Autopsy Final Report Findings and Corneal Transplantation: A Retrospective Review

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Donor screening for the possible introduction of a transmissible disease is a paramount concern for eye bankers, the Food and Drug Administration,(FDA), and the Eye Bank Association of America, (EBAA). The combination of the donor risk assessment interview or (DRAI) and the mandated serologic testing for infectious viral disease markers has been highly successful in assuring the safety of allograft tissues for transplantation. However, especially for cornea transplantation due to the time limits for maximum viability of the endothelial cells needed to restore vision, information that might have adversely affected the determination of donor eligibility does not become available until after the tissue has been transplanted. This retrospective study reviews histology findings and autopsies where myocarditis, or other potential contraindication was not reported until days or weeks after the corneal transplantation had occurred.

METHOD

A review of histology and autopsy finding for cornea donors over a ten year period were examined for the reports of a non-documented myocarditis where donor eligibility or corneal suitability might be a question had it been known at the time of transplantation. The review consisted of those cornea donation cases between January 1, 2009 and Nov.15, 2019 where deviation or recall reports contained information documented on medical examiner or other autopsy examination on cornea donor cases that might have affected the original determination of donor eligibility.

There were 26 total cases found during this time interval review that had histology findings that could be evaluated for potential suspected myocarditis or other pathology findings suggestive of potential infection had the autopsy finding been available within the time for tissue placement. During this time interval there were 1350 donors from this medical examiner population.

RESULTS

Of twenty-six cases reviewed, 15 had autopsy reports of either active, acute or possible myocarditis. In addition, there were autopsy findings of pneumonia, heroin toxicity or bacterial or viral infections and one non-required serology finding of Epstein Barr virus IgM, not discoverable in the medical history or physical examination. The myocarditis cases are summarized in Table 1 and the other potential contraindication cases are documented in Table 2. Cause of death or other medical /social history abbreviations are documented in Table 3. In all of these cases, there was no information available at the time of tissue recovery or prior to placement for transplantation, that would have indicated the conditions reported in these delayed autopsy or microbiology findings. No adverse reactions consistent with a demonstration of myocarditis were reported.

DISCUSSION

Myocarditis is an inflammatory disease of the heart, which may have infectious or non-infectious causes, although viral etiology is often suspected.[1] The clinical manifestations of myocarditis are highly variable, ranging from subclinical disease to fatigue, chest pain, heart failure, cardiogenic shock, arrhythmias, and sudden death.[2] Many cases of myocarditis likely go undetected because they are subclinical or present with nonspecific signs and therefore it is not surprising that nothing in the DRAI was identified to cause a donation of the corneas to be considered unsuitable.[3,4,5] With the other findings in the case reviews,

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Table 1

Donor #	Age/ Sex	DOD	Report Received	Results	COD/Medical History
2008-1119	62/M	9/6/2008	2/19/2009	possible viral myocarditis	Probable MI
2010-1579	4/F	10/1/2010	10/20/2010	myocarditis	Trauma/MVA
2012-1747	19/F	11/8/2012	11/21/2012	lymphocytic myocarditis	Hanging
2012-1783	44/M	11/13/2012	3/18/2013	myocarditis	SI GSW to head
2014-0787	48/F	5/23/2014	8/28/2014	myocarditis	Sudden cardiac death/Jaw Pain
2014-0881	7/M	6/11/2014	6/24/2014	myocarditis	Chromosome 14 deletion/pulmonary HTN
2015-1831	14/F	11/11/2015	11/25/2015	active myocarditis-FDA rejected report no sepsis/symptoms sepsis	SI GSW to head
16-000552	39/M	8/11/2016	8/29/2016	myocarditis	Sudden cardiac death; PMH-kidney stones, smoker
16-000143	21/M	3/19/2016	5/27/2016	myocarditis	Brain Injury -skateboarding accident in 2011-in chronic pain/multiple pain meds/Possible oral OD
17-001452	11/M	5/29/2017	7/11/2017	myocarditis	BFI-MVC
17-002019	33/M	11/23/2017	12/8/2018	myocarditis	BFI-Auto vs Pedestrian
17-00178	57/M	9/18/2017	1/5/2018	myocarditis	Sudden cardiac death/HTN/ETOH abuse
18-003184	39/M	10/30/2018	3/10/2019	myocarditis	Sore throat, strep throat for few days-on antibiotics/agonal breathing-to ER in v-fib. PMH-URI 3 month's prior-received antibiotics and it resolved. No other sig. PMH
19-003861	29/M	4/23/2019	7/3/2019	acute lymphocytic myocarditis	SI GSW to head. Had a cold last few days
19-004295	17/M	8/20/2019	8/30/2019	active lymphocytic myocarditis	SI GSW to head. PMH migraines/concussions

heroin toxicity was diagnosed by toxicology findings, there was no history on the screening interview of drug use, and neither the trained technical recovery team nor the medical examiner reported any evidence of intravenous drug administration. This finding, though always a concern when drugs are reported, would not cause the donor eligibly or tissue suitability, with concomitant nonreactive serology and lack of evidence of IV drug use, to lead to an automatic exclusion. The bacterial reports in blood cultures however are much more problematic. As seen in Table 2 the organisms isolated consisted of pathogenic stains of cocci, gram negative rods and yeast. A reexamination of donor

