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SUCCESSFUL PREGNACY OUTCOME IN A CASE OF OSTEOGENESIS IMPERFECTA WITH HIPOPITUITARISMUS

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Abstract

Osteogenesis imperfecta (OI), first described in the seventeenth century is a rare inherited connective tissue disease, characterized by bone fragility, low bone mass and susceptibility to bone fractures with variable severity. Osteogenesis imperfecta (OI) or brittle bone disease is a phenotypically diverse disorder caused by deficiencies in the synthesis of type I collagen.

Case presentation

We present hereby a case of a pregnant woman with osteogenesis imperfecta and hypopituitarism. Pregnancy was achieved with IVF procedure and hypertension occurred in 32 gestational weeks of pregnancy. Multidisciplinary team approach was mandatory and resulted in the delivery of a live baby girl in 37 gestational weeks of pregnancy.

The successful outcome of this high-risk pregnancy and delivery can be attributed to collaboration between different specialty teams and planning for the known complications that may affect pregnancy and delivery in women with these genetic skeletal disorders.

Keywords: hypopituitarism, osteogenesis imperfecta, pregnancy, childbirth.

Introduction

Osteogenesis imperfecta (OI), first described in the seventeenth century is a rare inherited connective tissue disease. It is characterized by bone fragility, low bone mass and susceptibility to bone fractures with variable severity [1].

Women with osteogenesis imperfecta, most commonly type I, may have successful pregnancies, but their pregnancies usually are complicated by the many associated conditions seen in those with this disease. This is accompanied with an increased risk to both the mother and fetus. [2-3].

We hereby present a case of pregnant woman with OI and hypopituitarismus. Her case history includes pregnancy induced hypertension, status post IVF et ET (noeffect) whose care required a multidisciplinary team approach, and resulted in the delivery of a live baby girl.

Osteogenesis imperfecta (OI), or brittle bone disease, is a phenotypically diverse disorder caused by deficiencies in the synthesis of type I collagen.

It is the most common inherited disorder of connective tissue. OI principally affects bone, but also impacts other tissues rich in type I collagen (joints, eyes, ears, skin and teeth). It usually results from autosomal dominant mutations (more than 800 have been identified) in the genes that encode the α1 and α2 chains of type I collagen.

The fundamental abnormality in OI is too little bone resulting in extreme skeletal fragility. Other findings include blue sclera caused by decreased collagen content making the sclera translucent and allowing partial visualization of the underlying choroid hearing loss related to both a sensorineural deficit and impeded conduction due to abnormalities in the bones of the middle and inner ear and dental imperfections (small, misshapen, and blue- yellow teeth) secondary to a deficiency in dentin.

Osteogenesis imperfecta can be separated into four major clinical subtypes that vary widely in severity. The type 2 variant is at one end of the spectrum and is uniformly fatal in utero or during the perinatal period. It is characterized by extraordinary bone fragility with multiple intrauterine fractures. In contrast individuals with the type 1 form have a normal life span, but experience childhood fractures that decrease in frequency following puberty [4].

Advances in medicine mean that more women affected by skeletal disorders survive into their reproductive years, desire fertility and become pregnant. There is a need for serious consideration of pregnancy and preconception counseling. [5-6].

Women with osteogenesis imperfecta, most commonly type I, may have successful pregnancies [2-7].

The overall prevalence is 6 – 7 in every100,000 cases, and it affects 1 in every 20,000 or 1 in every 30,000 cases pregnant women [8,9].

Bisphosphonate therapy remains the mainstay of medical treatment in OI and has been shown to decrease bone pain, enhance well-being, improve muscle strength and mobility and decrease fracture incidence. [10]

The anesthesia team should be consulted during pregnancy regarding plans for delivery. [11]

It is of the utmost importance to seek anesthesiologic evaluation in early pregnancy, due to the possible challenges these patients may present [10]. In fact, general anesthesia could be complicated by intubation difficulties due to short neck, temporal and occipital pro ejections, and prominent mandible, while spinal anesthesia could be more challenging due to spinal deformities.[12].

