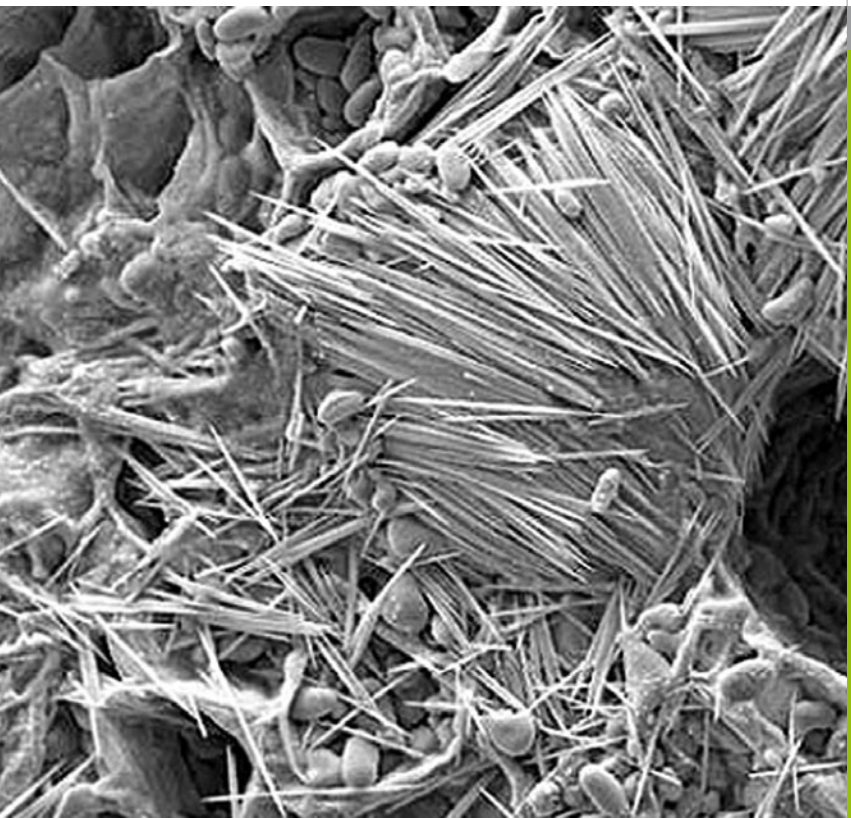
SWISS SOCIETY OF NEONATOLOGY

A combined liver-kidney transplant recipient with type 1 primary hyperoxaluria gives birth to a premature infant



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A 25-year-old woman with primary hyperoxaluria type 1 consulted our clinic of obstetrics with the desire to become pregnant. Three years earlier, she had developed end-stage renal failure and, after a short period of hemodialysis, she had undergone a cadaveric combined liver and kidney transplantation. Initial immunosuppression consisted of mycophenolate, tacrolimus and prednisone. At the time of the first appointment in our obstetric clinic, renal function was mildly impaired with a plasma creatinine of 190 µmol/l (normal < 130 µmol/l). Blood pressure was normal and there was no proteinuria. Her immunosuppressive regimen was changed to azathioprine instead of mycophenolate, whereas the therapy with tacrolimus and prednisone was continued.

A first pregnancy ended in spontaneous early abortion. During the second pregnancy, the mother presented with increasing proteinuria from the 19th week of gestation. At 27 5/7 weeks of gestation, intrauterine growth restriction and absent diastolic flow in the umbilical artery were noted. Lung maturation was induced. A caesarean section was performed at 28 0/7 weeks of gestation because of a silent CTG. A female infant was born with a birth weight of 700 g (P 3-5), a length of 31 cm (P <3) and a head circumference of 23.5 cm (P 5-10). Adaptation was excellent with Apgar scores of 8, 9, and 9 at 1, 5 and 10 minutes, respectively. Arterial umbilical cord pH was 7.32. Clinical examination was normal without any dysmorphic features (Fig. 1).

The baby girl required supplemental oxygen (maximal FiO2 0.25) for the first three days of life. Enteral and parenteral nutrition were started on the first day of life. Because of the maternal treatment with immunosuppressive drugs the girl was not breast fed. Parenteral fluids were stopped on the 10th day of life. Her weight increased along the 3rd percentile. An ultrasound scan of the kidneys and the urinary tract showed normal renal size and anatomy. Apart from „typical" problems of prematurity, the neonatal course was uneventful and the little girl was discharged home with a weight of 1750 g seven weeks after birth at a postmenstrual age of 35 0/7 weeks. Urinary oxalate/creatinine ratio, measured at 20 weeks of age, was normal at 141 mmol/mol (normal < 325 mmol/mol), and the baby was thriving (Fig. 2).