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Table 2

Donor #	Age/ Sex	DOD	Report Received	Results	COD/Medical History
2009-1091	39/m	7/27/2009	9/3/2009	Pneumonia per late report from x-ray	Probable MI
2012-1839	66/M	11/25/2012	12/3/2012	blood culture Fusobacterium	Fall from Ladder-anoxic brain injury-organ case
2014-1431	19/M	9/17/2014	11/10/2014	EBV IGM reactive suggestive of current infection	BFI-fell 14 ft. off forklift -landed on head-organ donor
2015-0155	41/M	1/27/2015	2/27/2015	blood culture Enterococcus F.	Cardiac event-anoxic brain injury-organ donor
16-000619	7/M	8/30/2016	9/7/2016	blood culture S. Aureus	Fell off bike-Acute HA-ICH-Organ case-3 days hospitalization
17-002045	33/f	11/30/2017	3/.13/2018	Heroin toxicity	Cardiac related autopsy pending
17-001752	44/M	9/17/2017	9/29/2017	blood culture Enterococcus F.	BFI-On bicycle-hit by car-SDH/SAH-failed Organ Donor-hospitalized 5 days-lungs could not be placed; Ht not recovered due to murmurs, lungs r/o 2'function
17-002006	50/M	11/19/2017	3/2/2018	Bronchopneumonia	Hypertensive CVD/gastric sleeve 11/10/17
17-001822	2/F	9/28/2017	3/2/2018	Bronchopneumonia	Upper Respiratory symptoms past few days-SOB. PMH-ischemic encephalopathy, holoprosencephaly, seizures, DI, G-tube feedings
18-002517	22/M	4/28/2018	5/10/2018	blood culture Strep vesticularis	BFI/MVA- Organ case-DCD-Hospitalized 1 day
19-003924	18/M	5/11/2019	6/20/2019	blood culture Candida albicans	Sudden frontal HA/ICH, ant. Communicating aneurysm, DI. PMH-shaken baby syndrome-wheel chair bound . Hospitalized 2 days

Report of blood cultures is delayed in part due to initial time of growth and identification and receipt of information from the testing facility.

Table 3

Abbreviation	Meaning	Abbreviation	Meaning
BFI	Blunt force injury	ICH	Intracranial hemorrhage
CVD	Cardiovascular disease	MI	Myocardial infraction
DCD	Donation after cardiac death	MVA	Motor vehicle accident
DI	Diabetes insipidus	MVC	Motor vehicle collision
ETOH	Alcohol	OD	Over dose
GSW	Gunshot wound	PMH	Prior Medical History
HA	Headache	SI GSW	Self-inflicted GSW
HTN	Hypertension	URI	Upper respiratory infection

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medical chart or admission history as well as time interval for organism growth, number of organism positive blood culture bottles and whether the cultures were pre or post mortem would assist in determining the likelihood of contamination verses septic complications.[6,7] There were also 3 cases of pneumonia diagnosed on autopsy which could have been of significance had the condition been reported on screening rather than just at the autopsy final.[8] In such cases, further investigation for any factors, which could be suggestive that the pneumonia had led to a possible systemic sepsis documented in medical chart or on the donor history screening might have been instituted including, but not limited to, contact with treating physicians or primary care physician if known. These three cases had no such documentation of symptoms or treatments to indicate a septic concern. There was one case of a serology finding not included in the routine screening panel, the Epstein Barr Virus reactive test for EBV IGM. Here too with the virus serology there was no history or current information to support a question of the donor eligibility. Nevertheless, in all of these incidences no complications were reported in the post-transplant outcome review.

There are limitations in retrospective post-transplant review as recipients could be lost to follow up before complications, if any, were manifest and could be reported to the transplanting surgeon. An undiagnosed myocarditis could exist pre-transplant or develop post-transplant, related or unrelated to the transplant, and as in these donors not be identified until the recipients autopsy should autopsy later occur. In addition as a final autopsy report contains not only the description of the gross autopsy findings, but requires the culmination of multiple pieces of additional information, including toxicology, histology, other ancillary testing, and reports of law enforcement investigations, the release of reports may exceed the optimal or required time for ocular transplantation. Because of the complexity of these reports, The National Association of Medical Examiners (the professional organization that credentials medical examiner offices) only requires a final autopsy report to be completed within 60-90 days of the initial autopsy.

Conclusions: The optimal time from death to preservation and preservation to transplantation presents the screening process with limitations to both the collection of the tissue and in the collection of post- mortem data, which is often unavailable until days or weeks post transplantation. Evaluation of this delayed information and reporting of it to the transplanting physician or other appropriate agencies, i.e. FDA and EBAA, when it becomes available can be problematic. The true origin of the myocarditis is generally unknown. It could be of an infectious cause i.e. viral infection, but it could also not be infectious in nature. The Broncho- pneumonia may have presented a risk of a systemic process or be limited to the respiratory system and unlike lobar pneumonia is less likely to be caused by Streptococcus but may be the result of a hospital acquired infection which is also problematic.[9,10] The data from all of these cases poses challenge and uncertainty to the eye-banking professional and medical director in evaluation of its relationship to recipient risk. However, in these cases it is important to note that no complication were reported in six to nine month transplantation follow up. In the case of myocarditis a diagnosis post cornea transplant might never be reported as it could as with these donor cases not show manifestations except on autopsy. It is then not possible to know definitely, from the data in hand, if the lack of reported contraindications can be totally attributed to the avascular nature of the cornea, the lack of true sepsis in the donor, or other contributing unknown factors of the donor's history or the recipient's robust health. It does however, reemphasize the necessity for those involved with transplantation of corneas to continue to be diligent in the collective evaluation and reporting of late post-mortem data to better assess donor screening for the risk factors in cornea transplantation and support the current data of low transmission of disease currently associated with cornea transplantation.

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