Undesired pregnancies should be avoided entirely. Pregnancy in OI poses a major life- threatening risk to both mother and child [13].

Case presentation

We hereby present a case of pregnant woman with OI and hypopituitarism. Her case history includes pregnancy induced hypertension, status post IVF et ET (no effect), breech presentation of the baby, whose care required a multidisciplinary team approach. She was admitted to the University Clinic for Gynaecology and Obstetrics, Skopje in the 35th week of gestation to terminate her pregnancy and resulted in the delivery of a live baby girl in the 37 gestational weeks of pregnancy.

The patient was diagnosed by an endocrinologist as nanosomia at the age of 5 years. There is a positive family history of osteogenesis imperfecta in a cousin and the cousin's grandchildren.

Laboratory tests of growth hormone showed unmeasurable values. Magnetic resonance imaging of the pituitary gland was performed on the patient with a finding of empty cellar and with an ectopic neurohypophysis. Due to T4 (thyroxine) deficiency, therapy with Euthyrox tablets was started.

At the age of 13 an LHRH (luteinizing hormone-releasing hormone) test was performed with a low value, after which the induction of puberty began with ,FGem patches and then with contraceptives (Jasmin) which she received regularly.

Her medical history revealed several fractures in childhood leading to a diagnosis of OI based on the clinical picture and examination, showing vertebral densitometry-3,7; on the left femur=-0.2; on the right femur=-0.4.

Treatment with growth hormone masked the picture and prevented the occurrence of fractures. However, in puberty the patient developed a curvature of the lower legs (microfractures or insufficient calcium deposit in the grown bone due to a mild form of osteogenesis imperfecta type 1).

This curvature of the lower legs was first noticed at the age of 12 which is very typical for osteogenesis imperfecta in children, so a detailed examination of the skeleton was made. Examination showed decreased bone density with typical curvature of the tibia and fibula.

