Liver transplantation in glycogen storage disease type I

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Abstract

Glycogen storage disease type I (GSDI), an inborn error of carbohydrate metabolism, is caused by defects in the glucose-6-transporter/glucose-6-phosphatase complex, which is essential in glucose homeostasis. Two types exist, GSDIa and GSDIb, each caused by different defects in the complex. GSDIa is characterized by fasting intolerance and subsequent metabolic derangements. In addition to these clinical manifestations, patients with GSDIb suffer from neutropenia with neutrophil dysfunction and inflammatory bowel disease.

With the feasibility of novel cell-based therapies, including hepatocyte transplantations and liver stem cell transplantations, it is essential to consider long term outcomes of liver replacement therapy. We reviewed all GSDI patients with liver transplantation identified in literature and through personal communication with treating physicians.

Our review shows that all 80 GSDI patients showed improved metabolic control and normal fasting tolerance after liver transplantation. Although some complications might be caused by disease progression, most complications seemed related to the liver transplantation procedure and subsequent immune suppression. These results highlight the potential of other therapeutic strategies, like cell-based therapies for liver replacement, which are expected to normalize liver function with a lower risk of complications of the procedure and immune suppression.

Introduction

Glycogen storage disease type I (GSDI) is an autosomal recessive inborn error of carbohydrate metabolism caused by defects in the glucose-6-phosphate transporter (G6PT)/glucose-6-phosphatase (G6Pase) complex [1,2]. G6PT/G6Pase complex plays a crucial role in interprandial glucose homeostasis and consists of a catalytic subunit, glucose-6-phosphatase-α (G6Pase-α) encoded by the G6PC gene and a glucose-6-phosphatase transporter (G6Pase), encoded by the SLC37A4 gene. Deficient activity of G6Pase-α causes GSDIa [3] and deficient activity of G6PT causes GSDIb [4]. GSDI is a relatively rare disorder with an incidence of 1:100,000, represented in 80% of the patients by GSDIa and in 20% by GSDIb [5].

G6Pase catalyzes the final step in glycogenolysis and in gluconeogenesis in the lumen of the endoplasmic reticulum in primarily liver, but also kidney and intestine, by hydrolyzation of glucose-6-phosphate (G6P) to glucose and inorganic phosphate. Because G6Pase affects both glycogenolysis and gluconeogenesis, inactivating mutations in the G6PC or the SLC37A4 gene result in severely reduced fasting tolerance. Clinical complications in patients include hepatomegaly, nephromegaly, hypoglycemia, hyperlipidemia, hyperuricemia, lactic acidemia, and growth retardation [5]. In addition to the clinical manifestations in GSDIa, patients with GSDIb generally also suffer from neutropenia, impaired neutrophil function and inflammatory bowel disease.

Prevention of hypoglycemia is crucial in the treatment of GSDI [5]. This is achieved by frequent feedings during day and night or nocturnal gastric drip feeding. Any feeding problem can result in a hypoglycemic event, with risk of cognitive impairment, seizures and finally death. This represents a constant threat for patients and their parents, severely affecting quality of life.

Despite progress in the treatment of GSDI, metabolic control remains challenging and hepatic, renal and/or immunologic complications may arise. Because of the prominent hepatic manifestations in GSDI, orthotopic liver transplantations have been performed [5]. Short-term outcome of liver transplantation for GSDI is encouraging, but very few papers report long-term follow-up. With the advent of less invasive cell-based therapies, including hepatocyte transplantations and liver stem cell transplantations,
which might become a therapeutic option for all patients with GSDI, it is eminent to know the long-term outcomes of liver specific therapies. We therefore reviewed short-term and long-term outcomes of liver transplantsations in GSDIa and GSDIb patients.

Methodology

English-language literature was systematically reviewed through searches in PubMed and in the references of relevant publications to find all GSDIa and GSDIb liver transplantsations published in literature. Through personal communication with treating physicians, we completed information and identified additional cases.

