial carcinoma,” or “lymphoepithelioma,” and found reports of 13 cases of primary ocular adnexal lelc. The primary sites included lacrimal gland, lacrimal sac, naso-lacrimal duct, conjunctiva, and eyelid. Of the 13 cases, 11 were well documented and are included in our analysis. Table II summarizes patient demographics, tumour characteristics, and pathology results. Table III describes treatment and outcomes.

5. DISCUSSION

Diagnosis and management of ocular adnexal malignancies remain a great challenge because of their unique location and heterogenous histologic types. A variety of malignancies occur in ocular adnexa, with lymphoma, malignant epithelial tumours of lacrimal gland, and neurogenic tumours being the most common. Lymphoepithelioma-like carcinoma of the ocular adnexa is very rare.

As Table II shows, the lacrimal glands, lacrimal drainage system, eyelid, and conjunctiva are potential primary sites for the development of lelc. Of the
11 cases summarized here, 6 involved men, and 4, women (the sex of the 11th patient was not given). Ages ranged from 45 to 95 years (median: 66 years); the youngest patient at our centre was 21 years of age.

The clinical manifestations of ocular adnexal LELC varied from site to site: diplopia and proptosis were commonly seen in lacrimal gland tumour; epiphora was a common symptom in lacrimal sac tumour; rhinorrhea and epistaxis were seen in nasolacrimal duct tumour; and a palpable mass was usually the only manifestation in conjunctiva or eyelid tumour. Otherwise, cervical lymph node swelling might be the only complaint. The primary tumour ranged from 2 cm to 4.5 cm in the greatest dimension. Most patients had well-confined tumours. Tumours with involvement of adjacent structures were seen in 2 patients from the literature and in patient 1 from our centre.

The association between EBV and LELC varies by site and by patient ethnicity. Infection with EBV is associated with LELC of salivary gland and lung in Asian patients. It is also associated with LELC of stomach and thymus independent of ethnicity. In previous studies, EBV infection was confirmed by ISH in tumours of the lacrimal sac (n = 2) and nasolacrimal duct (n = 1, Table i). All positive cases reported occurred in Asian patients. Accordingly, the ISH for EBV was positive in all 4 patients at our centre. The association between EBV and LELC in ocular adnexa therefore seems to be restricted to Asian populations. Furthermore, results at our centre showed uniform expression of EBERs in primary tumour, locally recurrent tumour, and metastatic lymph nodes. Those results suggest that detection of EBV in a metastatic site might be diagnostic, especially when the primary tumour in ocular adnexa is not easily accessible.

Given the rarity of ocular adnexal LELC, the optimal therapy is unclear. At our centre, 3 patients underwent surgical excision as initial definitive treatment. However, all patients experienced disease relapse, with a median DFS of 9 months. In the literature, 6 patients underwent surgical excision, followed by postoperative radiotherapy. Only 1 experienced disease relapse (at 6 months after therapy); the others lived free of disease for 6–36 months after therapy. Based on those observations, LELC in ocular adnexa appears to have a tendency to regional relapse, and postoperative radiotherapy seems to be effective for disease control. That hypothesis is consistent with results from a recent study by Skinner et al. on epithelial cancers of the lacrimal apparatus, which
<table>
<thead>
<tr>
<th>Reference</th>
<th>Race</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Presentation</th>
<th>Tumour origin</th>
<th>Tumour size (cm)</th>
<th>Gross appearance</th>
<th>Tumour stage</th>
<th>IHC positivity</th>
<th>Epstein–Barr virus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leung et al., 1996</td>
<td>Chinese</td>
<td>45</td>
<td>F</td>
<td>Left submandibular swelling for 6 months</td>
<td>Lacrimal sac</td>
<td>4x3x2.5</td>
<td>Homogenous, partially encapsulated</td>
<td>None</td>
<td>Sub-mandibular</td>
<td>CAM5.2</td>
</tr>
<tr>
<td>Bloching et al., 2000</td>
<td>White</td>
<td>61</td>
<td>M</td>
<td>Diplopia, conjunctivitis, chemosis, proptosis</td>
<td>Lacrimal gland</td>
<td>2</td>
<td>Homogenous, encapsulated</td>
<td>None</td>
<td>Cervical and parotid</td>
<td>CK</td>
</tr>
<tr>
<td>Rao et al., 2002</td>
<td>White</td>
<td>63</td>
<td>F</td>
<td>Dry eyes, fullness, proptosis, diplopia for several months</td>
<td>Lacrimal gland</td>
<td>3.1x2.9x2.8</td>
<td>Homogenous, partially encapsulated</td>
<td>None</td>
<td>None</td>
<td>Pan-keratin</td>
</tr>
<tr>
<td>Ho et al., 2005</td>
<td>White</td>
<td>67</td>
<td>M</td>
<td>Subcutaneous eyelid lesion for 8 months</td>
<td>Eyelid</td>
<td>NA</td>
<td>Well circumscribed</td>
<td>None</td>
<td>None</td>
<td>CK, EMA</td>
</tr>
<tr>
<td>Liu et al., 2009</td>
<td>Chinese</td>
<td>82</td>
<td>M</td>
<td>Epiphora, proptosis exotropia for 18 months</td>
<td>Lacrimal sac</td>
<td>NA</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>CK5, CK6</td>
</tr>
<tr>
<td>Tam et al., 2010</td>
<td>NA</td>
<td>61</td>
<td>F</td>
<td>Right nasal obstruction, rhinorrhea, epistaxis for 6 months</td>
<td>Naso-lacrimal duct</td>
<td>2.3x1.3x1.3</td>
<td>Polypoid</td>
<td>Maxillary bone</td>
<td>None</td>
<td>NA</td>
</tr>
<tr>
<td>Blasi et al., 2011</td>
<td>White</td>
<td>79</td>
<td>M</td>
<td>Left upper lid ptosis</td>
<td>Lacrimal gland</td>
<td>2.0x1.5x1.0</td>
<td>Dis-homogeneous, well-defined</td>
<td>Eyelid</td>
<td>None</td>
<td>CK AE1/3, EMA</td>
</tr>
</tbody>
</table>

