FAMILIAL MOSAIC TURNER SYNDROME WITH SHORT STATURE AND PRESERVED FERTILITY DUE TO A RING X CHROMOSOME WITH DISTAL XP22.3 AND XQ26 DELETION

SHARON LIM1, Caroline Brain2, Melissa Lees3, Kamila Jagiello4, Evelien Gevers5
1Paediatric Department, Broomfield Hospital, MHE NHS Trust, Chelmsford, United Kingdom
2Department of Paediatric Endocrinology, Great Ormond Street Hospital, London, United Kingdom
3North Thames Regional Genetics Service, Great Ormond Street Hospital, London, United Kingdom
4Cytogenetic Service, Great Ormond Street Hospital, London, United Kingdom
5William Harvey Research Institute, Queen Mary, University of London, and Royal London Children’s Hospital, Barts Health NHS Trust, London, United Kingdom

INTRODUCTION
Mosaicism X is characterised by loss of oocytes at the pachytene stage of meiotic prophase during female development, resulting in ovarian agenesis at birth. Fully normal women with Turner syndrome is usually a result of tissue mosaicism, with one cell line containing two normal X chromosomes. Fertility has occasionally been reported in women with a structural X chromosome rearrangement. We describe a family where the mother had a clinical diagnosis of Turner syndrome, with mosaicism for 45,X and a ring X chromosome, who achieved 3 pregnancies, two of which resulted in the live births of healthy females. One daughter was also mosaic for the ring X chromosome, and the other daughter had monosomy X in all cells analysed.

CASE HISTORY
Patient 1
12 years old and recently moved from Poland
Referred for investigations of short stature (Ht SDS -2.1)
Maternal height 142.9 cm (1.3 SD), paternal height 176.1cm (0.67 SD)
Birth weight 2.63 kg at 37 weeks (2.60 SD)
Compared to mean weight for gestational age of 3400 g (15th centile)
Birth length 49 cm (3.5 SD)
Proportionate short stature
Non-dysmorphic
 Tanner stage 2
Bone age: 11 years at a chronological age of 12.25 years.
Height: 145 cm at 12.0 years
Normal renal USS and echocardiogram

Patient 2
Younger sister of patient 1
Spontaneous puberty and menarche aged 12.
Yrs
Spontaneous menarche aged 12.8 years
AMH in the normal range
Bone age: 11 years at a chronological age of 12.25 years.
Height: 145 cm at 12.0 years
Normal renal USS and echocardiogram

Patient 3
Daughter of patient 1
Bone age: 11 years at a chronological age of 12.25 years.
Spontaneous puberty and menarche aged 12.
Yrs
Height: 145 cm at 12.0 years
Normal renal USS and echocardiogram

RESULTS
Karyotype in Patient 1: 45,X[20]/46,X[10] Iocation of genes in the stable X chromosome shown in red
Karyotype in Patient 2: 45,X (50 metaphases)

CONCLUSION
We present an unusual family with familial Turner Syndrome. The presence of the unstable ring X chromosome is likely to account for the familial Turner syndrome. Structural rearrangements of the X chromosome can be associated with fertility, which is thought to be related to the positions of the breakpoint. Spontaneous puberty and menarche occurred in the mother and her two daughters may be related to tissue mosaicism and intact X chromosome regions proximal to Xq22 and Xq26 which play a role in ovarian development and maintenance. However, raised gonadotrophins and undetectable AMH in the daughters and are in line with fluctuating ovarian function and developing ovarian failure. Only time will tell whether the daughters may be fertile like their mother.

REFERENCES
A high-resolution X chromosome copy-number variation map in fertile females and women with primary ovarian insufficiency. Setiawan A, Katzenhöfer, Michelle Wood-Trager, Tianjiao Chu, Huaying Jiang, and Aleksandar Rajkovic. Genetics in Medicine, 2019; 21:2275-2284

ACKNOWLEDGEMENTS
I would like to give special thanks to Melissa Lees and Evelien Gevers for the enormous time and effort spent in the preparation of this poster.

CONTACT INFORMATION
sharonlim@nhs.net
evelien.gevers@nhs.net

Monosomy X is characterised by loss of oocytes at the pachytene stage of meiotic prophase during female development, resulting in ovarian agenesis at birth. Fully normal women with Turner syndrome is usually a result of tissue mosaicism, with one cell line containing two normal X chromosomes. Fertility has occasionally been reported in women with a structural X chromosome rearrangement. We describe a family where the mother had a clinical diagnosis of Turner syndrome, with mosaicism for 45,X and a ring X chromosome, who achieved 3 pregnancies, two of which resulted in the live births of healthy females. One daughter was also mosaic for the ring X chromosome, and the other daughter had monosomy X in all cells analysed.