OPEN ACCESS

Bruck syndrome in pregnancy

Shravya Manohar,[1] Adam Jakes,[1] Ingrid Watt-Coote,[2] Asma Khalil[3]

[1]Obstetrics and Gynaecology, St George's University Hospitals NHS Foundation Trust, London, UK
[2]Maternal Medicine, St George's University Hospitals NHS Foundation Trust, London, UK
[3]Fetal Medicine, St George's University Hospitals NHS Foundation Trust, London, UK

Correspondence to
Professor Asma Khalil;
asma.khalil@stgeorges.nhs.uk

Accepted 13 April 2024

SUMMARY

Bruck syndrome is a rare, autosomal-recessive condition associated with features of both arthrogryposis and osteogenesis imperfecta. It is characterised by congenital large joint contractures with pterygia and bone fragility, leading to fractures and deformities, along with a short stature caused by progressive skeletal deformities. There are fewer than 50 described cases of Bruck syndrome in the literature, with no reported cases in pregnancy. We describe a case of a successful pregnancy in a woman with Bruck syndrome.

In pregnant women with Bruck syndrome, we recommend a multidisciplinary approach including input from obstetric and fetal medicine specialists, midwives, anaesthetists, geneticists, occupational therapists and physiotherapists.

BACKGROUND

Bruck syndrome is a rare, autosomal-recessive condition associated with features of both arthrogryposis and osteogenesis imperfecta.[1] It is characterised by congenital large joint contractures with pterygia and bone fragility, leading to fractures and deformities, along with a short stature caused by progressive skeletal deformities.[2]

There are fewer than 50 described cases of Bruck syndrome in the literature, with no reported cases in pregnancy. We describe a case of a successful pregnancy in a woman with Bruck syndrome.

CASE PRESENTATION

A woman in her 20s with osteogenesis imperfecta and significant lower limb contractures presented in her first pregnancy. She had conceived spontaneously with her husband. Her body mass index (BMI) was 15 kg/m^2 (weight 30 kg and height 130 cm) and was wheelchair-bound. She had a short stature with significant bilateral lower limb contractures, pterygia of both knees and mild pectus carinatum.

Her medical history included osteogenesis imperfecta diagnosed in childhood which had resulted in multiple fractures and severe scoliosis requiring spinal-fusion surgery with Harrington rods. There was no family history of osteogenesis imperfecta or skeletal problems. Her parents were consanguineous.

She also had chronic iron deficiency anaemia, with a booking haemoglobin of 80 g/L (normal range: 120–160) and ferritin of 7 ng/mL (13–150). There was no evidence of haemoglobinopathy, and a blood film demonstrated normocytic red blood cells with no evidence of haemolysis or atypical cells. Serum vitamin B_{12}, folate and coeliac serology were within the normal range. Two years prior to pregnancy she underwent a gastroscopy and colonoscopy, which were reported as normal but poorly tolerated and technically difficult due to her physical deformities. The patient declined further endoscopic investigation in pregnancy and was managed conservatively with three single unit blood transfusions and two intravenous iron infusions. Omeprazole was prescribed empirically, and her care was discussed a number of times in the haematology and gastroenterology multidisciplinary team meetings.

She was referred to a clinical geneticist, where a homozygous *FKBP10* gene mutation was identified, confirming Bruck syndrome at 27 weeks of pregnancy. *COL1A1* and *COL1A2* were both analysed, and no pathogenic variants were identified in either of these genes. As the condition is a very rare autosomal-recessive condition and the partner was not a blood relative, it was felt that the risk of the fetus being affected was minimal and partner testing was not indicated.

Utmost care was taken during antenatal examinations in view of her significant lower limb contractures, with an additional risk of fractures during pregnancy and further restricted mobility. Symphysis-fundal height measurements were not possible; therefore, serial growth scans were required.

The first-trimester and mid-trimester anomaly ultrasound scans were normal. Her combined screening test result for common trisomies was low risk. She was offered serial growth scans every 4 weeks. A fetal echocardiogram at 29 weeks demonstrated a structurally and functionally normal heart with a small pericardial effusion around the right ventricle. At 34^{+6} weeks the fetus demonstrated normal growth and resolution of the pericardial effusion.

