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Research Article

HCV Antibody, Patient Therapy and Ocular Tissue Donation: Is a Review of Donor Criteria Warranted

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Abstract

Hepatitis C serology reactivity in donors whose medical history does not suggest a reason for deferral continues to be of concern in ocular tissue availability. With the current treatments for Hepatitis C reporting cure of this often-occult disease it may now be time to consider if the Hepatitis C antibody only reactive donors might be acceptable for transplantation. This study reviews cases between May 2018 and May 2021 where screening, by Food and Drug Administration Regulation CR21 1271 and Eye Bank Association of America guidelines and standards, did not identify a cause for deferment of the donation. Sixty-two reactive serology donors with 20 reactive for Hepatitis C antibody only were identified in the 3660 donors during this interval. With a need to screen and defer donors for an increase in viral and other risk criteria, the ability to remove a potential, now possibly unnecessary, deferral reason could provide valuable tissues for corneal and other tissue transplants.

Keywords: *Hepatitis C Antibody; Donor Screening; Tissue Availability*

Abbreviation

HCV: Hepatitis C Virus

Introduction

Allograft tissue rejection following tissue recovery from reactive serology remains an area of concern for all tissue banks. The concern is for the loss of a potentially vital grafts; financial expenditures, donor family distress, employee risk and stress, and overall mission compromise. This loss post recovery is frequently from a serology that is only reactive in the antibody testing and of course had a donor history that was unremarkable for any history of hepatitis or other infectious disease. Reactivity for HCV is frequent in this category of antibody positive serologies. Hepatitis C treatment has advanced with hepatologist now reporting cures in over 90% of hepatitis C patients with treatment with a variety of drugs [1-6]. These patients are now regarded as not infected and not a risk of disease transmission. Therefore, the risk to the transplantation of their tissue, especially in avascular tissue like corneas, would seem to be eliminated. This retrospective review looks at three years of serology reactive data on tissue transplant donors for the potential of more tissue availability from HCV antibody reactive serology where no other markers were reactive.

Methods

Reactive serology on tissue donors between May 2018 and May 2021, 3660 total donors, was examined for the number of reactive markers for Hepatitis B, Hepatitis C and HIV during this three-year period. There were 211 reactive donors (5.7% of recovered donors). Of this 211 the data was further analyzed for a corollary of Hepatitis C antibody. Hepatitis C donors were reviewed for the serology markers for NAT (nucleic antigen), HBc and HC antigen and antibody to insure that antibody was the only reactive marker. Data was analyzed for frequency within the total number of serology reactive donors and total donors within the same 3-year period. Data was analyzed in two ways based on difference in proportions [12].

Results

Hepatitis C antibody was the only reactive maker found in 20 of the 62 reactive serology donors (Table 1). HIV reactive serology was found in 10 donors (Table 2) in which 3 of these 10 were also reactive for Hepatitis C. Hepatitis C reactivity was present in combination with other serology markers in 21 donors (Table 3) where donor deferral would have been necessary. The Hepatitis C antibody only results represent 32% of the 62 donors. Hepatitis B in conjunction with a reactive Hep C reactive result was identified in 34% and HIV 16% with 5% also Hepatitis C Reactive. These reactive results represent unexpected findings in carefully screened donors utilizing the DRAI (Donor Risk Assessment Interview) which has deferred from donation any potential donors with a previous history of these diseases and/or high risk behaviors. There was no notable difference in age, sex, race, or cause of death between any of the serology reactive groups. There were 41 males and 21 females. Heart related incidence was the most common cause of death with no indication of Hepatitis or HIV involvement. The donors ranged in age from 42 to 73 with a mean age of 60. Of these 62 positives the following analysis was made.

DIN #	Age/Race/Gender	COD	Reactive Serologies
18-002618	68 / W / M	Cardiac	HCV Ab
18-002968	56 / W / F	Cardiac	HCV Ab
18-002971	51 / W / M	MI / CAD	HCV Ab
18-003282	52 / H / F	Other - GI Bleed	HCV Ab
19-003493	53 / W / F	Other - Pending Autopsy	HCV Ab
19-003551	55 / B / M	Cardiac	HCV Ab
19-003576	58 / W / F	Cardiac	HCV Ab
19-003682	55 / M	Seizure disorder	HCV Ab
19-003684	60 / H / M	CVA / Stroke	HCV Ab
19-003709	64 / B / F	Cardiac	HCV Ab
19-003817	70 / H / F	Cardiac	HCV Ab
19-003880	64 / W / M	CHF	HCV Ab
19-004103	42 / H / M	Blunt Force Injuries	HCV Ab
19-004151	69 / W / F	CVA / Stroke	HCV Ab
20-004845	71 / W / F	Other - Resp Failure	HCV Ab
20-005086	73 / W / M	Cardiac	HCV Ab
20-005341	64 / W / M	Cardiac	HCV Ab
20-005396	60 / W / M	Cardiac	HCV Ab
20-005598	62 / W / M	ICH	HCV Ab
20-005706	63 / W / F	Cancer - Lung	HCV Ab
20 HCV Ab reactive donors by demographics and cause of death.			