Results

We identified 58 patients with GSDIa who underwent a liver transplantation between 1982 and 2012 (Table 1, Additional file 1: Table S1); 3 of these patients received a second liver transplantation. The average age at transplantation was 20 years (range: 4.3-50 years). A living-related transplantation was performed in 16 cases. 6 Patients underwent a combined liver-kidney transplantation (Table 2). The immunosuppressive regime consisted of steroids, combined with cyclosporine in 12 patients, with cyclosporine and azathioprine in 17 patients and with tacrolimus in 9 patients. The specific immunosuppressant medication was not reported in 22 cases (Table 1).

The indication for liver transplantation varied and included hepatic adenomas/liver abnormalities/focal nodular hyperplasia (29 patients), poor metabolic control (27 patients), growth retardation (13 patients, some with delayed puberty and sexual maturation), renal failure (5 patients, 3 of whom received a combined liver-kidney transplantation), bleeding complications leading to anemia (1 patient) and acute pancreatitis due to severe hypertriglyceridemia (1 patient).

4 Patients with GSDIa died; 1 due to rejection related liver failure (15 years after 1st liver transplantation, 1 year after 2nd liver transplantation with combined kidney transplantation), 1 committed suicide 3 years post-transplantation, 1 because of metastatic hepatocellular carcinoma 4 months after transplantation, and 1 because of pancreatitis and sepsis 2 months post-transplantation. All other patients were alive at time of follow-up (range several months to 11.3 years post-transplantation). In all cases, liver function was good and metabolic control normalized, without a specific dietary regime. In 13 cases, catch-up growth was mentioned (Table 3). The patients with catch-up growth reported were all children or teenagers and for 2 of these, sexual maturation was also reported. In addition, one patient of 27 years old showed an increase of 5.4 cm in height 2 years after transplantation.

The complication reported most frequently was acute or chronic renal failure. Acute renal failure occurred in 8 patients, including 1 patient with pre-transplantation renal failure. One of these 8 patients required temporary dialysis. Chronic renal failure was seen in 6 patients after transplantation and 2 of these patients required dialysis. In addition, 1 case of gouty arthritis was reported 4 years post-transplantation. It is unclear whether this was due to renal failure. None of the patients who had received a combined liver-kidney transplantation developed renal failure.

Transplantation associated complications were seen in 18/58 patients and included hepatic artery thrombosis (2 patients), late portal vein thrombosis (2 patients), hepatic vein obstruction (2 patients), prolonged drainage (2 patients), acute (steroid responsive) rejection (5 patients), chronic rejection (3 patients) and a never functioning liver transplant (2 patients). Complications that might have been caused by immune suppression included hypertension (4 patients), starting one month after transplantation and reversible insulin-dependent diabetes (3 patients), starting within the first week after transplantation (Table 4). In addition, various infections were reported (5 with cytomegalovirus 1 month after transplantation and 1 patient with hepatitis 4 years after transplantation).

Liver transplantation was performed in 22 patients with GSDIb between 1991 and 2012, at an average age of 10 years (range 1–44 years) (Table 1, Additional file 1: Table S2). One patient had a kidney transplantation 2 years prior to the liver transplantation, with good function of both grafts reported 8 months after liver transplantation (Table 2). Indications for liver transplantation in GSDIb patients included poor metabolic control (21 patients) and/or recurrent infections (10 patients), growth retardation (3 patients), and oral and anal ulcer (1 patient). Immune suppression after transplantation involved cyclosporine in 1 patient and tacrolimus in 16 patients. The immune suppressive medication was not reported in the other 6 patients.

At follow-up, 1 patient had died 1.4 months after transplantation, due to systemic infections. In all patients, metabolic abnormalities were corrected by transplantation. Catch-up growth was reported in 2 cases (Table 3). In 14 patients, neutropenia improved, while in 7 patients neutropenia persisted. One report mentioned prolonged bleeding time and bruises after several years. 7 Patients had transplantation associated complications, including anemia in the first days after the transplantation (1 patient) and various infectious diseases shortly after transplantation (6 patients). Complications potentially associated with immune suppressive therapy included 1 patient with hepatitis B, seven months after transplantation, and 1 patient with cytomegalovirus infection several years after transplantation (Table 4). 1 patient developed tacrolimus encephalopathy.
## Table 1 Indication and follow-up of GSDIa and GSDIb liver transplantation

