Nursing care of the patient with cornea graft rejection

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The best thing you can do for your patient with a corneal transplant is educate them about graft rejection. The better medical and pharmaceutical diagnosis and treatment are understood, the better nursing interventions necessary to help your patients keep their cornea grafts clear for a lifetime can be performed.

Warning signs and symptoms
Educate patients every chance you get on the early warning signs and symptoms of corneal transplant rejection. There are three warning signs or symptoms of corneal transplant rejection. They are 1) decreased vision, 2) redness, and 3) pain.

The most common and reliable way a patient notices early transplant rejection is by the first warning symptom, decreased vision (Alldredge & Krachmer, 1981). Beginning after the first postoperative day, and throughout their life, patients should test their vision daily. An easy way for them to do this is to have them select an object on the wall, such as a clock or picture. They then cover their unoperated eye and back away until the borders of that object begin to blur or appear unclear. Have them notice how far away the object is when this occurs and start at this same point everyday. As the vision improves, it will be necessary to back farther away to establish a new distance from which the object can just be seen. If the object cannot be seen as well as it was on the previous day from the same distance, then the vision has decreased (University of Iowa Hospitals and Clinics, 1992).

Explain the difference between fluctuating vision and decreased vision. For the first year and a half after surgery, the surface of the cornea won’t be stable and vision will fluctuate. Teach patients that if vision is worse but can vary by position of the head or squinting to get better, then this is probably due to finding a better refractive plane on the corneal surface. If, on the other hand, the vision will not get any better no matter what the patient does, then this is probably indicative of transplant rejection.

Teach your patients to inspect daily for any increased redness of the eye. Postoperatively, the eye may be red because there may be inflammation and blood in the tissues due to the trauma of surgery. After a few weeks, the blood should absorb and inflammation should disappear and the eye should become more white. If the conjunctiva becomes more red at any time, it may be a warning of corneal transplant rejection.

Also teach your patients to notice any discomfort in or around the eye. Initially, there may be some discomfort around the eye postoperatively, but this should resolve in a few days. If the eye becomes uncomfortable in any way, it could be a warning of corneal transplant rejection.

If any combination of only one, two, or all three of the corneal transplant warning signs persist for a period of 24 hours, then instruct the patient to contact your office or the ophthalmologist on call. Stress the importance of beginning the habit of setting aside a certain time of day to perform these three simple tests to evaluate the condition of the cornea. The gift of a corneal transplant can last a lifetime by doing these few short checks everyday (Smith, 1982).

Symptoms patients report in addition to those already covered may include: irritation, photophobia, and tearing. Even if the cause of the irritation and tearing is from a loose suture, the patient should still be seen as soon as possible. Loose stitches that are not removed in a timely manner can become the cause of graft rejection from the increase in vasculature to the area. In addition, it can provide a tract for an infection to enter the eye—which if left untreated may lead to endophthalmitis.

Types of rejection
Depending on the type and severity of the rejection, and the awareness of the patient, the rejection may or may not be symptomatic (Wilson & Kaufman, 1990). Patients will be anxious once they hear the diagnosis of rejection. The will want to know their chances of recovery, if they have lost their graft for good, or what outcome they can expect.

An epithelial rejection most likely will be asymptomatic. If left untreated, donor epithe-
Malignant cells are destroyed causing an epithelial defect. In a study by Alldredge and Krachmer (1981), the average onset was found to be three months after surgery with an incidence of about 10% in patients followed for one year. Epithelial rejections shouldn’t occur after one year because all epithelial cells at that point will be the recipient’s, not the donor’s.

Subepithelial infiltrates (SEI’s) are usually an asymptomatic sign of rejection first described by Alldredge and Krachmer (1978). They are found immediately beneath Bowman’s layer, seen only in the donor tissue. With corticosteroid treatment they will rapidly disappear, but some residual scarring may remain (Wilson & Kaufman, 1990). Some physicians believe this is part of the epithelial rejection process. Average time of onset was 10 months with a frequency of about 15% (Alldredge & Krachmer, 1981).

Appearing as an immunologic arc, a stromal rejection commonly presents simultaneously with endothelial rejection making it a difficult condition to detect. It has only been demonstrated in rabbits and there is little information regarding its occurrence in humans (Wilson & Kaufman, 1990).

An endothelial rejection usually begins as a line at a vascularized area of the peripheral donor cornea. Damage to the endothelium inhibits normal corneal hydration function, therefore causing stromal edema. If left untreated, it will result in irreversible diffuse endothelial damage. Average time of onset for an endothelial rejection is eight months, with a range of 2 weeks to 29 months (Alldredge & Krachmer, 1981). Frequency ranges from 0% to 60%, average of 29%, depending on which study you refer to.