**Note:** IHC = Immunohistochemistry, PCR = Polymerase chain reaction, EMA = Epitope mapping.
showed better DFS in patients who received postoperative radiotherapy.

Lymphoepithelioma-like carcinoma of the head and neck is reported to be sensitive to radiotherapy, with good locoregional control\(^5\). In the ocular adnexa, the disease also seems to be radiosensitive. In 3 patients at our centre, radiotherapy alone or combined with chemotherapy achieved complete remission of locally recurrent tumour, without relapse in the radiation fields during follow-up. Thalacker et al.\(^14\) reported a case (not included here because of the unavailability of the full text) of nasolacrimal duct LELC treated with radiotherapy and chemotherapy. Their patient achieved complete remission and lived for 2.5 years free of tumour.

Therefore, for LELC of ocular adnexa, we recommend surgery plus adjuvant radiotherapy to primary sites. When surgery is not an option, a combination of radiotherapy and chemotherapy might be an alternative. It is noteworthy that ocular radiosensitivity and orbital anatomy are unique challenges for radiotherapy. Protection of the radiosensitive ocular tissues, such as the lens and retina should therefore be considered\(^21\). Among the patients at our centre, 1 developed serious side effects 2.5 years after conventional radiotherapy at 60 Gy. After similar doses of intensity-modulated or three-dimensional conformal radiotherapy, another 2 patients experienced no obvious decline in vision at a follow-up of 2 months and 3 years respectively. Complications might therefore be able to be minimized with the use of the new technical advances in radiotherapy.

Chemotherapy was described as an integral part of treatment for LELC in several sites\(^6,22,23\). Pulmonary LELC with regionally advanced disease responded favourably to chemotherapy with cisplatin–5FU\(^6,22\). In all 3 patients with locoregionally recurrent tumour at our centre, neoadjuvant chemotherapy with cisplatin–5FU achieved partial remission; however, given the limited number of patients, more investigation is needed to confirm that approach.

Survival in ocular adnexal epithelial malignancies varies by site and histology. The 5-year survival rate in epithelial lacrimal apparatus cancers ranges from 40% to 80%\(^20\). Mortality rates for eyelid squamous cell carcinoma and conjunctiva squamous cell carcinoma range from 2% to 40% and from 0% to 8%, respectively\(^24\). As for LELC of the ocular adnexa, 3 patients at our centre survived for 22, 33, and 76 months after surgery. As Table II shows, 8 of 11 cases reported in literature were followed after treatment. All patients were alive at the last follow-up, after a follow-up time of 6–36 months (median: 24 months). Only 1 patient at our centre died of distant metastasis after a survival of 38 months. This particular patient had a huge recurrent tumour, with extensive erosion of adjacent structures. It appears that the advanced stage of the tumour was associated with poor outcome. However, because of the small number
of cases and short follow-up, the overall survival in ocular adnexal LELC is difficult to assess. Moreover, it is advisable to assume that the prognosis of ocular adnexal LELC varies by site. More cases, with longer-term follow-up, are needed to address this issue.

6. CONCLUSIONS

Lymphoepithelioma-like carcinoma is a heterogenous entity among ocular adnexal malignancies. Lacrimal glands, the lacrimal drainage system, eyelid, and conjunctiva are potential primary sites for the development of this disease. For early and locoregionally advanced disease, complete excision of tumour plus postsurgical radiotherapy seems to achieve satisfactory disease control. The tumour seems to respond well to radiotherapy and cisplatin–5FU chemotherapy, but the role of chemotherapy in surviving advanced disease needs to be further clarified. Because of the low incidence of this entity, further investigation is needed to determine optimal treatment and prognosis. Further efforts with a larger number of cases and longer-term follow-up are warranted.

7. ACKNOWLEDGMENTS

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8. CONFLICT OF INTEREST DISCLOSURES
The authors have no financial conflicts of interest to declare.

9. REFERENCES


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