



Extrahepatic biliary atresia in combination with possible toxic cholestasis due to Glibenclamide in a case of neonatal diabetes

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Introduction

More than 20 gene loci are known to cause monogenic neonatal diabetes today. A definite mutation can be found in 65-70% of all cases. Mutations in the ATP sensitive potassium channel can frequently be treated by sulfonylurea. Glibenclamide is one of the drugs known to inhibit the bile salt export pump (BSEP). However most drug induced cholestasis cases regarding Glibenclamide are reported in adults.

Methods

We report about a boy with neonatal diabetes due to a KCNJ11 missense mutation diagnosed in the age of 2 weeks. Early diagnosis was possible because the mother has the same mutation and received Glibenclamide for several years without any complications. In pregnancy metabolic control of the mother was worse with HbA1c always above 10% (86 mmol/mmol).

Results

Glibenclamide was started in the boy with very low doses (0.0125mg/kgKG) immediately after diagnosis with an age of 3 weeks. At this time no signs of hyperbilirubinemia were obvious.

Cholestatic icterus developed with the age of 9 weeks. Glibenclamide was stopped immediately. We suspected a drug induced cholestatic icterus. However Liver biopsy showed signs of extrahepatic cholestasis but also possible toxic signs. There was no improvement with conservative treatment. Intraoperative exploration and cholangiography showed an extrahepatic biliary atresia. Biliodigestive anastomosis with Y-Roux (Kasai) was established by the pediatric surgeons. Diabetes is in remission at the moment. Cholestasis has completely recovered. The boy developed two episodes of cholangitis within the first months after biliodigestive anastomosis. Within the last 8 months there were no further complications and Bilirubin is within the normal range. Liver function tests are normal. Motoric and psychosocial development are appropriate.

Conclusions

Cholestasis due to glibenclamide has to be taken into account when treatment is initiated in neonates with monogenic diabetes. Therefore we would recommend to monitor cholestatic parameters in a certain algorithm.

Tab 1. Total bilirubin over the live span of our patient given in $\mu\text{mol/l}$. The arrow marks the time of surgery (biliodigestive anastomosis)

