From ascites to rejection: further recognizing antibody mediated rejection in pediatric living donor liver transplantation through case report

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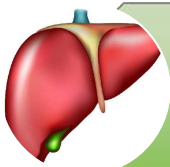
Declaration

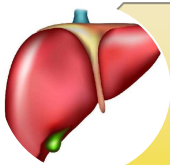
- ***Conflicts of interest:*** The authors have declared no conflicts of interest to this work.

- ***Funding：*** This study is granted by Nature Science Foundation of Tianjin (No. 21JCYBJC01600).

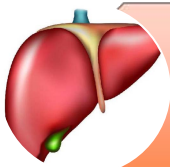
Introduction



Antibody mediated rejection (AMR) is fewer than T cell mediated rejection in pediatric liver transplantation



However, it is difficult to make the precise and timely diagnose of AMR, until combination of clinical manifestations, histopathology, C4d staining and donor specific antibody (DSA)



Our aim is to summarize the diagnosis and prognosis of AMR in pediatric recipients after living donor liver transplantation (LDLT), especially one unique type of AMR manifested by refractory ascites

Patients and Methods

Total 5 pediatric recipients whose primary disease was biliary atresia were performed LDLT with grafts of left-lateral segment in our study. Piggy-back technique and Roux-en-Y hepaticojejunostomy for hepatic vein and biliary reconstruction were used in surgeries, respectively. Repeated liver biopsies were performed and DSA was detected by Luminex.

Table 1. Characteristics of recipients

Cases	*Gender*	*Age at LDLT (Months)*	*Blood group (D/R)*	*Intra-MP in operation*	*Bax in and post-LT*	*IM post-LT*
1	Male	7	O+/O+	10mg/Kg	10 mg × 2	Tac+MP
2	Male	6	O+/O+	10mg/Kg	None	Tac+MP
3	Female	12	A+/O+	10mg/Kg	10 mg × 2	Tac+MP
4	Female	9	O+/A+	10mg/Kg	10 mg × 2	Tac+MP
5	Male	10	O+/O+	10mg/Kg	10 mg × 2	Tac+MP

Results

■ In case 1 and case 2, the abnormal syndromes were manifested as a large amount of ascites in abdomen or hydrothorax, with normal graft's function except hypoproteinemia

■ In case 3 to case 5, the abnormal syndromes were manifested as abnormal graft function

■ The ultrasound, enhanced computed tomography scan and hepatic vein angiography ruled out vascular complications in all of cases

■ DSA showed positive in all of recipients, specifically against HLA-DQ and DR

■ After AMR was confirmed, the patients were received additional mycophenolate mofetil (MMF), rituximab, bortezomib, plasmapheresis and intravenous immunoglobulin (IVIG)

■ The prognosis was not optimistic, in which three were performed by re-transplantation and one was received conservative therapy without improvement

■Only case 3 recovered well to normal graft function without re-transplantation

Results: the process and prognosis of AMR

Cases	*Interval from LTx to AMR (Months)*	*Trough concentration of Tac （ng/ml）*	*Clinical manifestations*	*Treatments*	*Prognosis*	*Follow-up (Months)*
1	50	6.1	Hypoproteinemia, ascites and hydrothorax	Tac + MMF (supplemental) Rituximab × 2	Conservative therapy and re-transplantation if necessary	12
2	38	2.1	Hypoproteinemia, ascites	Tac + MMF (supplemental) Rituximab × 1 IVIG × 3	Re-transplantation	64
3	1	3.3	Abnorminal graft function	Tac + MMF (supplemental) Plasmapheresis × 2 Rituximab × 1 IVIG × 7	Normal graft function, Pulmonary infection	86
4	2	3.3	Abnorminal graft function	Tac + MMF (supplemental) Plasmapheresis × 1 Bortezomib × 5 IVIG × 17	Re-transplantation	87
5	1	10.0	Abnorminal graft function	Tac + MMF (supplemental) Plasmapheresis × 3 Rituximab × 1 IVIG × 14	Re-transplantation	80

Results: . DSA and graft pathology

Cases	*Types of DSA*	*Locus of DSA*	*MFI*	*C4d*	*Pathological manifestations*
1	Class I negative Class II positive	DQ, DR	14629 -20167	(-)	Inflammatory cells infiltrated in the periportal area. The epithelial cells of biliary duct in the interlobular are focally degenerated. Perivenular inflammatory cells are found in Zone 3.
2	Class I weakly positive Class II strongly positive	A31 DQ, DR	3852 > 18000	(+)	The periportal area is enlarged with fibrous hyperplasia. The epithelial cells of biliary duct in the interlobular are degenerated. The interlobular veins are mildly dilated.
3	Class II strongly positive	DQ	13707	(+)	The epithelial cells of biliary duct in the interlobular are degenerated. The mild pericentral phlebitis appeared.
4	Class II strongly positive	DQ, DR	13783 3793	(+)	The epithelial cells of biliary duct in the interlobular are degenerated. The interlobular veins are mildly dilated.
5	Class II medium positive	DQ	18640	(-)	The epithelial cells of biliary duct in the interlobular are degenerated. The interlobular veins are mildly dilated. The mild pericentral phlebitis appeared.

Discussion and Conclusions

AMR post-LT could present with hepatic venous outflow obstruction (HVOO) or sinusoidal obstruction syndrome (SOS), besides graft dysfunction

When acute AMR is diagnosed, most patients have already failed steroid recycle and T cell-depleting-antibody therapy for steroid-resistant rejection and receive B-cell or plasma cell depletion, with or without plasmapheresis and/or IVIG

Re-transplantation is one of the valid treatment strategies, in case of patient's condition can't be maintained by conservative therapies.

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