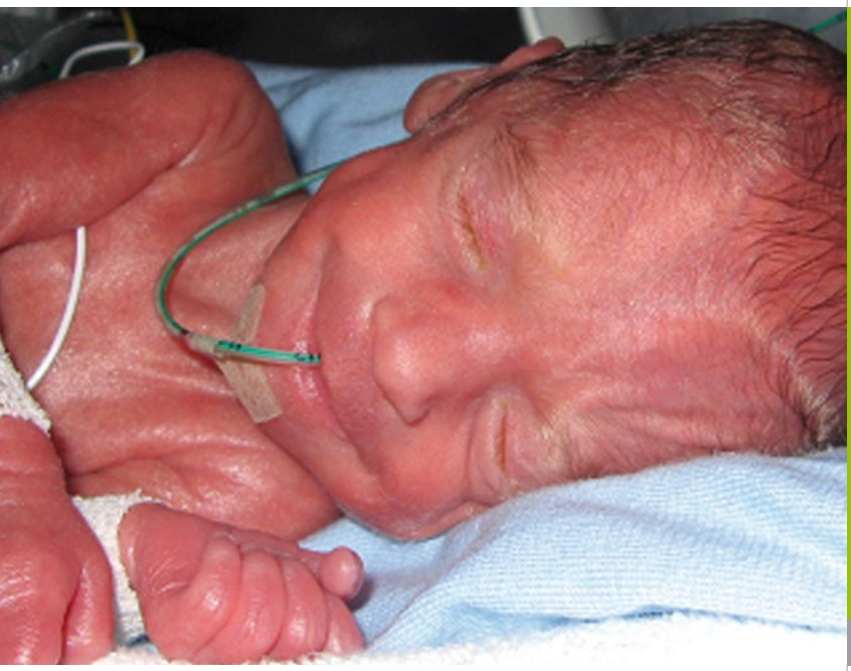

Fig. 1

The premature baby on the fifth day of life.

Fig. 2

The girl at six months of corrected age.

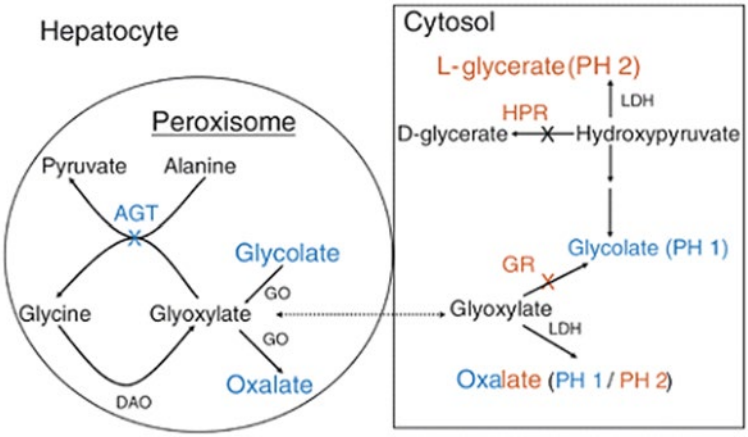

Fig. 3

Oxalate metabolism in patients with primary hyperoxaluria types 1 and 2; reproduced with permission from (1).