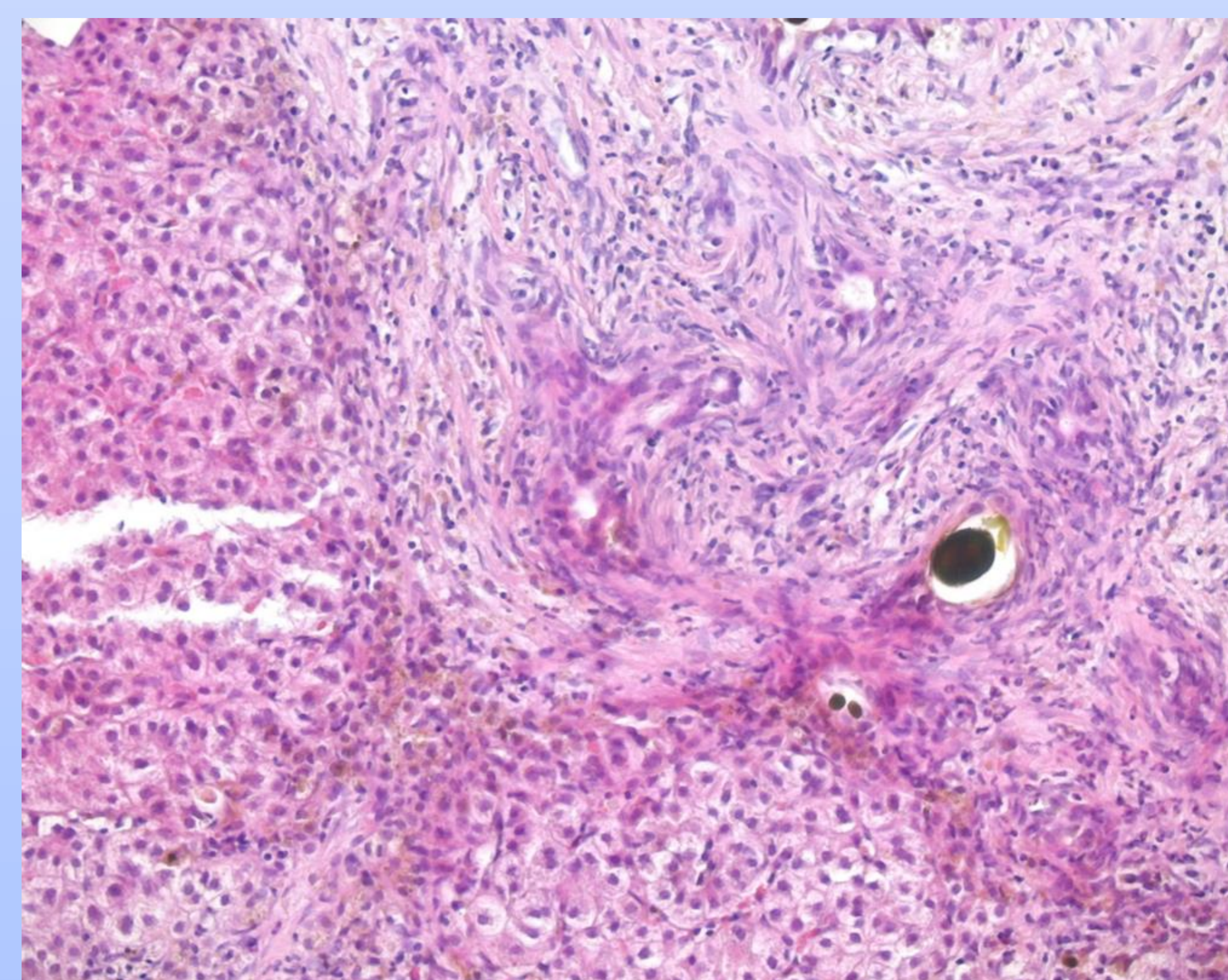
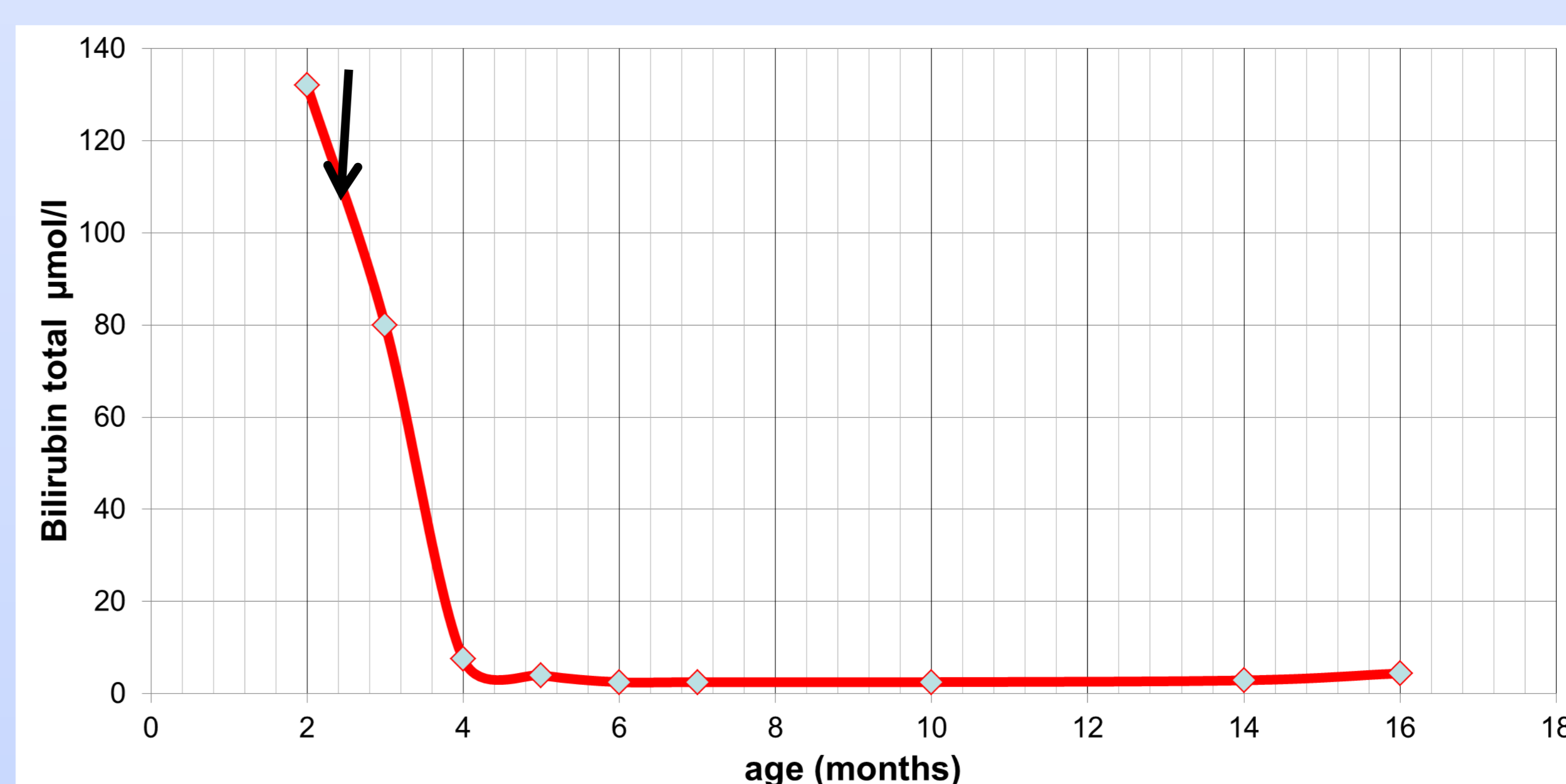


Fig. 1. liver biopsy showing a portal field with bile plugs are found in principal bile ducts within portal tracts. No deficiency of portal-tract bile duct numbers is discerned. Patient's gallbladder was hypoplastic, a usual feature of extrahepatic biliary atresia (not shown).

Discussion

Glibenclamide is used frequently to treat neonates with monogenic diabetes. To date there is no case of drug induced cholestasis reported in neonates. Extrahepatic biliary atresia seems to develop either intrauterine but in some cases even after birth. Causing factors are not known exactly. We hypothesize that the coincidence of extrahepatic biliary atresia in a patient treated with glibenclamide because of neonatal diabetes could be partially explained by drug induced cholestasis. Another possible explanation could be the diabetes of the mother. Biliary atresia is more frequent in mothers with gestational diabetes.

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