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## CASE REPORT

# Increased fertility in a woman with classic galactosaemia

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**Summary:** A 27-year-old caucasian female with classical galactosaemia due to Q188R homozygous mutation is reported. At 18 years she had triplets and at 23 years a further pregnancy. All infants are well.

A 21-year-old caucasian female was diagnosed at the age of 2 weeks with classic galactosaemia with vomiting, cataracts, failure to thrive and 'liver problems'. Since menarche at age 11 years, her menstrual cycle had been irregular with periods of amennorrhoea lasting up to 6 months. At the age of 16 years, her periods became regular, until her unplanned triplet pregnancy at the age of 18 years.

During the 17th week of pregnancy her galactose 1-phosphate (Gal-1-P) level was 4.12 mg/dl (normal range < 1) and Gal-1-P uridyltransferase (GALT) level 0 and 0.34 $\mu$mol/h per g Hb respectively on two different measurements (galactosaemia 0–0.7; normal range 18.5–32.9). Mutation studies indicated that she was homozygous for the common mutation Q188R. During the 29th week of pregnancy, she developed pre-eclampsia and azotaemia. Over the subsequent 36 h, she developed deteriorating renal function (creatinine 2.2 mg/dl, microscopic haematuria with red blood cells, hyaline and granular casts, creatinine clearance 40.8 ml/min (normal range 88–128 ml/min), and 240 mg/24 h proteinuria (normal 50–80 mg/24 h).

She had an emergency Caesarian section at 29 weeks gestation. Five days later, her renal function was normal. At birth, triplet A had Apgar scores of 6, 8, and 9 at one, five, and ten minutes, respectively, weighed 1760 g, measured 51 cm, and had a head circumference of 31 cm. Triplet B had Apgar scores of 8, 9, and 9 at one, five, and ten minutes, weighed 1580 g, measured 41 cm, and had a head circumference of 30 cm. Triplet C had Apgar scores of 8, 9 and 9 at one, five, and ten minutes, weighed 1450 g, measured 44 cm, and had a head circumference of 29 cm. The triplets had respiratory distress at birth related to their prematurity and required intubation and surfactant treatment. They had mild hyperbilirubinaemia, which was treated with phototherapy. Screening for galactosaemia was normal in the triplets.

Postpartum she took oral contraceptives, which she discontinued after 21 months. Hormonal testing for amenorrhoea revealed luteinizing hormone (LH) level of

38.82 mIU/ml (U/L) (postmenopausal range 16–64 U/L), and follicle-stimulating hormone (FSH) level was 94.19 mIU/ml (U/L) (postmenopausal level 18–153 U/L), suggesting ovarian failure. She was treated with lactose-free cyclical oestrogen/progesterone combination therapy and maintained satisfactory galactose 1-phosphate levels.

She became pregnant again 5 years later at age 23 years. The pregnancy progressed unremarkably and a male infant was delivered vaginally at 41 weeks gestation, birth weight 3742 grams, length 53.5 cm and OFC 32.8 cm. No dysmorphic features or cataracts were noted. The triplets age 5 years and the baby age 10 months all have normal growth parameters and developmental milestones.

Waggoner and colleagues (1990) and Gibson (1995) reviewed pregnancies in galactosaemic females ranging in age from 17 to 30 years, many of whom were either black and/or had the variant type. Sauer and colleagues (1991) reported successful pregnancy after oocyte donation to a woman with ovarian failure in classic galactosaemia. The authors also reported six further pregnancies in three women with galactosaemia, two of whom developed premature ovarian failure soon after delivering a normal infant. Briones and colleagues (2001) reported a woman also homozygous for the Q188R mutation who had pregnancies at ages 20 and 22 years.

The premature ovarian failure in this patient appears to have been accelerated by the pregnancy. There is no previous report of increased fertility in galactosaemia associated with the severe homozygous Q188R mutation as seen in this woman. Despite premature ovarian failure documented by elevation of the FSH and LH 21 months after the triplet pregnancy, she had sufficient residual activity to conceive again and deliver a healthy male. The woman's young age may be an important factor, as many of the reported pregnancies were in younger females. As in previous reports, no adverse outcome in the four offspring was observed. Further studies are indicated to determine the factors leading to preservation of ovarian function in some women with galactosaemia, thus helping to develop strategies to preserve fertility.

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