An elective caesarean section at 37^{+0} weeks was recommended due to her significant lower limb contractures, scoliosis, short stature and the risk of an unplanned caesarean section. Anaesthetic review recommended a general anaesthetic due to the technical difficulties and unreliable spread of regional analgesia.

Pre-delivery lung function testing demonstrated a restrictive pattern, but this was thought to be the result of pressure from the gravid uterus on the diaphragm. Following delivery, this was expected to improve.

A multidisciplinary simulated theatre trial was performed together with the patient to address the difficulties in positioning, the instruments required, access to the lower abdomen, lower uterine segment and delivering the baby. The simulation

Check for updates

© BMJ Publishing Group Limited 2024. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Manohar S, Jakes A, Watt-Coote I, *et al*. *BMJ Case Rep* 2024;**17**:e257696. doi:10.1136/bcr-2023-257696

BMJ Case Rep: first published as 10.1136/bcr-2023-257696 on 10 September 2024. Downloaded from http://casereports.bmj.com/ on September 30, 2024 by guest. Protected by copyright.

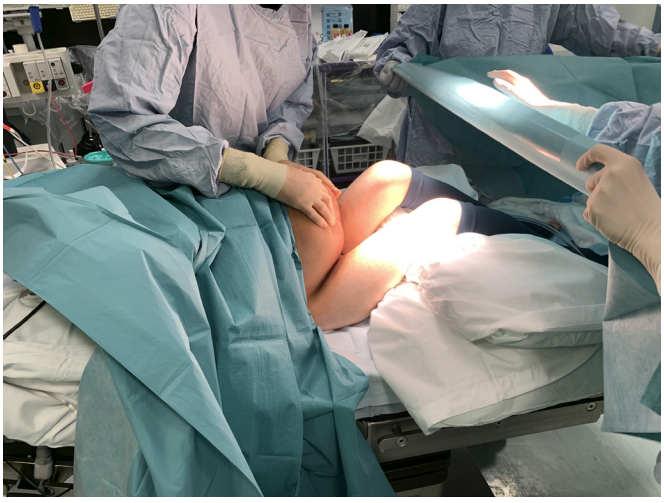

Figure 1 Access to the lower abdomen was limited due to contractures.

involved anaesthetists, obstetricians, neonatologists, midwives and theatre staff.

An occupational therapist performed a home visit to identify any difficulties with her home setup and offerred adaptations to support her recovery and activities of daily living. They also recommended the use of a weighted doll to highlight any additional challenges caring for a newborn baby with her limited mobility and contracted limbs.

OUTCOME AND FOLLOW-UP

At 36^{+4} weeks' gestation, she presented with spontaneous contractions. Her haemoglobin was 64 g/L (120–160) and a single unit red blood cell transfusion was administered. A caesarean section was performed under general anaesthesia. The multidisciplinary team in theatre consisted of two consultant and three registrar obstetricians, two anaesthetic consultants and one anaesthetic assistant, one consultant and one registrar paediatrician, two senior neonatal nurses, two scrub nurses, two midwifery-support workers and two theatre staff. A low transverse skin incision was used to enter the abdomen, but a high transverse uterine incision was required due to lack of access to the lower uterine segment (figure 1). A female infant was born in good condition weighing 2.11 kg with APGAR scores of 8 at 1 min and 9 at 10 min.

Blood loss was 500 mL which led to a haemoglobin drop from 96 g/L to 64 g/L, requiring another single unit red blood cell transfusion. She was managed in the obstetric high-dependency area, with obstetric, anaesthetic, midwifery, tissue viability, occupational therapy and pain team input. Postoperative pain management was challenging and used cautiously due to her low BMI. A patient-controlled analgesia allowed small-bolus opioids to be used when required. She did not require respiratory support postoperatively. Anti-thromboembolic stockings were used for thromboembolism prophylaxis as low molecular weight was avoided due to the unexplained iron-deficient anaemia.

She was discharged after a 1 week hospital stay and had an uneventful postnatal period.