| Indications | GSDIa (n = 58) | GSDIb (n = 22) |
|-------------|---------------|---------------|
| Year of transplantation | 1982 – 2012 | 1991 – 2012 |
| Indications | | |
| Hepatic adenomas or liver abnormalities (mostly focal nodular hyperplasia) | 29 [6-22] | |
| Poor metabolic control | 27 [6,8,10,14-16,19,21,23-27] | 21 [13,28-34] |
| Growth retardation | 13 [10,14-16,23,24,27] | 3 [32,33,35] |
| Recurrent infections | | 10 [28,33,34] |
| Renal failure | 5 [36] | |
| - Of which also kidney transplant | 3 [17,26,37] | |
| Bleeding complications (anemia) | 1 [27] | |
| Pancreatitis | 1 [24] | |
| Anal and oral ulcers | | 1 [30] |
| Immunosuppressive regime | | |
| Cyclosporine | 12 [6,7,9,10,12,14,15,17,21,26] | 1 [28] |
| Cyclosporine + azathioprine | 17 [16,23,25,38,39] | - |
| Tacrolimus | 9 [16,18,21,36] | 16 [30,31,33-35] |
| Not reported | 22 | 6 |
| Outcome and complications GSDIa | | |
| Short-term (≤1 year) | Long-term (>1 year) | |
| Normalization liver function | 58 (all) | - |
| Catch-up growth | - | 13 [10,13,14,23,25,39] |
| Sexual maturation | - | 2 [25] |
| Re-OLT | 2 [16,23] | 1 [20] |
| Death | 1 (pancreatitis and sepsis) [25] | 3 (rejection related liver failure, suicide, metastatic hepatocellular carcinoma) [19], PC |
| Renal failure | 6 [21] | 4 [20] |
| - Of which already pre-transplant | 1 [39] | |
| - Requiring dialysis | 1 [12] (temporary) | 2 [27], PC (permanent) |
| - Gouty arthritis (due to renal failure?) | - | 1 [14] |
| Metastatic hepatocellular carcinoma | 1, PC | |
| Transplantation associated | | |
| - Hepatic artery thrombosis | 2 [16,23] | |
| - Portal vein thrombosis | - | 2 [6,16] |
| - Hepatic vein obstruction | 2 [25] | |
| - Prolonged drainage | 2 [25,39] | - |
| - Rejection | 5 [14,20,21,38,39] | 3 [6,9] |
| - Never functioning liver after transplantation | 2 [23,24] | |
| Therapy (immune suppression) associated | | |
| - Hypertension | 4 [25,39] | - |
| - Insulin-dependent diabetes (reversible) | 3 [8,9,21] | - |
| - Infections (CMV, hepatitis) | 7 [21,25,39] | 1 [14] |
| Outcome and complications GSDIb | | |
| Short-term (≤1 year) | Long-term (>1 year) | |
| Normalization liver function | 23 (all) | |
| Catch-up growth | - | 2 [32] |
| Death | 1 (systemic candidiasis) [40] | |
soon after transplantation, which was resolved upon withdrawal of tacrolimus. None of the reports described renal complications.

**Discussion**

In this review, we show that liver transplantations sustainably corrected fasting tolerance and the induced metabolic abnormalities associated with GSDIa and GSDIb, thereby immensely improving quality of life for patients. In addition, catch-up growth was seen in most patients with growth retardation (13/13 (100%) and 2/3 (67%) in GSDIa and GSDIb patients, respectively).

The extra-hepatic symptoms of the disease might however persist after liver transplantation. In GSDIa patients, renal failure was the most common complication (14/58 (24%) of patients) and 3/14 (21%) required dialysis. The natural course of renal function in GSDI patients shows a biphasic pattern [41]. We identified only 1 patient with both pre- and post-transplantation renal failure; renal function was restored in the other 4 patients with pre-transplantation renal dysfunction. Notably, 3 of these 4 patients had received a combined liver-kidney transplantation. In the other patients, renal dysfunction developed after transplantation. It is yet unclear whether post-transplantation renal failure in GSDI represents progression of the disease, a secondary reaction to poor metabolic control, toxicity from immune suppressive medication after liver transplantation, or a combination. Strikingly, none of the GSDIb patients developed renal failure. We are unaware of a pathophysiological mechanism to explain why GSDIa patients would be more prone to develop renal failure than GSDIb patients, nor has this been observed in our experience with GSDI patients. Potentially, this is a coincidental finding due to the relatively small number of patients evaluated.

