A Case Report: Organs From a Donor With Highly Virulent Zoonotic Outbreak Strain of *Streptococcus agalactiae* Serotype III, Multilocus Sequence Type 283 Infective Endocarditis Did Not Result in Transmission With Adequate Prophylactic Antibiotic Cover

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ABSTRACT

In 2015, an outbreak involving a highly virulent zoonotic outbreak strain of *Streptococcus agalactiae* serotype III, multilocus sequence type 283 occurred in Singapore with increased neurologic complications, septic arthritis, and spinal infections in healthier patients. We report a case of a successful dual kidney transplant from a deceased donor with infective endocarditis and disseminated infection with the same strain of *S agalactiae* and we review the current literature.

ORGAN transplantation gives patients a new lease on life; however, there is an increasing scarcity of suitable organ donors around the world. One of the concerns in the selection of donors is the presence of donor-transmitted infections. The selection criteria, with regards to infection, of these donors have been less strict in the recent years due to increasing evidence for low rates of donor-transmitted infections from what was previously deemed an absolute contraindication due to transplant complications [1,2]. Some of these infections may be detrimental to the recipient, hence a risk-benefit ratio will need to be considered in every recipient and donor evaluated for transplant. Reports of successful solid organ transplantation from donors with infective endocarditis (IE) still remain exceedingly uncommon.

In 2015, a nationwide outbreak of invasive *Streptococcus agalactiae* infections caused by *S agalactiae* serotype III, multilocus sequence type (MLST) 283 was reported in Singapore [3–5]. This was later shown to be related to the consumption of raw freshwater fish, namely Asian bighead carp and snakehead fish in a Chinese-style raw fish dish called "yusheng"; the outbreak curbed after local health authorities advised the cessation of sale of raw fish dishes involving the implicated fish [3–5]. *S agalactiae* serotype III, MLST 283 appeared to infect healthier patients [5,6]. Clinical manifestations of this strain of *S agalactiae* were unusual because it is associated with a severe clinical course with septicemia and a higher incidence of neurologic complications, septic arthritis, and spinal infections [5–7].

We report one such patient who received dual kidney transplantation from a donor with a virulent *S agalactiae* IE.

CASE REPORT

The donor was a 59-year-old man with a history of diabetes who was admitted for fever and right knee pain with swelling. He was found to have disseminated *S agalactiae* infection causing IE, endophthalmitis, septic arthritis of the right knee, and lumbar spondylodiscitis.

His blood cultures and knee fluid on admission grew *S agalactiae* with a penicillin mean inhibitory concentration of <0.12 mg/L. This was typed and found to be serotype III MLST 283 in keeping with the outbreak strain [3–7]. He did not report raw fish consumption but worked as a dishwasher in a kitchen. A transthoracic echocardiogram showed an aortic valve vegetation measuring 0.8×0.3 cm in keeping with the diagnosis of IE. He was treated with 1 day of intravenous co-amoxiclav, 4 days of piperacillin/tazobactam, followed by ceftriaxone, until he died 7 days later. Blood cultures on day 4 of admission were negative. He underwent a right knee arthroscopic washout on day 8 of admission. He deteriorated acutely on day 9 of admission with a drop in conscious level and was found to have a large intracranial bleed with midline shift. He was pronounced brain-dead 3 days later, on day 12 of admission.

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0041-1345/17
http://dx.doi.org/10.1016/j.transproceed.2017.06.004

Urine microscopy and urine cultures on admission and on date of death did not demonstrate infection. At the time of organ recovery, there was no macroscopic evidence of pyelonephritis. Preimplantation biopsies were also performed to determine organ allocation, and these also did not show any histologic evidence of infection. Because the Remuzzi histologic score was 4/12, 2 kidneys were implanted into our recipient. Endotracheal tube cultures taken on day of donor death revealed a pansensitive *Pseudomonas aeruginosa*, and corresponding blood cultures were negative.

Our recipient was a 65-year-old woman with 13 years' duration of end-stage renal failure attributed to drug-induced interstitial nephritis.

She underwent a dual deceased donor kidney transplantation complicated in the immediate postoperative period by perianastomotic bleeding secondary to an arterial spurter in the perinephric fat at the upper pole of the superiorly placed graft. This necessitated exploration of the renal allograft, hemostasis and evacuation of hematoma on same day of transplantation, and multiple transfusions of blood products.

She received intravenous basiliximab 20 mg preoperatively and on postoperative day 4 and intravenous methylprednisolone 500 mg preoperatively and on postoperative day 1, followed by oral prednisolone 20 mg that was later slowly tapered. She also received mycophenolate mofetil 750 mg twice a day and tacrolimus 3 g twice a day titrated to a target level of 8 to 10. She also sustained ischemic hepatitis and a type 2 myocardial infarction. There was no delayed graft function noted.

