Donor Eligibility/Suitability

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Summary

Donor eligibility and suitability determinations are key to maintaining a safe and effective donor pool. A careful reading and understanding of FDA regulations and guidance documents and Eye Bank Association of America (EBAA) Medical Standards are usually sufficient to make eligibility and suitability decisions. This commentary explores some of the more ambiguous situations that may be encountered. When regulations and standards do not provide clear guidance, consultation with the eye bank's Medical Director is warranted.

Federal regulations[1,2] and guidance documents[3-6] state that donors are eligible if they are free from risk factors for or clinical evidence of relevant communicable diseases (RCDs), free from risks associated with xenotransplantation, and if tests for RCDs are negative or nonreactive. A responsible person must determine and document the eligibility of a donor prior to tissue release. While some eligibility and suitability decisions are straightforward, others may be more complex.

In addition to eligibility criteria, eye banks must determine if a tissue is suitable for its intended use. These determinations are typically uncomplicated, and in the United States are governed by the Eye Bank Association of America (EBAA) Medical Standards[7]. However, with the proliferation of different keratoplasty techniques, some suitability decisions may be less clear.

The following case presentations explore some of the potentially difficult decisions faced by eye bankers in making eligibility and suitability determinations. They were originally presented at the Eleventh Annual HCT/P Regulation Conference in March, 2015 in Bethesda. This annual conference offers eye and tissue bankers an opportunity to explore these issues in depth. The cases are presented in stages in an outline form, revealing more information at each step, with decision points along the way.

Case 1: Is This Dementia?

Donor History: Hospital Record Review

- Seventy-five-year-old female donor
- Cause of death: respiratory failure
- Underlying medical diagnosis: chronic obstructive pulmonary disease (COPD)
- Admitted from emergency room (ER) after two to three days of increasing shortness of breath (SOB) at home
- Progressive downhill course in hospital, culminating in removal from life support
- Death note summary by treating hospital physician lists "dementia" among several diagnoses
- Review of ER and hospital records show no other mention of dementia, although patient was at times confused or poorly responsive

Donors with a diagnosis of dementia are ineligible as cornea donors because of the risk of transmission of prion disease. Is the above history sufficient to conclude that the donor had dementia and was therefore ineligible?

Although a diagnosis of dementia is present in the death note summary, there is no other mention of it in the remainder of the medical record. There is insufficient information to come to a conclusion. The hospital record is only a portion of the information available for review.

Medical/Social Interview: Daughter

- Donor was sometimes confused at home
- Confusion was associated with episodes of severe SOB or "if she let her blood sugar get way out of control."
- At other times, she was "pretty normal, other than occasionally forgetful."

Is this enough information to conclude that there was no dementia?

The family interview offers potential alternative explanations for episodes of confusion other than dementia. However, family members are not medical professionals and are not capable of making or excluding a diagnosis of dementia.

Treating Hospital Physician Interview

- Thought he recalled seeing dementia mentioned somewhere in the patient's past medical history
- Included dementia on death note summary for sake of completeness

- Never evaluated donor specifically for dementia
- Clinical impression was that poor responsiveness and confusion were related to inadequate oxygenation associated with COPD

Can dementia be ruled out now?

Information obtained from the treating hospital physician offers more conclusive evidence that the episodes of confusion and poor responsiveness in the hospital were not due to dementia. However, the treating physician has no detailed knowledge of the patient's pre-admission status, other than a vague recollection that dementia was mentioned somewhere in the patient's past medical history. There is still a potential that the patient had dementia as well as other medical reasons for episodes of confusion.

Primary Care Physician Interview

- Patient had severe COPD and diabetes mellitus, poorly controlled at times
- She was occasionally confused when hypoxic and/or hypoglycemic
- There was no clinical evidence or history of dementia

This history allows a confident exclusion of a diagnosis of dementia. The case demonstrates the importance of gathering all available information.