Incidence
Overall, the body will attempt to reject the cornea in 20% of the cases. If the corneal transplant rejection is treated early in its course, 90% of the cases can be reversed with medications (University of Iowa Hospitals and Clinics, 1992). Therefore, it cannot be emphasized enough how extremely important it is for the patient to recognize the signs and symptoms of impending rejection as early as possible and report them to the ophthalmologist.

As mentioned earlier, a rejection reaction can happen at anytime in the patients’ life—days, weeks, or years after the transplant. They have been reported to occur anywhere from a very rare 2 days (due to an antigen presensitization) to 40 years after transplantation. Most likely, they will occur in the first year—between 3 to 9 months.

Since it takes about 2 to 3 weeks to build an immune reaction, then technically, the diagnosis of rejection should only be made in a successful graft that has remained clear for at least 10–14 days (Wilson & Kaufman, 1990). This way, rejection can be differentiated from primary graft failure.

All three types of rejection decrease in frequency with the increase in age of the recipient (Alldredge & Krachmer, 1981). In my experience, as children go through growth spurts, they will have increased rejection episodes. They need to be watched very closely, and know to return to the clinic at the first sign of rejection for treatment.

Generally, if all goes well, topical steroids will be tapered down to about once a day by four months postoperatively. This is a particularly opportune time to remind patients once again of the warning signs of rejection and give them a little wallet sized card with the warning signs and the clinic phone number close at hand (Figure 1).

### Warning Signs of Corneal Transplant Rejection

1. Decreased vision
2. Increased redness of the eye
3. Discomfort in or around the eye

If signs persist for 24 hours, call the Eye Clinic at (000) 000-0000 from 8:00 a.m. until 5:00 p.m. Monday–Friday.

After 5:00 p.m. or on weekends and holidays, call (000) 000-0000 and ask to speak with the eye resident on call. [Insert correct phone numbers and clinic times to customize wallet card for patients.]

**Figure 1**

Potential risk factors
Studies have shown several potential risk factors that increase the rate of immune related cornea allograft rejection 25–50%. They are corneal vascularization, previous graft failure, and large or eccentric grafts. Because the normal cornea is avascular, it has what is known as a relative immune privilege (Wilson & Kaufman, 1990). Conditions that make the cornea vascularized break that privilege by introducing the donor graft to the nearby vas-
Nursing care of the patient with cornea graft rejection

Continued from page 35

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Other potential risk factors are bilateral grafts and age of the recipient. After an extensive review of the literature, Wilson and Kaufman (1990) determined that "since the risk of rejection is greatest in the first year after a transplant, it is probably sensible to wait at least 12 months after the transplantation of the first eye before grafting the second eye." Alldredge and Krachmer (1981) found rejection more frequent in patients younger than 50 years of age as compared to patients older than 50 years of age.

Circumstances once perceived as potential risk factors, but that have been found not to change the chances of graft survival, are the method of corneal preservation, sex and race of the donor to the recipient, pregnancy, or previous blood transfusions (Wilson & Kaufman, 1990).

Preventive Measures
It is possible, although unlikely, that a rejection could be brought about by a nonspecific stimulation of the immune system, as may be possible from undergoing dental work or receiving a flu shot. Some physicians believe steroids need to be increased to cover this burst from the immune system. A schedule of steroid drops used at qid [4 times per day] the day before and the day of the dental work or flu shot may be prescribed. This is followed by a quick taper of tid [3 times per day] for three days, bid [2 times per day] for one week, then back to their normal routine scheduled of qd [everyday] or qod [every other day]. Other physicians prefer to just have the patient pay particular attention to the warning signs and symptoms of transplant rejection and call if any change is noticed. This might be risky due to the fact that some rejection episodes occur without the patient being aware of them.

HLAs (human leukocyte antigens) are the primary stimuli in corneal allograft rejection. HLA antigens have been detected in all layers of the cornea, with the largest quantities in the corneal epithelium (Wilson & Kaufman, 1990). Studies have been inconclusive regarding HLA matching or tissue typing in the incidence of graft rejection. Limitations with HLA matching are the high variability of antigens in the human population and the next to impossible task of acquiring a high level match.

Treatment
Treatment is undeniably more effective if rejection is diagnosed early and treatment begun immediately. The first line of attack will be to combat the rejection with steroids. It will most commonly begin with hourly corticosteroid drop instillation, with the addition of an oral dose, depending on the severity of the reaction.

