primary aims of the trial was to assess whether repeated scrap-
ing improved outcomes. The result of longer healing times in
fungal ulcers may be influenced by this. Re-epithelialization
is a difficult end point to measure, particularly in fungal kera-
titis, so this result should be interpreted with some caution.
Other factors associated with fungal and bacterial keratitis
cases, such as geographic location of the patients, could act
as confounders in this study. Selection bias could occur be-
cause use of topical antibiotics prior to presentation is more
common than antifungal use, and culture-negative bacterial
ulcers may be milder. However, the results of this study sug-
gest that fungal keratitis has a higher risk of perforation and
may have worse overall outcomes compared with bacterial
keratitis.

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Clinicopathological Findings in Persistent Corneal Cowpox Infection

Cowpox viruses (CPXVs) belong to the genus Orthopoxvirus.1 In-
creasingly, CPXV infections have been reported in domestic cats,
rats, and exotic zoo animals, with humans potentially being in-
fected through direct contact with these animals.1 Typically, a
CPXV infection becomes apparent through the development of
small skin lesions. Healing comes with scar formation and can
take several weeks. Complications and severe courses have been
reported in immunocompromised individuals.2

Report of a Case | In February 2009, a 49-year-old woman pre-

tended to a local clinic with a swollen eyelid and phlyctenular
changes of the cornea in her right eye. She received antibiot-
ics and steroid eyedrops for 2 weeks, but she developed a corre-

nal infiltration and marginal ulceration and her best-
corrected visual acuity (BCVA) decreased to 20/100.3 Because
of skin lesions on her shoulder that developed after direct con-
tact with a rat suspected of being infected with CPXV, she was
also tested for a CPXV infection. That was confirmed by real-
time polymerase chain reaction from conjunctival and skin swab samples. The CPXV infection of the eye was probably
caused by smear infection. Involvement of Staphylococcus au-
reus was shown by a swab, so she was given cefuroxime so-

dium and local antibiotics. Corneal infiltration then resolved,
but limbal ulceration worsened. Four months after the initial
infection, conjunctival swabs were negative for CPXV. From
then on, she received steroid eyedrops to control inflamma-

tion, ofloxacin eyedrops because of subtotal erosion, and lu-
bricants. From her general medical history, she solely re-

ported a 22-year history of type 1 diabetes mellitus.

In March 2010, she presented at the University Eye Hos-
pital Freiburg because of increasing corneal melting with per-
sistent corneal erosion (Figure 1, A and B). Her BCVA was count-
ing fingers. Penetrating limbal keratoplasty was performed.
Postoperatively, her BCVA was 10/200 (Figure 1C) and she re-
ceived immunosuppressive treatment with mycophenolate
mofetil.3 Three weeks later, the patient presented with scle-
rasis, transplant erosion, and ocular hypotension. Her BCVA was
reduced to 1/50. The patient received prednisolone, 100 mg/d, and cidofovir, 350 mg, intravenously once weekly because reactivation of a CPXV infection was suspected. The ocular changes improved, and the intraocular pressure values became normal, no longer hypotensive, with an epithelialized edematous transplant. Her BCVA was limited to hand movements. The cidofovir therapy was maintained. Cidofovir is, in fact, approved for *Cytomegalovirus* retinitis in patients with AIDS. The local therapy consisted of dexamethasone sodium phosphate, 1%, every hour. Two weeks later, the patient presented with transplant erosion and decompensated intraocular pressure due to extensive anterior synechiae. Intraocular pressure normalized after operative revision. Epithelialization took place, but the transplant remained bullous. Three months after transplantation, failure of the graft was evident. There was no inflammation.

Examination of the corneal explant revealed widespread destruction of the Bowman layer. The epithelium was missing in the central part. Diffuse infiltration of lymphocytes and neutrophil granulocytes was seen. Eosinophilic granular structures were found between stromal lamellae and within some keratocytes (Figure 2A). Histological changes were congruent with chronic keratitis as well as infectious crystalline keratopathy (Figure 2B). Interestingly, the corneal explant tested positive for CPXV DNA by polymerase chain reaction. Also, electron microscopy of the corneal explant revealed numerous Orthopoxvirus particles in different stages and locations of the cornea (Figure 2, C and D).