DISCUSSION

The incidence of Bruck syndrome is estimated to be less than one in a million.[3] It is caused by a deficiency of bone-specific telopeptide lysyl hydroxylase, which results in aberrant crosslinking of bone collagen. This leads to ineffective collagen synthesis and reduced function of osteoblasts, resulting in bone fragility, fractures and subsequent deformities, and congenital large joint contractures. Cognitive function is normal, as well as teeth, sclera, vision and hearing. It is an autosomal-recessive condition and can be divided into two genetic types. Bruck syndrome type 1 is a result of a homozygous mutation in the *FKBP10* gene. Bruck syndrome type 2 is a result of a homozygous mutation in the *PLOD2* gene.[2] Both genes are located on chromosome 17.

COL1A1 and *COL1A2* gene mutations are associated with abnormalities of type 1 collagen seen in conditions such as osteogenesis imperfecta and Ehlers-Danlos syndrome. These mutations are not found in Bruck syndrome.

The diagnosis can be suspected prenatally via ultrasound with the identification of antenatal fractures with contractures and further genetic testing to confirm the diagnosis.[4] Treatment involves the use of bisphosphonates and orthopaedic surgery, including osteotomies, intramedullary stabilisation and spinal fusion. Occupational therapy and physiotherapy are essential to optimise tasks of daily living.[5]

This is the first reported case of pregnancy in a woman with Bruck syndrome. The main obstetric risks anticipated were preterm birth and the risks of an unplanned, complicated caesarean section out of hours without the appropriate personnel. This was suggested due to the significant risk of preterm delivery in pregnant women with osteogenesis imperfecta and other collagen disorders.[6]

The risks pertaining to Bruck syndrome were fractures and restricted mobility with advancing gestation. Care was taken to support the patient's contracted limbs without force to avoid dislocation or fracture, especially while mobilising and positioning the patient under general anaesthesia.

The anaesthetic challenges included airway assessment and the possibility of difficult intubation. It was essential to minimise neck and jaw manipulation and reduce the risk of fractures/atlanto-axial injury. Lung function tests showed all measures (forced vital capacity, forced expiratory volume in 1 s and peak expiratory flow) were around 45% of their predicted values, indicating restrictive lung disease due to chest wall/thoracic spine deformities. Preoperative lung function testing was used to predict the need for postoperative respiratory support.

Managing blood loss was challenging due to the relatively normal-sized uterus in a person of small stature, together with the limited surgical access. This meant that the anticipated blood loss was likely to be higher than a routine caesarean section in a woman of normal stature. In addition, the patient's circulating blood volume was small, and so the capacity to tolerate this blood loss was reduced. Managing this required the ability to transfuse blood quickly through large bore cannulas and rapid infusion devices, and careful surgical attention to haemostasis.

Surgical challenges included positioning and access to the lower abdomen during caesarean section due to her severe lower limb contractures. A high uterine incision was required due to the lack of access to the lower uterine segment. This increases the risk of postpartum haemorrhage and subsequent uterine rupture in subsequent

BMJ Case Rep: first published as 10.1136/bcr-2023-257696 on 10 September 2024. Downloaded from http://casereports.bmj.com/ on September 30, 2024 by guest. Protected by copyright.

pregnancies. Anti-thromboembolic stockings were used due to the unavailability of gradual compression stocking for her size. Prophylactic anticoagulants were avoided in view of her undiagnosed cause of chronic anaemia. Blood loss was meticulously managed due to her anaemia and low weight.

Patient's perspective

I am an individual who has the condition Bruck syndrome, and I am a full-time wheelchair user. Never did I imagine that I could, first, possibly get pregnant and, second, that my baby could be delivered safe and sound, but with the help and assistance of the amazing healthcare team, this all became true.

I was unfortunately in hospital every month throughout my pregnancy due to my haemoglobin dropping quite drastically and in urgent need of a blood transfusion, which was handled with so much care from every department within the hospital. A plan was even put in place so that I didn't have to go through A&E in order to get the blood transfusion.

