

Atrium Health

Introduction

Although single antigen and screening beads are highly sensitive and important tools for evaluating pre-transplant compatibility, a patients clinical status or associated treatment often interferes with interpretation. It is important to take such factors into account when making a comprehensive assessment for transplantation. In this case study, we evaluate a patient with protein-losing enteropathy (PLE) in the context of failing Fontan physiology after pediatric palliative treatment for hypoplastic left heart syndrome (HLHS) and the resulting impact to detection of anti-HLA antibody.

Background

Hypoplastic left heart syndrome is a congenital defect in which the left ventricle, mitral, and aortic valves are underdeveloped or completely closed (fig. 1). Treatment for this condition is palliative and requires a series of three surgeries known as the Norwood, Glenn, and Fontan procedures¹ (fig. 2). Long term, it is possible for cardiac output to decrease to the point of the Fontan procedure being deemed a failure. At this point, the patient may require a heart transplant.

In the Fontan procedure, venous blood is diverted directly to the pulmonary artery, thereby increasing systemic venous pressures². The increased pressure can cause protein to be lost via the intestines (lymphangiectasia) as a means to lower the pressure. This uncompensated loss of plasma protein is a syndrome known as protein-lost enteropathy (PLE) and is acquired in up to 18% of patients undergoing the Fontan procedure³. This syndrome presents as nonselective hypoproteinemia with reduced albumin and immunoglobulin levels. PLE can be very mild to severe in patients with elevated systemic venous pressures such that antibody to HLA may not be detectable.

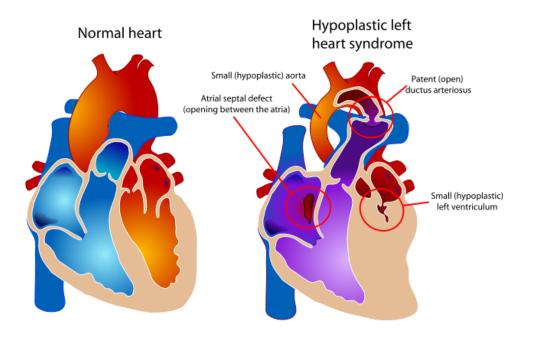


Figure 3. Due to PLE, patients serum IgG levels remained low leading up to transplant. After improved condition after transplant, IgG levels increased. This correlates with sharp increase in detectable HLA antibody post-transplant (fig. 4).

A donor heart with HLA typing of A23,33 B53,65 Cw04,08 DR1 DQ5 DQA1*01 DPA1*01 DPB1*04:02, 104:01 was offered for this patient. A virtual crossmatch determined DPB1*104:01 as a potential weak DSA based on surrogate bead DPB1*03:01 (fig. 4a). The antibody was weak enough to be considered within the risk parameters of the transplant program and the offer was accepted.



Patient is a 15-year-old male born with HLHS who was palliated with the Fontan procedure. The patient experienced chronic systolic and diastolic heart failure, leading to the need for a heart transplant. As a complication of heart failure and the Fontan procedure, the patient also had longstanding PLE.

Case Study: Protein losing enteropathy may pose a hidden danger to prospective heart transplant patients