**Discussion** | To our knowledge, this is the first report of corneal melting necessitating corneal transplantation due to a CPXV infection. Ocular complications following CPXV infection involving swelling or ulceration of eyelids, conjunctivitis, and superficial keratitis have rarely been reported. Histological changes correlate with former reports of viral-induced corneal erosion. It seems that if the epithelial barrier is defective, keratocytes may especially be prone to infection.

Topical and systemic immunosuppression as well as the immune privilege of the eye may have supported viral persistence and disease course. Potentially, the immunosuppres-
sive therapy (prednisone, mycophenolate) prevented any reaction against CPXV, facilitating viral persistence and the graft failure. It is unclear whether the underlying diabetic condition had any effect on disease progression. No specific antiviral therapy exists for CPXV infection, but the application of cidofovir probably inhibited viral replication. Nevertheless, therapeutic options are limited, underscoring the potential risk of CPXV infection to humans.

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Regional Nodal Recurrence of Sebaceous Carcinoma of the Caruncle 11 Years After Primary Tumor Resection

Sebaceous carcinoma is a rare cancer with a predilection for the periocular region. The vast majority of cases of metastasis of sebaceous carcinoma are detected within 5 years after diagnosis and management of the primary tumor.1-5 Herein, we describe a case of regional nodal recurrence of sebaceous carcinoma of the caruncle 11 years after primary tumor resection.

Report of a Case | A 69-year-old man presented to our institution in June 2012. Eleven years earlier, in September 2001, he had been diagnosed as having sebaceous carcinoma of the left caruncle, which was surgically excised by a Mohs surgeon with reportedly negative margins. Since 2001, the patient had undergone ocular examination and magnetic resonance imaging annually and scans with results that had been negative for recurrence. However, examination in March 2012 revealed an enlarged left submandibular lymph node, which was initially treated with oral antibiotics with no improvement. The node was surgically excised, and pathologic examination confirmed metastatic sebaceous carcinoma with extracapsular extension. The patient was referred to our institution for further evaluation and treatment.

At presentation to our institution, the pertinent findings on examination included scarring and webbing of the caruncle, scar tissue along the canaliculi, and a palpable scar at the site of recent lymph node excision. Computed tomography of the head and neck with contrast showed operative changes in the neck but no evidence of tumor recurrence at the left caruncle. Findings on ultrasonography of the neck were negative for lymphadenopathy, and computed tomography of the thorax with contrast showed no evidence of metastatic disease. A completion neck dissection was recommended. In July 2012, the patient underwent neck dissection with concurrent biopsy of the left caruncle including conjunctival map biopsies. Pathologic examination of the excised left caruncular tissue showed scar tissue but no tumor; the conjunctival map biopsy results were negative for tumor. Twenty-five lymph nodes were dissected, and all were free of disease. Given that the previously excised positive lymph node demonstrated extracapsular extension, postoperative adjuvant irradiation of the nodal basins of the neck was recommended.

Discussion | Clinically evident nodal metastasis developed in this patient 11 years after treatment of primary sebaceous carcinoma of the left caruncle. To our knowledge, regional or distant metastasis of primary sebaceous carcinoma has not previously been reported this late after excision for any primary tumor location.

Review of the literature reveals reported rates of regional nodal metastasis of 4% to 20% for sebaceous carcinoma of the eyelid and conjunctiva.1-5 In a recent analysis of 50 patients with eyelid sebaceous carcinoma from our institution, we found that primary tumors classified as T2b or more extensive or at least 10 mm in greatest diameter were associated with an increased risk of regional nodal metastasis.7 On the basis of this observation, we recommended sentinel lymph node biopsy in patients with either of these primary tumor characteristics to detect micrometastasis not detected by palpation or routine imaging of regional lymph nodes.

In another recent report of sebaceous carcinoma from all head and neck sites, higher histologic grade was associated with a higher rate of regional metastasis, and 12 of 79 poorly differentiated eyelid sebaceous carcinomas (15%) metastasized, compared with 0 of 19 well-differentiated cases.6 The standard local treatment for sebaceous carcinoma is complete surgical excision with negative margins. Mohs surgery or similar techniques with frozen-section control of margins are often advocated for skin cancer to achieve negative