Case 2: After the Fact. Viral Hepatitis?

Summary of Case

- Medical Examiner (ME) case
- Donor eligibility information, including donor screening and testing, is all negative prior to distribution
- Autopsy results received three months after distribution of corneas showed active hepatitis on pathology slides
- ME cannot verify whether hepatitis was infectious or immune

Was the eye bank justified in releasing the tissue?

Can a donor eligibility determination be made prior to receipt of autopsy results when it is known that an autopsy will be performed?

Federal regulations require that donor eligibility determinations must be based on a review of donor screening and testing (CFR §1271.50) and that the screening includes a review of "relevant medical records" (CFR §1271.75)[2]. While some records must be reviewed, others must be reviewed "if available" (CFR §1271.3(s))[2]. Medical examiner reports and autopsy results are considered relevant medical records. Is it reasonable for an eye bank to release tissue while autopsy results or final ME reports are still pending?

The FDA addresses this specific situation in the donor eligibility guidance documents[5]. The donor eligibility guidance states that "available" means that a record or information exists, or is pending, and can be obtained through due diligence, within a reasonable amount of time. A "reasonable" amount of time is defined as a period that would allow for collection of important information without compromising the utility of the tissue. Corneas and autopsy reports are specifically addressed, noting that since corneal tissue must be used before receipt of an autopsy report, the report could not be obtained in a reasonable time period. Under these circumstances, it is not necessary to wait to review the final report of autopsy results prior to distribution of the corneas.

What are the eye bank's responsibilities?

Based on the FDA donor eligibility guidance, it was appropriate to use the available information when considering the donor's eligibility, including the presumed cause of death and other relevant preliminary autopsy findings and all other information obtained about the donor, and to release the tissue based on that available information. It is also the bank's responsibility to review the final autopsy report when available. If information in the final report indicates that the donor is ineligible, the bank must file an HCT/P deviation report with the FDA within 45 days (CFR §1271.350(b))[2].

In addition to the FDA requirements, the EBAA Medical Standards state that information received after release of tissue that indicate risk of transmission of a relevant communicable disease must be reported to the eye bank medical director, the EBAA office, the consignee and the FDA. When notifying the consignee, it is extremely helpful to offer some advice regarding the meaning of the information. This is typically done in consultation with the eye bank's medical director, and on occasion with outside consultation with a specialist familiar with the result in question. In the case cited above, the concern is for the potential of transmission of hepatitis B or C. While cases of hepatitis B transmission through corneal transplantation were reported prior to the onset of donor testing [8], the likelihood of transmissible hepatitis B in a donor with negative hepatitis B surface antigen and antibody to core antigen is exceedingly low[9]. Nevertheless, recommending testing of the recipient is a reasonable precaution.

Case 3: Risk Factors and Adequacy of Donor Screening

Donor History and Examination

- Nineteen-year-old male donor
- Cause of death: multiple trauma secondary to motor vehicle accident
- No significant past medical history
- Social history: was incarcerated in local juvenile detention center
- Examination: homemade tattoos suspicious for shared needles and ink

Is this donor eligible?

Donor eligibility guidance states that relevant risk factors would render a donor ineligible if in juvenile detention, lock up, jail or prison for more than 72 consecutive hours in the preceding 12 months. In addition, persons who have undergone tattooing, ear piercing or body piercing in the preceding 12 months, in which sterile procedures were not used, e.g., contaminated instruments and/or ink were used, or shared instruments that had not been sterilized between uses were used also have relevant risk factors which would render them ineligible.

Medical/Social Interview: Mother

- Detention occurred two years ago
- Tattoos were obtained two years ago in juvenile detention center
- No contact with donor in since that time
- Answers most risk questions with "I don't know."