On postoperative day 2, a chest radiogram showed right mid to lower zone infiltrates suggestive of pneumonia. Investigations showed raised C-reactive protein of 50.1 mg/L (normal: 0.2–9.1 mg/L) and a raised white cell count at 13.38×10^9/L (normal: $4.0–10.0 \times 10^9$/L). She was treated with intravenous ceftriaxone and later intravenous meropenem followed by intravenous piperacillin/tazobactam for 7 days. Antibiotics were then de-escalated to intravenous ceftriaxone 2 g daily for a total duration of 2 weeks. On day 10 post-transplant, she developed right lower limb swelling. Imaging of her abdomen showed an acute hematoma causing extrinsic compression on the right external iliac vessels near the vascular anastomosis of the superiorly placed graft. This was deemed secondary to previous bleeding episode because she remained well with a stable hemoglobin level. She was discharged stable 14 days post-transplant. On discharge her C-reactive protein level had trended down and was normal at 7.1 mg/L (normal: 0.2–9.1 mg/L). Her estimated glomerular filtration rate (Modification of Diet in Renal Disease) was 52 mL/min/1.73^2. Urine cultures immediately postoperatively and 1 week off antibiotics were negative.

Four months post-transplant, she presented with fever and chills and was found to have a urinary tract infection complicated by a pan-sensitive *Escherichia coli* bacteremia. Urinalysis showed white cells in keeping with infection, although corresponding urine cultures were negative. There was no *S agalactiae* isolated in her multiple blood and urine cultures during the admission. Repeat imaging of her abdomen revealed no collection within her abdomen and near complete resolution of her previously noted hematoma. She was treated with 1 week of ceftriaxone followed by oral ciprofloxacin for another 1 week and has recovered well.

She has remained well without recurrence of *S agalactiae* infection 6 months after the transplantation. Post-transplantation routine surveillance urine cultures have been negative for *S agalactiae*, and her C-reactive protein and white blood count are normal with a stable renal function and good graft function.

DISCUSSION

We describe a successful renal transplantation of a patient with IE. We were concerned initially due to the virulent nature of the *S agalactiae* in this recent outbreak. *S agalactiae* has been increasingly shown to affect the elderly, immunocompromised, diabetics, and cirrhotic patients [8]. It has also been reported to cause post-transplant complications such as renal abscesses [9].

Previous efforts made to characterize *S agalactiae* strains in 2006 found that *S agalactiae* serogroup type III MLST 283 was significantly associated with isolation from "invasive" sites such as blood, spinal fluid, peritoneal fluid, and joint aspirate [10], suggesting that this particular strain of *S agalactiae* is of increased virulence. The experience from the 2015 outbreak in Singapore echoes these findings, showing an association formation of invasive infection such as meningitis, joint infections, and spinal infections [5–7].

Successful transplant involving donors with endocarditis has been reported, but numbers remain few thus far [11–13]. Historically case reports of donor infection with *Staphylococcus aureus* and *Pseudomonas* have had reported complications of mycotic aneurysm formation and poor graft function post-transplant [2]. However, there are increasing reports that refute the old dogma. A previous review of heart and liver transplants showed that use of organs from donors with unrecognized bacteremia did not show a higher incidence of poor graft and survival [14]. A further retrospective analysis found no significant difference in graft complications and 12-month survival from infected versus noninfected donors [15].

To date, only 9 donors with IE involving 17 solid organ transplants (summarized in Table 1) have been described in the literature with a range of various organisms implicated [11–13]. Miceli et al described contrasting experiences with regards to liver transplantation from a donor with IE, probably secondary to a difference in virulence of organisms implicated in the endocarditis; one recipient of liver transplant from a donor with enterococcal IE complicated by donor-related infected intra-abdominal hematoma had a less complicated clinical course than the recipient who received an organ from a donor with methicillin-resistant *S aureus* [11]. A case series found 4 organ donors with left-sided IE over a 4-year period. The organisms implicated included coagulase-negative Staphylococcus (*Staphylococcus hominis* and *Staphylococcus epidermidis*) and *Streptococcus viridans*. They reported that 6 of 7 recipients were alive with functioning grafts, whereas only one transplantectomy needed to be performed due to a cause unrelated to infection [13].