In GSDIb patients, persistent neutropenia was the most important complication (7/22 (32%) of patients). Neutropenia in GSDIb has recently been attributed to a second G6P hydrolase, called G6Pase-β [42]. The G6PT/G6Pase-β complex maintains glucose homeostasis and function in neutrophils. Deficiency of the G6PT/G6Pase-β complex in neutrophils leads to impaired endogenous glucose production and enhanced endoplasmic reticulum stress, oxidative stress and apoptosis, leading to neutropenia [42]. Migration of neutrophils from the blood to inflamed tissues (e.g. intestines, liver adenoma) might further contribute to the neutropenia [43]. It remains unclear why neutropenia improves after liver replacement in some patients and persists in others. It is possible that improved metabolic control and general well-being result in decreased inflammation, leading to higher blood neutrophil concentrations. Second, immediate increase in neutrophil count after liver transplantation might be related to the neutrophilic effect of steroid therapy. However, recurrence of neutropenia after steroid tapering has not been reported. Finally, host/donor bone marrow chimerism has been observed after

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**Table 1 Indication and follow-up of GSDIa and GSDIb liver transplantation (Continued)**

| Neutropenia                          | -                     | 14 [31,34,35] |
|--------------------------------------|-----------------------|---------------|
| -Improved                            | 6 [34]                |               |
| -Persisted                           | 1 [33]                | 7 [13,29,30,32,33] |
| Thrombocytopenia                     | 1 [28]                |               |
| Transplantation associated           |                       |               |
| -Infection                           | -                     |               |
| -Anemia                              | -                     |               |
| -Rejection                           | -                     | 1 [13]        |
| Therapy (immune suppression) associated |                 |               |
| -Infection                           | 1 [30]                | 1 [26]        |
| -Tacrolimus encephalopathy           | 1 [35]                |               |

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**Table 2 Follow-up of combined liver-kidney transplantation**

| Combined liver-kidney transplantation | Year of transplantation [ref] | Age at transplantation | Current age (if alive) | Outcome and complications |
|---------------------------------------|------------------------------|------------------------|------------------------|--------------------------|
| GSDIa                                 | 1996 (2nd OLT and KT) [20]   | 30                     | 1                      | 1.3 years: PT died at age 31 |
|                                       | 1996 [37]                    | 34                     | 52                     | 4.1 years: alive          |
|                                       | 2000 [26]                    | 19.5                   | 34                     | 2 years: normal liver and kidney function |
|                                       | 2004 (publication) [17]      | 25                     | 35                     | 4 months: normal liver and kidney function |
|                                       | 2011 (publication) [36]      | 30                     | 33                     | 7 months: good condition, both grafts functional |
| GSDIb                                 | 2003 (2y later OLT) [33]     | 32                     | 41                     | 8 months: good liver function and normal kidney function |
liver transplantation [44]. Donor-derived leukocytes, co-transplanted with the liver graft, can migrate into the recipient’s immune system and bone marrow. This phenomenon may result in both long-term tolerance induction and induction of enzymatic activity in extra-hepatic tissue. Clearly, although the molecular mechanism causing congenital neutropenia in GSDIb has now been elucidated, many aspects of the phenotype remain poorly understood.