The history of incarceration and tattoos is over twelve months old, and therefore does not in and of itself necessitate a determination that the donor is ineligible. Is the medical/social history interview adequate? Can a responsible person make a donor eligibility determination in this case without obtaining answers to all relevant risk questions in the donor medical/social history interview? If additional information cannot be obtained from an alternate historian, the history is inadequate to make a donor eligibility determination, and the donor must be considered ineligible.

Case 4: Tissue Suitability

Donor Eligibility

- Fifty-seven-year-old male
- Cause of death: cardiopulmonary arrest secondary to myocardial infarction
- Eligible based on unremarkable donor screening, exam and testing

Tissue Recovery

- Cornea-scleral rim recovery
- Body refrigerated beginning three hours post-mortem
- Normal penlight exam
- Uncomplicated, atraumatic excision procedure
- Death to preservation time: twelve hours

Tissue Evaluation

- Mild inferior epithelial exposure
- Trace stromal folds
- Posterior crocodile shagreen
- Normal endothelium: cell density 2653 cells/mm^2, normal morphology

Posterior crocodile shagreen (Fig. 1) is characterized by cloudy central polygonal or rounded deep stromal opacities that fade anteriorly. It may be phenotypically indistinguishable from central cloudy dystrophy of Francois, it is non-progressive, and it is usually asymptomatic.

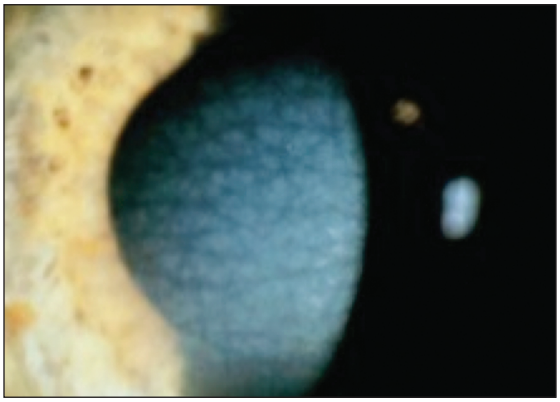

Figure 1. Posterior crocodile shagreen. Cloudy deep stromal polygonal opacities

EBAA Medical Standard D1.110[7] states that tissues "that pose a risk to the success of the surgery shall not be offered for surgical purposes." Lack of tissue clarity poses a risk to success. Is this tissue suitable for transplantation?

To determine tissue suitability, one must first consider the intended use of the tissue. Each of the following procedures utilizing corneal tissue are intended to provide an optically clear graft, and must be considered individually:

- Penetrating keratoplasty (PK)
- Superficial anterior lamellar keratoplasty (SALK)
- Deep anterior lamellar keratoplasty (DALK)
- Descemet stripping automated endothelial keratoplasty (DSAEK)
- Descemet membrane endothelial keratoplasty (DMEK)

In PK, DALK and DSAEK, the posterior portion of the stroma affected by posterior crocodile shagreen is transplanted. The disease is typically asymptomatic, but there are no ophthalmic records available for review and the medical history interview was not revealing with respect to any eye disease. There are a number of unanswered questions here. Is the posterior stromal opacity visually significant? Would additional interface irregularities inherent to the DALK and DSAEK procedures present greater problems than after PK? Is the eye bank technician qualified to make those judgments? Consultation with the medical director is necessary. A conservative approach would be to defer use of the tissue for PK, DALK or DSAEK.

In SALK, only the anterior stroma is transplanted. In DMEK, only Descemet membrane and endothelium are transplanted. In both of these cases, the cloudy posterior stroma is not used. The tissue would be suitable for either of these uses. It would also be suitable for non-optical purposes, such as a patch or tectonic graft or a limbal stem cell graft.

CONCLUSION

FDA Guidance for Industry documents[3-6] and EBAA Medical Standards[7] offer guidelines for donor eligibility and tissue suitability determinations. When ambiguous situations arise, consultation with the eye bank's medical director is in order. When in doubt, deferral is the preferred course of action.

REFERENCES

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