Table 1: *HCV Ab only.*

DIN #	Age/Race/Gender	COD	Reactive Serologies
19-004309	57 / B / F	Cardiac	HIV 1/2 Ab, HIV NAT
19-004698	65 / W / M	Cardiac	HBsAg, HBc Total, HIV NAT, HCV NAT, HBV NAT
20-005153	67 / B / M	Cardiac	HBc Total, HIV NAT, HCV NAT, HBV NAT
20-005573	42 / H / F	Cardiac	HBc Total, HIV NAT, HCV NAT, HBV NAT
18-003152	59 / B / F	Caner - Pancreatic	HIV 1/2 Ab
19-003979	56 / W / M	Cardiac	HIV 1/2 Ab
19-004047	66 / W / F	Cardiac	HIV 1/2 Ab
20-005610	50 / W / M	Cardiac	HIV 1/2 Ab
21-005960	61 / H / F	Cardiac	HIV 1/2 Ab
21-006023	53 / W / M	Cardiac	HIV 1/2 Ab
10 HIV Reactive Donors by demographics and cause of death			

Table 2: *HIV reactive cases.*

DIN #	Age/Race/Gender	COD	Reactive Serologies
18-002908	46 / H / M	Blunt Force Injuries	HBc Total, HBV NAT, HBsAg, HCV Ab
18-002865	66 / W / M	Cancer - Lung	HCV Ab, HBc Total
18-002908	64 / W / M	Cardiac	HCV Ab, HBc Total
18-003071	63 / B / M	Cardiac	HCV Ab, HBc Total
18-003209	59 / F	Hypertensive CVD/Obesity and depression	HCV Ab, HBc Total
19-003444	71 / B / F	Cardiac	HCV Ab, HBc Total, HCV NAT
19-003784	70 / W / F	Cardiac	HCV Ab, HBc Total
19-004123	59 / W / F	Cardiac	HCV Ab, HBc Total
19-004185	60 / B / M	Cardiac	HBsAg, HCV Ab
19-004292	61 / W / F	Electrocution/Trauma	HCV Ab, HBc Total
19-004408	68 / B / M	Cardiac	HCV Ab, HBc Total
19-004698	65 / W / M	Cardiac	HBsAg, HBc Total, HIV NAT, HCV NAT, HBV NAT
20-005153	67 / B / M	Cardiac	HBc Total, HIV NAT, HCV NAT, HBV NAT
20-005153	70 / M	Anoxic Brain Injury	HCV Ab, HBc Total
20-005349	68 / B / M	ICH/ICB	HCV Ab, HBc Total, HCV NAT
20-005573	42 / H / F	Cardiac	HBc Total, HIV NAT, HCV NAT, HBV NAT
20-005631	60 / W / M	Cancer - Lung	HCV Ab, HBc Total
21-005900	50 / W / M	Trauma 2nd to MVA	HCV Ab, HBc Total, HCV NAT
21-006174	63 / H / M	Cardiac	HCV Ab, HBc Total
21-006177	50 / W / M	Other - Cardiac arrest	HCV Ab, HBc Total
21-006237	65 / W / M	Cardiac	HCV Ab, HBc Total, HCV NAT, HBV NAT
21 Reactive donors for HCV and Hepatitis B by demographics and cause of death			

Table 3: *HCV and HBV.*

3,660 potential donors.

n = 211 rejected donors.

Group 1: Of the 211 rejected donors, 62 were serology positive and therefore unusable.

$= {}^{62}/_{211} = 0.294$ (proportion of unusable due to serology).

Group 2: Of the 211 rejected donors, it was determined that 20 that were serology positive but could be used as donors meaning that only 42 were unusable.

$= {}^{42}/_{211} = 0.199$ (proportion of unusable).

Test #1:

Hypothesis test showing that (proportions are statistically different)

Test #2:

Hypothesis test showing that (0.294 is statistically greater than 0.199)

3,660 potential donors.

n = 211 rejected donors.

Group 1: Of the 211 rejected donors, 0 were usable.

$= {}^{0}/_{211} = 0$ (proportion of usable).

Group 2: Of the 211 rejected donors, 20 that were serology positive could be used as donors.

$= {}^{20}/_{211} = 0.095$ (proportion of usable).

*Note: Some statistical software will not perform calculations if one of the proportions is 0.

Test #1:

Hypothesis test showing that (proportions are statistically different).

Two sample proportion summary hypothesis test:

p_1 : proportion of successes for population 1

p_2 : proportion of successes for population 2

$p_1 - p_2$: Difference in proportions

$H_0 : p_1 - p_2 = 0$

$H_A : p_1 - p_2 \neq 0$

Hypothesis test results:

Difference	Count1	Total1	Count2	Total2	Sample Diff.	Std. Err.	Z-Stat	P-value
$p_1 - p_2$	62	211	42	211	0.09478673	0.041955756	2.2592068	0.0239

Figure A

Test #2:

Hypothesis test showing that p^1 > p^2 (0.294 is statistically greater than 0.199)

Two sample proportion summary hypothesis test:

p_1 : proportion of successes for population 1

p_2 : proportion of successes for population 2

$p_1 - p_2$: Difference in proportions

$H_0 : p_1 - p_2 = 0$

$H_A : p_1 - p_2 > 0$

Hypothesis test results:

Difference	Count1	Total1	Count2	Total2	Sample Diff.	Std. Err.	Z-Stat	P-value
$p_1 - p_2$	62	211	42	211	0.09478673	0.041955756	2.2592068	0.0119

Figure B

Two sample proportion summary hypothesis test:

p_1: Proportion of successes for population 1.

p_2: Proportion of successes for population 2.