Our review shows that there are still many complications related to the liver transplantation procedure (18/58 (31%) in GSDIa and 8/22 (36%) in GSDIb patients), as well as complications suspected to be related to immune suppressive therapy (13/58 (22%) in GSDIa and 3/22 (14%) in GSDIb patients). In the light of these complications, novel therapeutic strategies, like hepatocyte and liver stem cell transplantations might represent attractive alternatives for liver transplantation in GSDI patients. Liver (stem) cells can be infused through the portal vein, which is considerably less invasive than liver transplantation and hence not associated with surgery related complications. We identified 3 GSDIa and GSDIb patients, treated with hepatocyte transplantations (Additional file 1: Table S3, Additional file 1: Table S4). Normalization of metabolic parameters was observed in all patients after transplantation and no therapy-related complications were mentioned. This concurs with previously reported beneficial effects from human hepatocyte transplantations for different hepatic indications (metabolic, acute and chronic liver failure) [45]. However, these beneficial effects were short-lived and effects subsided within months. Similarly, metabolic improvement decreased in one of the GSDI patients treated with hepatocytes after 3 years and eventually subsided completely [46]. Nevertheless, these case reports show that cell-based therapies can restore liver function for at least a limited period, which might be beneficial in acute situations awaiting a liver transplantation.

Liver stem cell transplantations might provide additional advantages. Stem cells are highly proliferative and have the potential to bypass the current shortage of donor livers by expansion in vitro or in vivo upon engraftment. Furthermore, liver stem cell transplantations might require less immune suppression. For allograft survival after solid

| Catch-up growth | Year of transplantation [ref] | Age at transplantation | Current age (if alive) | Catch-up growth |
|-----------------|--------------------------------|------------------------|-----------------------|----------------|
| GSDIa           | 1986 [23]                       | 6                      | 34                    | 2 years: catch-up growth |
|                 | 1987 [10]                       | 27                     | 54                    | 2 years: catch-up growth (5.4 cm) |
|                 | 1993 [13]                       | 11.8                   | 33                    | Yes: time of follow-up not mentioned |
|                 | Between June 1994 and December 2005 [25] | median 7.3 (n = 4) | Unknown               | The mean height-for-age increased from <10th percentile (at t = 0) to 50th percentile at 5 years |
|                 | Between 1996 and 2001 [39]      | 4.3-14.5 (n = 4)       | 20-30                 | 2 years: catch-up growth |
|                 | 1999 (publication) [14]         | 15                     | 30                    | 8 years: catch-up length growth (−6SD to −1.5SD) |
|                 | 1999 (publication) [14]         | 17                     | 32                    | 6 years: catch-up length growth (−2.5SD to −1.5SD) |
| GSDIb           | 2004 (publication) [32]         | 8                      | 18                    | Yes: time of follow-up not mentioned |
|                 | 2004 (publication) [32]         | 11.1                   | 21                    | Yes: time of follow-up not mentioned |

| Therapy-associated complications | Therapy-associated complication | Follow-up time [ref] |
|----------------------------------|---------------------------------|----------------------|
| GSDIa                            | Diabetes (n = 3)                | Acute: diabetes mellitus (1 patient) [9,21] |
|                                  |                                  | −2 days: insulin-dependent diabetes (1 patient) [9] |
|                                  |                                  | −3 days: for following 5 days insulin pump (1 patient) [8] |
|                                  | Hypertension (n = 4)            | −1 month: 4 patients, 2 received short term treatment with antihypertensive medication [25,39] |
|                                  | Infection (n = 8)               | Acute: CMV (2 patients) [21] |
|                                  |                                  | −1 month: CMV (5 patients) [25,36,39] |
|                                  |                                  | −4 years: hepatitis C (1 patient) [14] |
| GSDIb                            | Infection (n = 32)              | −7 months: hepatitis B (1 patients) [30] |
|                                  | Encephalitis                    | Acute: tacrolimus encephalitis (1 patient) [35] |
organ transplantation, all patients require life-long immune suppression, with serious associated side effects, including toxicity, malignancy development and infectious complications. Human fetal-liver derived hepatocytes have been given for end-stage decompensated liver cirrhosis without immune suppression, based on the concept that fetal cells do not express HLA yet [47]. Short term outcomes were promising, but long term follow up has not been reported. This illustrates that progenitor cell-based therapies might be given without or with reduced immune suppression. In this context, autologous transplantation with genetically corrected stem cells [48,49] and hepatocyte-like cells generated from autologous induced pluripotent stem cells [50] have exciting potential for the future.

