

initial visual field loss, following successful medical involution of the pituitary tumor, the chiasm itself may herniate into an enlarged and relatively empty sella. In some cases, this may result in traction and kinking of axons with renewed loss of function.⁹ Likewise, although the intracranial pressure diminishes following cerebrospinal fluid leaks, deterioration of visual function can also be expected when the brain, no longer buoyed by fluid, settles onto the skull base and compresses the chiasm with pressure points between the brain and pituitary fossa.¹⁰ Keeping such alternative processes in mind, one can comprehend the futility of using functional testing such as visual evoked potentials to monitor the progression of optic gliomas.

To summarize, spontaneous regression of gliomas is not a rare occurrence and can be accompanied by loss of vision.³ Some medical practitioners misinterpret loss of function, either clinically or by means such as visual evoked potentials, as evidence of tumor progression. This can misguide them to initiate unproven treatment modalities for gliomas that are already beginning to shrink. They may subsequently attribute efficacy to a purported remedy for an eventually detected reduction of glioma size. Particularly when trying to assess the beneficial effects of future therapies in investigational trials, such errors should not be allowed to occur.

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Substance P Concentration in Human Amniotic Membrane

Amniotic membrane can act as a biological bandage contact lens to the ocular surface, with therapeutic anti-inflammatory properties. The analgesic benefits of this intervention are believed to be due to mechanical protection. Amniotic membrane is also used in the treatment of neurotrophic corneal disease. Substance P is a neurotransmitter released by C-terminal nerve endings. It mediates acute inflammation and is known to play a role in modulating pain sensation. Substance P is also known to promote proliferation of various cell types, including epithelial and nerve progenitor cells.^{1,2} In this in vitro pilot study, we investigated the relationship between amniotic membrane and substance P.

Methods. This study was approved to use surplus tissue from 6 previously harvested amniotic membranes. The original samples were washed, prepared, and stored using standard techniques to ensure no contamination from blood. Residual pieces were defrosted and washed 4 times in phosphate-buffered saline. Sections measuring 0.5 × 0.25 cm were used throughout. The tissue was sonicated for 1 minute in phosphate-buffered saline and 0.5% Triton X and spun in a Jouan microfuge for 10 minutes at 400 rpm. This was analyzed using a Parameter Substance P competitive enzyme immunoassay (R&D Systems).

Results. Substance P was present in amniotic membrane samples at a range between 4000 and 6000 pg/mL. (Samples were diluted 1:50 to enable analysis.) In comparison, substance P levels in independent saliva and serum samples from volunteers in the research team ranged between 8 and 200 pg/mL in saliva and between 1200 and 1300 pg/mL in serum. We were unable to demonstrate uptake of substance P following incubation with the saliva or serum by this method owing to the very high concentration of substance P in amniotic membrane.

Comment. This pilot study demonstrates that substance P is present in very high concentrations in amniotic membrane. This exceeded the concentrations in our control sources of serum or saliva and was found despite several months of storage. Substance P has been identified in amniotic fluid in mid to late gestation.³ Further investigation would be required to elucidate whether this is the source of amniotic membrane's substance P. Urine is known to be a rich source of substance P, and fetal urine is produced from 12 weeks after conception. We wonder whether protective absorption of substance P by amniotic

membrane from amniotic fluid in utero is the source of our findings.

Eyedrops containing substance P and insulinlike growth factor have been tried with some success in therapy for nonhealing neurotrophic corneal ulcers. Substance P and insulinlike growth factor are believed to act synergistically in promoting corneal epithelial proliferation.^{4,5} Our positive identification of substance P in amniotic membrane may offer further insights into its mode of action in healing the ocular surface. Tseng et al⁶ investigated 31 eyes of 26 patients with cytologically proven limbal deficiency who received amniotic membrane transplants, and all showed rapid epithelialization and reduced inflammation except for the 2 eyes with atopy. It has been our clinical observation that some atopic patients can experience unexplained ocular surface irritation following treatment with amniotic membrane. Substance P is known to degranulate mast cells.¹ We wonder whether substance P released by amniotic membrane could provide a partial explanation for this phenomenon in atopic individuals and could have contributed to the failure of treatment in the 2 patients of Tseng and colleagues.

We have demonstrated that substance P is present in very high concentrations in amniotic membrane. Further study to identify the hitherto unrealized substances involved in the scavenging of damaging agents by amniotic membrane may permit development of specific topical preparations to treat the ocular surface.

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Epstein-Barr Virus-Positive T-Cell Lymphoma Involving the Lacrimal Gland of an Adult

Systemic T-cell lymphomas metastatic to the orbit are much rarer than non-Hodgkin B-cell neoplasms (predominantly marginal zone and follicular).¹ We describe an adult with an Epstein-Barr virus (EBV)-positive T-cell lymphoma of the lacrimal gland associated with multiorgan disease that was not of the expected natural killer/T-cell subtype.² Because of the unusual clinical findings and imaging study results, the diagnosis was elusive. A lacrimal biopsy evaluated with an EBV probe established the correct diagnosis; this technique should probably be used for all unusual or atypical orbital lymphomas.

Report of a Case. A 57-year-old man developed abrupt right eye swelling and erythema with chemosis that worsened over 6 days and was nonresponsive to intravenous antibiotics (**Figure 1A**). He had had a febrile illness with fatigue for 4 years. Earlier lung, liver, and bone marrow biopsies revealed an EBV-positive T-cell lymphoma with a clonal rearrangement of the T-cell receptor gene. Visual acuity was 20/20 OU. The motility was moderately decreased and there was no proptosis. Magnetic resonance imaging showed enlargement of the lacrimal gland on the right side with a nonenhancing center (**Figure 1A**) and bilateral involvement of the extraocular muscles (**Figure 1B**). Biopsy of the periorbita (**Figure 1C**) and lacrimal gland (**Figure 1D**) showed chronic inflammation with necrosis (**Figure 1C** and **D**) and scattered larger cells with ground-glass nuclei (**Figure 1C**). The lymphocytes were positive for CD3 and CD5 (**Figure 2A**) and negative for CD56; there were rare CD20-positive cells. Brown-Hopps, Steiner, and Gomori methenamine silver stains disclosed no organisms. In situ hybridization with an EBV probe demonstrated marked positivity in the lymphocytes in both the periorbita and lacrimal gland (**Figure 2B**). The lung biopsy showed a striking perivascular lymphocytic distribution (**Figure 2C**) with identical immunohistochemical and EBV-positive (**Figure 2D**) findings. Radiotherapy delivered to both orbits caused complete resolution of the patient's symptoms, and he has recently received an allogenic bone marrow transplant.

Comment. Ascending ductular and hematogenous infections of the lacrimal gland are vanishingly rare. Our patient's orbital "cellulitis" with lacrimal gland cavitation and no response to antibiotic therapy was confusing. The biopsy revealed necrosis of the lacrimal gland (probably at the margins of a sterile abscess) and the profuse presence of CD3- and CD5-positive T lymphocytes that were CD56 negative, thereby ruling out a natural killer/T-cell lymphoma. The number of T cells was much greater than that normally expected in the gland,³ and in situ hybridization established T-cell EBV positivity.