$p_1 - p_2$: Difference in proportions.

H_0: $p_1 - p_2 = 0$.

H_A: $p_1 - p_2$ 0.

Hypothesis test results:

Test #2:

Hypothesis test showing that (0 is statistically less than 0.095).

Two sample proportion summary hypothesis test:

p_1: proportion of successes for population 1.

p_2: proportion of successes for population 2.

$p_1 - p_2$: Difference in proportions.

H_0: $p_1 - p_2 = 0$.

H_A: $p_1 - p_2 \neq 0$.

Hypothesis test results:

Calculated using socscistatistics.com/tests/ztest/.

Discussion

It cannot be assumed the 20 hepatitis C antibody only reactive donors were treated and resolved cases. The stage of their disease response to serology testing however does indicate the possibility of the resolution of the virus. As the numbers of patients treated for Hepatitis C and reportedly, resolved increase, the potential for these individuals to become donors over time could also increase. The importance of this data is as a pilot study indicating the possibility that greater numbers of transplantable tissues could be made available. While 40 corneas for 40 patients may only influence the timing of surgical procedures or the selection of the appropriate tissue for a particular patient, if you look at making this type of donor tissue available across multiple centers, the numbers would increase exponentially. In addition, if this type of donor providing tissues were made available for bone and skin, transplantable allografts would increase in the thousands.

Published data reports the newer antivirals are, for the first time, creating a significant change in how the infection, Hepatitis C, is viewed by those involved in the care and treatment of this acute and chronic disease [7]. This data reports the cure of Hepatitis C within 12 weeks of treatment.

If only half of this 20 number were treated and resolved and became eligible donors, significantly more needed tissue allografts could be made available. This would include but not necessarily be limited to corneas, but also bone, tendons, cartilage, skin, vessels, heart values, and emerging specialty grafts. This does not even consider the number of organs currently in much greater demand than available for transplantation. The demands for DSAEK and DMEK tissues already place a strain on the availability of these specific types of tissue for corneal transplants.

Were the FDA, Food and Drug Administration, to reexamine the contraindications for donation in CFR 1271 of the Federal Registry and find that all HCV antibody only reactive donors were acceptable, the supply could be dramatically increased, potentially without an increased risk. Articles from the following publications [8-10], but not necessarily limited to those noted, support the non-infectivity of Hepatitis C treated patients with treatment of one of the following drugs: Sofosbuvir/Velpatasvir (Epciesa), Sofosbuvir/Ledipasvir (Harvoni), Glecaprevir/Pibrentasvir (Maviret), and Elbasvir/Gazoprevir (Zepatier) where patients are RNA non detectable at 6 to 12 weeks post treatment. Caution is emphasized in use of these drugs in individuals with an additional history of Hepatitis B, or HIV [11]. These individuals would not be candidates for tissue donation. No definite treatment cure for Hepatitis B is currently available. Though HIV treatment, but not cure, may now reduce viral loads to an undetectable serology level, these tissues are not indicated for transplantation based on history. Results for Hepatitis B and HIV were included only to emphasize that these donors would not provide suitable tissues for transplantation. Careful screening and detection of continuing therapy should provide the information necessary to defer these individuals from the donor pool. This does however, point to a concern for the application of the screening process since the testing for HIV might be less reliable, although this is unproven at present.

Testing for all required serology as found in CFR 1271 of the Food and Drug (FDA) regulation, American Association of Tissue Banks (AATB) and Eye Bank Association of America (EBAA) medical standards should continue to be performed on all tissue donor blood samples. Reactivity in any of these tests, with the exception of RPR where a confirmatory test is permitted, would currently cause defer-

ment of the donor/donor tissue. The only change is the possible utilization of tissue where only the Hepatitis C antibody test is reactive. In these cases, additional screening questions might be implemented to document treatment with the antiviral agents currently reported to affect cure.

Conclusion

While the number of HCV antibody only cases in this limited 3660 donor three-year history (62 potential donors with 20 Hepatitis C antibody only donors) is insufficient to base the impact on overall donor tissue availability, it does raise the question of a change in risk infectivity and points to the need for additional studies. As virial diseases appear to be on the increase worldwide adding more exclusionary criteria for allograft transplantation, the potential to eliminate one exclusionary criterion is intriguing. It suggests that a larger study might in fact determine a new standard for viewing the antibody only positive Hepatitis C donor given the current antiviral therapies and thereby make more safe allografts available for numerous surgical procedures where allograft tissue is the optimal treatment.

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