Despite promising, some complications might still occur after stem cell based therapies, including renal complications. New-born G6PC knock-out mice treated with bone marrow-derived myelomonocytic cells displayed restored G6Pase activity and improved liver functional parameters, without amelioration of renal involvement [51]. Similarly, there is concern that hepatic adenoma and carcinoma might develop in the cells with a defect G6PT/G6Pase complex with the use of cell-based therapies that do not replace all patient cells. However, a recent study has demonstrated that the occurrence of hepatocellular adenoma was prevented by gene therapy in G6pc−/− mice, despite partial and variable G6Pase activity, but with normalized blood metabolite profiles and glucose tolerance [52]. This concurs with the observation that development of hepatocellular adenoma and carcinoma appears to be related to the degree of steatosis and has been shown to regress with improved metabolic control [53], as is expected from cell-based therapies.

In conclusion, all GSDI patients reviewed in this article showed improved metabolic control and normal fasting tolerance after liver transplantation. This dramatically improved the quality of life of these patients, but a substantial number of patients experienced complications. Although some complications might be caused by disease progression, most seemed related to the liver transplantation procedure and subsequent immune suppression. These complications underscore the need for improvement of therapeutic strategies and emphasize the potential of novel (stem) cell-based treatments.

Additional file

Additional file 1: Information on individual GSDI patients undergoing liver transplantations.

Competing interests

The authors declare that they have no competing interests.

Authors’ contributions

SB identified all the cases to be included, analyzed and interpreted the data and drafted the manuscript. PS reviewed the manuscript. PS, GV and SF contacted treating physicians and reviewed the manuscript. In addition, GV and SF analyzed and interpreted the data. All authors read and approved the final manuscript.

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References

1. Chou JY, Jun HS, Mansfield BC: Glycogen storage disease type I and G6Pase-beta deficiency: etiology and therapy. Nat Rev Endocrinol 2010, 6:676–688.
2. Froissant P, Piraud M, Baudjelline AM, Vianey-Saban C, Petit F, Hubert-Buron A, Eberschweiler PT, Gajdos V, Labrune P: Glucose-6-phosphate dehydrogenase deficiency. Orphanet J Rare Dis 2011, 6:27-1172-6-27.
3. Lee KJ, Shelly LL, Pan CJ, Sidbury JB, Chou JY: Mutations in the glucose-6-phosphate transporter gene that cause glycogen storage disease type 1a. Science 1993, 262:580–583.
4. Hiraifa H, Pan CJ, Lin B, Moses SW, Chou JY: Inactivation of the glucose 6-phosphate transporter causes glycogen storage disease type 1b. J Biol Chem 1999, 274:5532–5536.
5. Rake JP, Visser G, Labrune P, Leonard JV, Ulteh K, Smit GP: Glycogen storage disease type I, diagnosis, management, clinical course and outcome. Results of the European Study on Glycogen Storage Disease Type I (ESGSD I). Eur J Pediatr 2002, 161(Suppl 1):S20–534.
6. Malatack JJ, Finegold DN, Iwatsuki S, Shaw BW Jr, Gartner JC, Zitelli BJ, Roe T, Starzl TE: Liver transplantation for type I glycogen storage disease. Lancet 1983, 1:1073–1075.
7. Coite CJ, Qublasky AH, Castelli MF: Hepatic adenomata in type I glycogen storage disease. Arch Pathol Lab Med 1987, 111:166–169.
8. Martinez Ibanez V, Margarit C, Tornro R, Infante D, Iglesias J, Allende H, Lloret J, Jimenez A, Boix-Ochoa J: Liver transplantation in metabolic diseases. Report of five pediatric cases. Transplant Proc 1987, 19:3803–3804.
9. Poe R, Snover DC: Adenomas in glycogen storage disease type I. Two cases with unusual histologic features. Am J Surg Pathol 1988, 12:477–483.
10. Kirschner BS, Baker AL, Thorp FK: Growth in adulthood after liver transplantation for glycogen storage disease type I. Gastroenterology 1991, 101:238–241.
11. Kay RM, Eckardt JJ, Goldstein LL, Busuttil RW: Metastatic hepatocellular carcinoma to bone in a liver transplant patient. A case report. Clin Orthop Relat Res 1994, 303:237–241.
12. Reid CJ, Hebert D: Acute renal failure complicating liver transplantation in twin sisters with glycogen storage disease type Ia. Transplant Proc 1996, 28:3629–3631.
13. Matern D, Starzl TE, Arnaout W, Barnard J, Bynon JS, Dhwawan A, Emond J, Haagsa MB, Hug G, Lachaux A, Smit GP, Chen YT: Liver transplantation for glycogen storage disease types I, III, and IV. Eur J Pediatr 1999, 158(Suppl 2):S43-548.
14. Faivre L, Houssin D, Valayer J, Brouard J, Hadchouel M, Bernard O: Glycogenesis in adulthood after liver transplantation on hepatic glucose metabolism in a patient with type I glycogen storage disease. Transpl Int 1996, 9:262–270.
15. Koestinger A, Gillet M, Chioriero R, Mosimann F, Tappy L: Effect of liver transplantation on hepatic glucose metabolism in a patient with type I glycogen storage disease. Transplantation 2000, 69:205–220.
16. Letur JP, Ciccariello O, Sempoux C, Dansse E, de Flandre J, Horsmans Y, Sokal E, Ott SC: Liver transplantation in patients with glycogen storage disease type Ia. J Inher Metab Dis 1999, 22:77–732.
17. Panaro F, Andorno E, Basile G, Morelli N, Botino G, Fontana I, Bertocchi M, DiDomenico S, Miggino M, Saltalamacchia L, Ghinolfi D, Bonfazi L,
Glycogen storage disease type Ia: a secondary cause for hyperlipidemia: report of five cases. 