Oral prednisone is usually prescribed at a dose of 80 mg/d [milligrams per day] (typically 1 mg/kg) [milligrams per kilogram of weight] for one week. It should be taken all at once with breakfast and is best tolerated when histamine blockers such as cimetidine or antacids are prescribed for the stomach at bedtime. After one week, the patient is re-examined and three things can happen. 1) The cornea looks better; in which case, the oral steroids can simply be stopped. 2) The cornea looks no better; in this case, the oral steroids are also discontinued. 3) The cornea looks a little better; then steroids are continued at 80 mg/d and gradually tapered as the condition of the cornea improves (personal communication, Jay Krachmer, M.D., July 1995).

Solu-Medrol is currently another form of immediate treatment, giving the patient a bolus of 125, 250, or 500 mg of steroid at the time of the visit. This is relatively safe; however, caution should be used in the elderly population, diabetics, and patients with hypertension. Patients should be counseled concerning the possible increase in appetite and metallic taste in their mouth. They may feel agitated, anxious, and could have problems of an underlying psychosis brought out.

If compliance is considered to be a potential problem, then a subconjuctival injection of steroid may be indicated before the patient leaves the office to insure some treatment will be instituted.

Cyclosporine appears to be a promising agent for the treatment of high risk corneal transplant patients. Usually monocural patients or patients who have previously had a failed graft due to a graft rejection would be candidates for this form of medical treatment. It primarily inhibits the early stages of antigen recognition. It doesn't cause an immediate reaction, but takes time to work. So, it is usually started preoperatively and used prophylactically in high risk patients. Remember, it only helps to prevent rejections, and therefore is not useful once the patient has a rejection in progress.

Systemically, cyclosporine is a powerful immunosuppressant, used extensively to sup-
press rejection following renal, cardiac, liver and bone marrow transplantation. Studies have shown it has the potential to induce numerous side effects including hypertension (50%), renal toxicity (25–38%), and neurotoxicity (Nussenblatt & Palestine, 1986). Patients also may complain of mild numbness and tingling of the extremities (90%), nausea and gastrointestinal distress (20%), as well as increased hair growth (25–45%), hyperplasia of the gums (25%), fine hand tremors (12–55%), and acne (6–8%) (Physicians Desk Reference, 1995).

The dose of cyclosporine for organ transplants is started at 10–14 mg/kg/day and tapered down to 3–10 mg/kg/day. The dose for cornea transplant patients is much lower, at a rate of about 5–7 mg/kg/day. Depending on the size of the patient, this generally turns out to be about 100 mg bid at an astronomical cost of about $350/month or $4200/year — currently covered for Medicare recipients. Cornea patients usually will be on this medication for about one year following penetrating keratoplasty.

Oral absorption is extremely erratic so monitoring the blood levels and adjusting the dosage is most important. This medication must be taken with food for proper ingestion. Patients should be advised to be consistent with their schedule of medication doses with regard to time of day and mealtime.

Acceptable cyclosporine blood levels depend on the assay used for testing but commonly should run at about 100–200 ng/ml [nanograms per milliliter] in adults. Compare your assay to what the literature describes. Test levels at least monthly until a consistent reading is demonstrated. Schedule patients for early morning appointments and have them hold off on their morning dose until their blood is drawn for accurate testing. This reveals the 12 hour level, which is what our assay requires.

Every four to six months, additional labs of blood urea nitrogen (BUN), serum creatinine, and liver function tests (including bilirubin) should be acquired to assess renal and liver function. Current studies suggest a guideline of no more than a 30% increase in serum creatinine from the preoperative baseline level (Nussenblatt & Palestine, 1986). While on cyclosporine, remind patients not to get any kind of vaccination or use potassium supplements, nephrotoxic drugs, or NSAIDS (nonsteroidal anti-inflammatory drugs).

The risks of side effects from systemic cyclosporine may be avoided through topical administration of cyclosporin A (CsA). When prescribed as a drop CsA is generally made up in 2% corn or olive oil. Most patients will complain of brief burning with drop instillation. If severe, some physicians have tried compounding the drug in artificial tears, however, proper absorption in the cornea cannot be guaranteed with either vehicle. In the future, a more hydrophilic derivative may need to be developed to better penetrate the epithelium and stroma for higher reliability (Belin, Bouchard, & Phillips, 1990).

With a little bit of knowledge, patience, and time — teaching your patients about cornea graft rejection can add new meaning to the old saying “An ounce of prevention is worth a pound of cure.”

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References