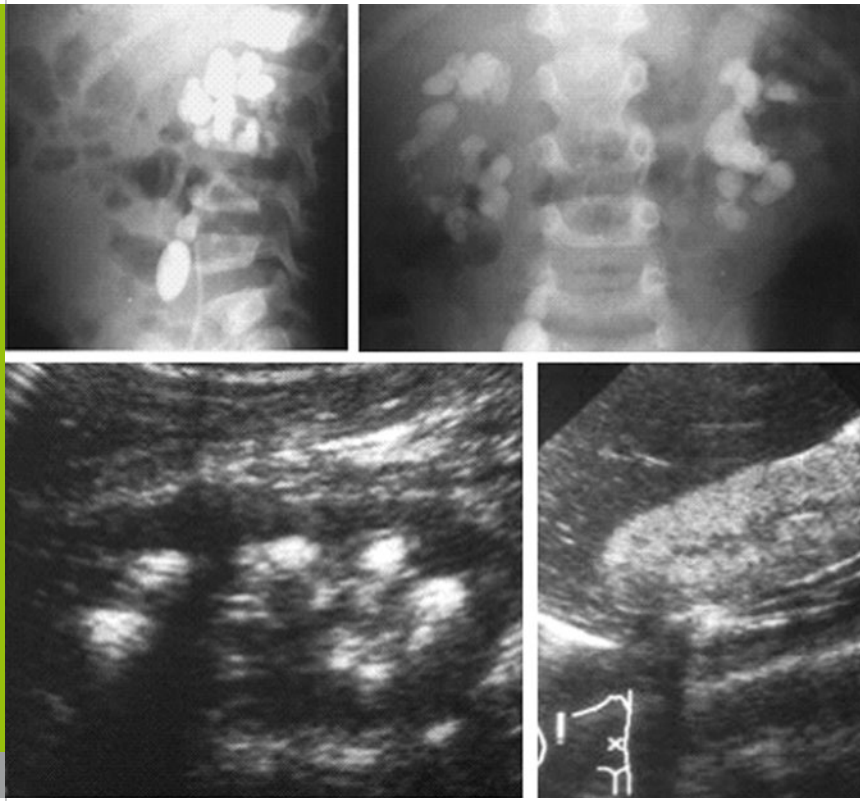

Fig. 4

Clinical hallmarks of primary hyperoxaluria: severe urolithiasis and nephrocalcinosis; reproduced with permission from (1).

Primary hyperoxaluria type 1 (PH1) is a rare autosomal recessive disorder caused by a deficiency of the liver-specific enzyme alanine-glyoxylate aminotransferase resulting in a reduced degradation of oxalate with subsequent hyperoxaluria and hyperoxalatemia (Fig. 3). Recurrent kidney stones and progressive medullary and cortical nephrocalcinosis lead to progressive loss of kidney function. The accumulation of oxalate can result in systemic oxalosis (Fig. 4) (1-3).

PH1 shows a broad clinical phenotype ranging from end stage renal failure in infancy or adulthood to „isolated" urolithiasis with maintained renal function (4). Diagnosis of PH1 is often delayed due to its rare occurrence and non-specific clinical presentation. Stones are typically composed of 100% calcium-oxalate-monohydrate. Conservative treatment consists of high fluid intake to dilute urine and oral citrate to inhibit urinary calcium-oxalate crystallization. So far, no therapy is available to either decrease oxalate synthesis or increase oxalate degradation.

Because of the liver-specific localization, the only cure of PH1 is liver transplantation. Most patients undergo combined liver-kidney transplantation when progressive chronic or end-stage renal failure has occurred. As PH1 is an autosomal recessive hereditary disease, the baby must be a heterozygous carrier of a mutation in the gene coding for PH1. Only in case of her father carrying also a heterozygous mutation she would have

a risk of 50% to suffer from PH1 (or in case of a de novo mutation). Genetic analysis of the father was offered, but finally the parents decided against testing.

Successful pregnancy after solid organ transplantation is possible and is occurring with increasing frequency. The rate of live births is high. The first pregnancy in a solid organ transplant recipient occurred in a renal transplant patient who subsequently delivered a healthy neonate in 1958. In the ensuing 50 years, more than 14‘000 pregnancies in women with transplanted organs have been reported (5). But even if a pregnancy after transplantation has become more common, it remains a high-risk situation for both mother and unborn child.

In the maternal transplant recipient, the main focus is on the effect of the pregnancy on maternal long-term graft function. Risk of irreversible loss of renal allograft function is low if renal function is stable. In patients with impaired graft function, risk of loss of function is increased during and after pregnancy (5, 6). Another maternal concern during pregnancy is hypertension either by deterioration of preexisting hypertension or the development of new hypertension and superimposed preeclampsia during pregnancy (5, 7). Immunosuppression is associated with an increased risk of infections, e.g., cytomegalovirus, toxoplasmosis, herpes simplex and varicella. Therefore, close prenatal screening and follow-up is recommended (7).

The rate of caesarean section in patients with kidney transplantation is as high as 60%, partially due to the high rate of obstetrical complications. However, the localisation of the transplanted kidney in the pelvis alone is not a reason per se to perform a caesarean section (7).

A high risk of preterm delivery and/or low birth weight has been reported for pregnancies after organ transplantations. In published registry reports, preterm live birth rate was estimated to be as high as 50% (8). Reported reasons were maternal (hypertension or preeclampsia, deteriorating renal function) or fetal complications (intrauterine growth restriction and fetal distress) (8). The mean gestational age at delivery in kidney transplanted women is 34 weeks (5) and the rate of intrauterine growth restriction is as high as 30-50%. A major concern is the in utero exposure to immunosuppressive or antihypertensive drugs. All immunosuppressive drugs cross the placenta. Because of limited clinical data, no reliable information is available and there are no prospective randomized trials regarding drug safety (9).

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