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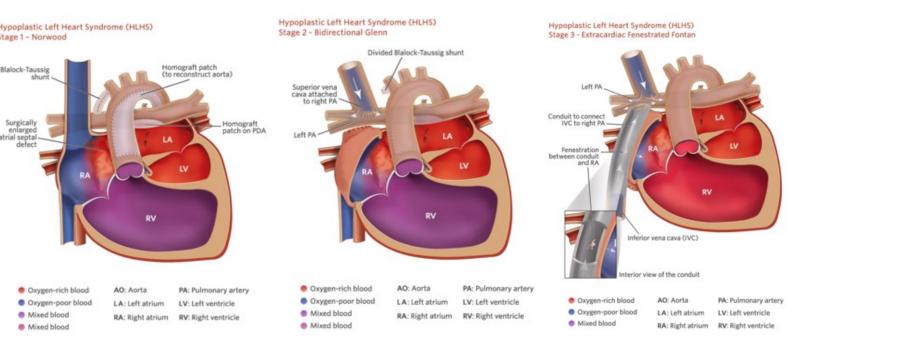
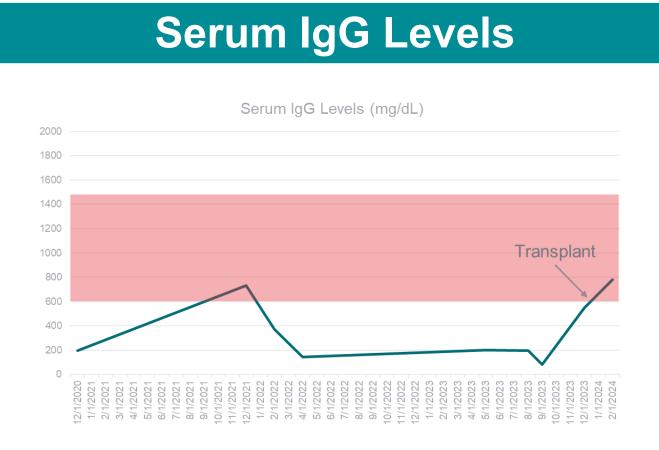


Figure 2. Norwood, Glenn, and Fontan procedures⁵

Patient Profile



Donor Offer

Upon admission, the patient was treated closely for heart failure and prescribed Milrinone. Increased serum protein was seen as a result. An admission sample was crossmatched retrospectively to find a strongly positive reaction. The sample was then reflexed to single antigen bead testing, which showed strong DEAV DSA correlating with decreased PLE. One month post op, biopsy showed moderate C4d staining and anti-HLA antibody saw a significant increase with a pattern matching previous testing.

This study illustrates the potential risk transplant patients with PLE face due to loss of serum proteins, including IgG. The significant increase in reactivity matching previous testing in this case suggests these antibodies were likely present pretransplant but were not detectable in the serum.

Centers should be aware of the possibility of unforeseen rejection when serum antibody levels stabilize after heart transplantation.

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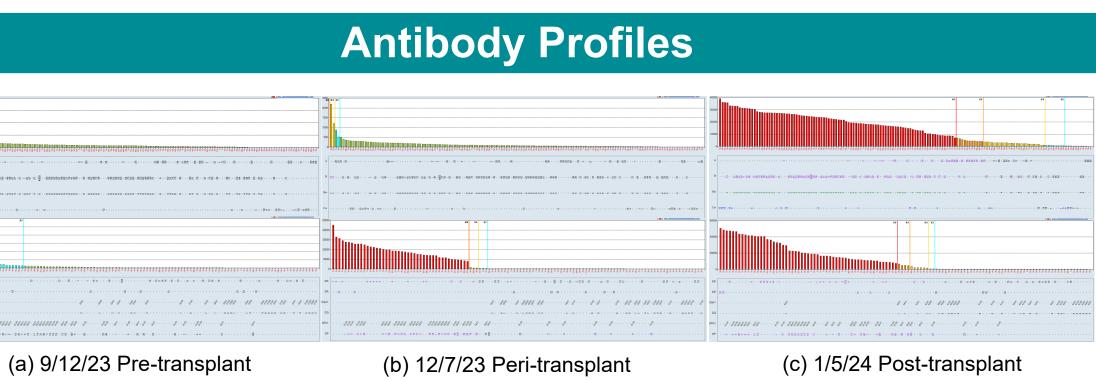


Figure 4 a-c. Single antigen profiles pre, peri, and post-transplant.

Postoperative Course

Conclusions

References

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2. Ozen, A., & Lenardo, M. J. (2023). Protein-Losing Enteropathy. The New England Journal of Medicine, 389(8). https://doi.org/10.1056/NEJMra2301594

3. Mertens, L., Hagler, D. J., Sauer, U., Somerville, J., & Gewillig, M. (1998). Protein-losing enteropathy after the Fontan operation: an international multicenter study. PLE study group. The Journal of thoracic and cardiovascular surgery, 115(5),

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4. Diagram of Healthy Heart and One with Hypoplastic Left Heart Syndrome. Photo placed into public domain by Mariana

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5. Staged reconstruction heart surgery. Children's Hospital of Philadelphia.

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