To our knowledge, this remains the first reported renal transplantation using organs from a deceased donor with a highly virulent zoonotic *S agalactiae* MLST 283 infection. We still remain concerned with regards to transmission of infection to the donor, especially in cases where the organisms are of increased virulence. Although IE is not an absolute contraindication to organ transplantation, caution should be undertaken along with steps with regards to administration of appropriate antibiotics to both donor and

Table 1. Summary of Clinical Details and Outcomes of Patients Who Received Organs From Donors With Infective Endocarditis

Recipient Age/Sex/No. of Transplant/Organ Received	Organism	Donor Valve(s) Involved/ Prior Pathology	Reason for Transplant	Antibiotic/Antibiotic Days Before Harvest	Antibiotic Days Post-Transplant	Blood Cultures Negative Prior to Transplantation	Graft Function/ Follow-up	Transmission
50/M/1st/right kidney [13]	*Staphylococcus epidermidis*	Prosthetic mitral valve/rheumatic mitroaortic valvulopathy	Nonaffiliated nephropathy	Cloxacillin/7	9	NS	Preserved/2 y	No
22/F/2nd/left kidney [13]	Coagulase-negative staphylococci	Native aortic valve/stenosis plus insufficiency	IgA nephropathy	Cloxacillin/2	0	NS	Loss/2 d	No
39/M/1st/liver [13]	*Streptococcus viridans*	Native aortic valve/stenosis plus insufficiency	Fulminant hepatitis	Cefepime/1; teicoplanin/1	5	NS	Preserved/21 mo	No
63/M/1st/left kidney [13]	*Streptococcus viridans*	Native aortic valve/stenosis plus insufficiency	Chronic pyelonephritis	Amoxicillin-clavulanate/7	5	NS	Preserved/21 mo	No
69/M/1st/right kidney [13]	*Streptococcus viridans*	Native aortic valve/stenosis plus insufficiency	Nonaffiliated nephropathy	Amoxicillin-clavulanate/7	5	NS	Preserved/21 mo	No
29/M/1st/liver [13]	*Staphylococcus hominis*	Native mitral valve/prolapse	Familial amyloid polyneuropathy	Aztreonam/4; vancomycin/2	7	NS	Preserved/13 mo	No
46/M/3rd/left kidney [13]	*Staphylococcus hominis*	Native mitral valve/prolapse	IgA nephropathy	Amoxicillin-clavulanate/3; aztreonam/3	7	NS	Preserved/13 mo	No
51/M/1st/liver [12]	*Enterococcus faecalis*	Native mitral valve/None	HCV cirrhosis	Aztreonam/10; vancomycin/10	3	NS	Preserved/7 y	No
24/F/1st/left kidney [12]	*Enterococcus faecalis*	Native mitral valve/none	Chronic pyelonephritis	Meropenem/10	3	NS	Preserved/7 y	No
31/M/1st/right kidney [12]	*Enterococcus faecalis*	Native mitral valve/none	Chronic pyelonephritis	Meropenem/10	3	NS	Preserved/7 y	No
59/M/1st/liver [11]	*Enterococcus faecalis*	Native mitral valve/none	Hepatitis C cirrhosis	Vancomycin, ampicillin/17	30	Yes	Preserved/9 mo	Yes
41/M/1st/liver [11]	MRSA	Native mitral valve/none	Primary sclerosing cholangitis	NS	21	Yes	Preserved/ 6–7 mo	Yes
NS/NS/NS/lung [16]	MRSA	Native mitral valve/none	NS	Vancomycin/NS	63	Yes	Preserved/1 y	Yes
NS/NS/NS/liver [16]	MRSA	Native mitral valve/none	Primary sclerosing cholangitis	Vancomycin/NS	14	Yes	Preserved/1 y	Yes
NS/NS/NS/left kidney, pancreas [16]	MRSA	Native mitral valve/none	Type 1 DM	Vancomycin/NS	5 doses	Yes	Preserved/NS	No
NS/NS/NS/right kidney [16]	MRSA	Native mitral valve/none	Type 2 DM nephropathy	Vancomycin/NS	5 doses	Yes	Preserved/NS	No
60/F/1st/dual kidney	*Streptococcus agalactiae*	Native aortic valve/none	Nonaffiliated nephropathy	Amoxicillin-clavulanate/1; piperacillin, tazobactam/4; ceftriaxone/7	14	Yes	Preserved/3 mo	No

Abbreviations: DM, diabetes mellitus; HCV, hepatitis C virus; MRSA, methicillin-resistant *Staphylococcus aureus*; NS, not significant.

recipient, ensuring that the kidneys are not involved in the septic episode, as well as close monitoring of the recipient. This supports the current guidelines of adopting a less restrictive donor screening criteria and may help with increasing the current donor pool.

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