18. Arikian C, Klicic M, Nart D, Ozgenc F, Ozkan T, Tokat Y, Yagci RV, Aydogdu S. Hepatocellular carcinoma in children and effect of living-donor liver transplantation on outcome. Pediatr Transplant 2006, 10(6):E286–E289.

19. Carreiro G, Villegas-Juarez CA, Coelho H, Busto S, Pannain M, Caro-Rattino A, Ribeiro Filho J. Orthotopic liver transplantation in glucose-6-phosphatase deficiency–Von Gierke disease–with multiple hepatic adenomas and concomitant focal nodular hyperplasia. J Pediatr Endocrinol Metab 2007, 20:545–549.

20. Davis MK, Weinstein DA: Liver transplantation in glycogen storage disease type Ia. J Hepatol 2009, 51:483–490.

21. Carvalho PM, Silva NJ, Dias PG, Porto JF, Santos LC, Costa JM: Hepatocellular carcinoma in children and effect of living-donor liver transplantation on outcome. Hepatol Transplant 2008, 12:137–145.

22. Reddy SK, Austin SL, Spencer-Manzon M, Koebele DD, Clay BM, Desai DM, Smith AD, Kishnani PS. Liver transplantation for glycogen storage disease type Ia. J Hepatol 2009, 51:483–490.

23. Labrune P. Glycogen storage disease type Ia: indications for liver and/or kidney transplantation. Eur J Pediatr 2002, 161(Suppl 1):S335–S335.

24. Iyer SG, Chen CL, Wang CC, Wang SH, Concejero AM, Liu YW, Yang CH, Yong CC, Jawan B, Cheng YF, Eng H. Long-term results of living donor liver transplantation for glycogen storage disorders in children. Liver Transplant 2007, 13:848–852.

25. Belingheri M, Ghio L, Sala A, Menfi F, Trevisi L, Ferrero A, Berardinelli L, Rossi G, Edefonti A, Parini R. Orthotopic liver transplantation for type I glycogenosis with reversal of cyclic neutropenia. J Pediatr Gastroenterol Nutr 1993, 16:465–467.

26. Jarzembowski TM, Valente U. Transplant Proc 2010, 42:1741–1746.

27. Boers et al. Orphanet Journal of Rare Diseases 2014, 9:47

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