I then had an appointment organised by the consultant, regarding the types of positioning I could do with my body comfortably, while being operated on which I appreciated very much, with all due respect to the healthcare team, I did have the fear due to my disability of waking up after the operation and being in severe pain as the doctors wouldn't have known what I could stretch or not within my body.

I had more regular scans of my baby with the consultant because of my disability, who kindly informed me of how the baby was doing and any forthcoming issues we may have incurred.

Then came the day of my biggest fear where I experienced pain, 3 weeks before the due date of my baby girl, and then rushed to the hospital and was once again dealt with so much care by the midwives, consultants and every doctor that I came across.

I was then told the c-section would be undertaken that very day as the baby was pushing down and wanted to come out and that it was safe for me to have the baby delivered earlier rather than later, whereby I could have experienced excruciating pain and it could be an understandable risk to my brittle bones.

As an individual with physical disability needs, the healthcare team looked after me from day 1 of my pregnancy till the very end where I had to stay in hospital after the c-section for about 7 days in order for me to be able to sit in my wheelchair comfortably.

I would very much like to thank the healthcare team in all that they did to look after me and have my baby delivered safely.

Learning points

- Bruck syndrome is a rare, autosomal-recessive condition associated with features of both arthrogryposis and osteogenesis imperfecta.
- In pregnant women with Bruck syndrome, we recommend a multidisciplinary approach including input from obstetric and fetal medicine specialists, midwives, anaesthetists, geneticists, occupational therapists and physiotherapists.
- It is likely that pregnant women with Bruck syndrome have a risk of preterm birth, which is seen in osteogenesis imperfecta and other collagen disorders.

Acknowledgements The authors thank Sahar Mansour, Cleave Gass, Carolyn Johnston, Karen Light, Katherine Bell and Matthew Cauldwell, who were all involved in the clinical care of the patient.

Contributors SM and AJ were responsible for drafting of the text, sourcing and editing of clinical images, investigation results, drawing original diagrams and algorithms, and critical revision for important intellectual content. All authors gave final approval of the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Consent obtained directly from patient(s).

Provenance and peer review Not commissioned; externally peer reviewed.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

REFERENCES

1 Dhaubhadel S, Baniya B, Joshi H, *et al*. Bruck Syndrome: A Rare Disorder in New-Born with Fractures and Contractures. *J Nepal Paedtr Soc* 2017;37:276–9.
2 Moravej H, Karamifar H, Karamizadeh Z, *et al*. Bruck syndrome - a rare syndrome of bone fragility and joint contracture and novel homozygous FKBP10 mutation. *Endokrynol Pol* 2015;66:170–4.
3 Parvin S, Dhali A, Biswas DN, *et al*. Bruck syndrome: a rare cause of reduced fetal movements. *BMJ Case Rep* 2021;14:e246786.
4 Berg C, Geipel A, Noack F, *et al*. Prenatal diagnosis of Bruck syndrome. *Prenat Diagn* 2005;25:535–8.
5 Santana A, Oleas-Santillán G, Franzone JM, *et al*. Orthopedic Manifestations of Bruck Syndrome: a Case Series with Intermediate to Long-term Follow-Up. *Case Rep Orthop* 2019;2019:1–7.
6 Ruiter-Ligeti J, Czuzoj-Shulman N, Spence AR, *et al*. Pregnancy outcomes in women with osteogenesis imperfecta: a retrospective cohort study. *J Perinatol* 2016;36:828–31.

BMJ Case Rep: first published as 10.1136/bcr-2023-257696 on 10 September 2024. Downloaded from http://casereports.bmj.com/ on September 30, 2024 by guest. Protected by copyright.

Copyright 2023 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit
https://www.bmj.com/company/products-services/rights-and-licensing/permissions/
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:
- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

Customer Service
If you have any further queries about your subscription, please contact our customer services team on +44 (0) 207111 1105 or via email at support@bmj.com.

Visit casereports.bmj.com for more articles like this and to become a Fellow

BMJ Case Rep: first published as 10.1136/bcr-2023-257696 on 10 September 2024. Downloaded from http://casereports.bmj.com/ on September 30, 2024 by guest. Protected by copyright.