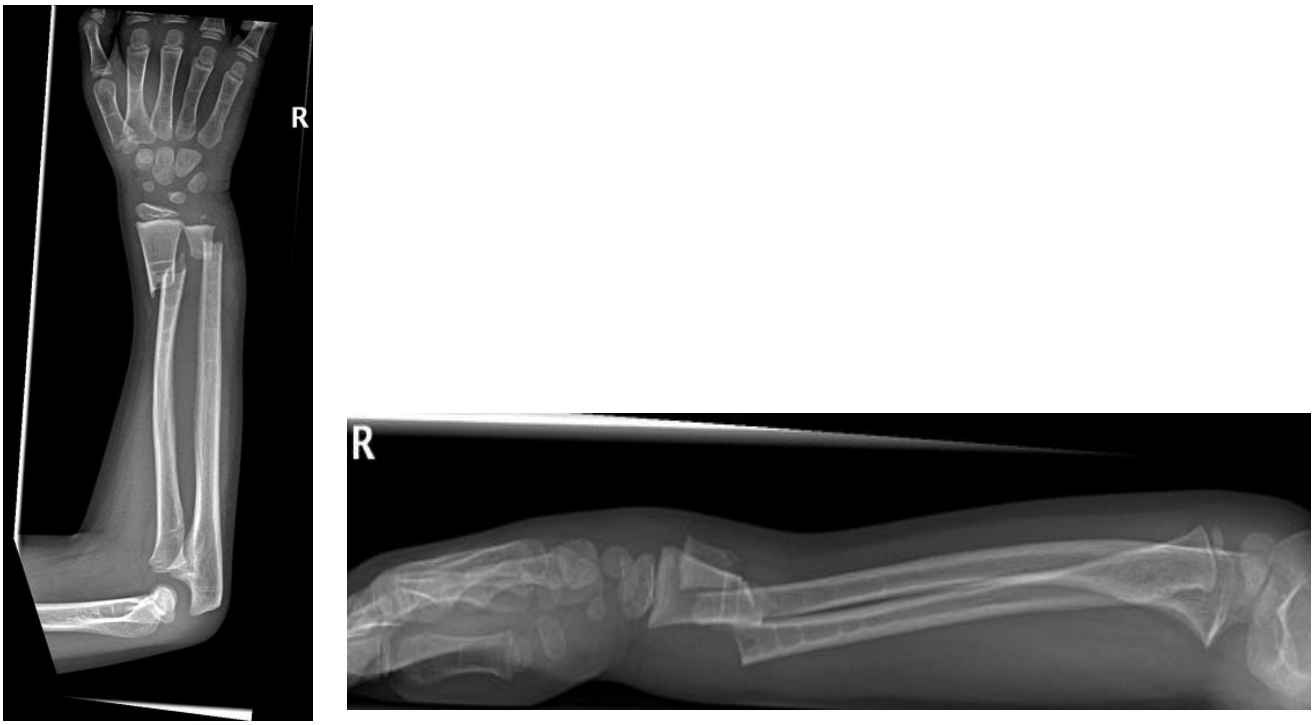

Figure 1. Distal radius fracture

Fractures of the patient from puberty onwards include: in 2014 fraktura radii lateralis sinistri partus distalis, in 2015 conquasation digiti IV-V manii dextri, fraktura phalangis distalis digiti mani IV lateralis dextri et contusion reg.phalangis digiti minimi lateralis dextri, in 2017 fractura radii dextri partus distalis et processus styloideus ulnae dextra, which was conservatively resolved with plaster immobilization.

Because of the hypopituitarism it was decided to give several doses of bisphosphonates.

The pregnancy was conceived with IVF procedure and went uneventful until 32 gestational weeks, when mild hypertension occurred.

At admission she had 153 cm height and 75 kg weight. It has blue sclera and triangular face which are characteristics of osteogenesis imperfecta. She had no scoliosis or kyphosis, and her cardiovascular examination was normal. Her abdominal examination revealed a uterus the size of a 37-week gestation.

A multidisciplinary team was involved in the management. The team included a specialist in obstetrics and gynecology, endocrinologist, pediatricians, anesthetists and midwives.

All necessary clinical and laboratory tests were performed on the patient according to protocol. After being admitted for a cesarean section, the patient was hemodynamically stable. Laboratorial examination such as CBC, renal function, blood glucose levels, and clotting factors did not show abnormalities. Also, feto-placental unit was monitored.

Preoperatively, the patient was prescribed antihypertensive, neuroprotective, hormonal and vitamin therapy.

Due to the complexity of diagnoses the patient was assigned for surgical termination of pregnancy, with transverse lower segment elective caesarean section under spinal anesthesia, at 37 weeks. The patient gave birth to a female fetus with a birth weight of 2950 g and a height of 49 cm.

The operative course went smoothly. Postoperatively, the patient was prescribed double antibiotic, antihypertensive, substitution therapy including one unit of SSP and one unit of human albumin 20%, uterotonic, rehydration, thromboprophylaxis and symptomatic therapy.

The baby was admitted to the neonatal intensive care unit and was being monitored by neonatologist. Genetic testing for OI was recommended.

Discussion

OI is a disease characterized by brittle bones and frequent fractures with minimal trauma leading to skeletal deformities. Type I is the most common subtype accounting for 60% of OI cases. It is also the mildest form. Type II accounts for 20% of OI cases and is the most severe and is lethal. Type III is severe and progressive and accounts for 20% of OI cases. It can be a result of germ cell mosaicism in 6% of cases. Type IV is the least common and is intermediate in its severity. [14]

Severe OI can lead to significant limb and spinal deformities leading many of those affected by OI type III to be wheelchair bound by the time they reach adulthood. Only a third of those with OI type III will survive into their adult years. [15].

Pregnancy in women with OI is complicated by the many associated conditions seen in those with this disease. Abnormal coagulation increases the risks of blood loss and hemorrhage during delivery. The heart muscle is made of type I collagen leading to an increased prevalence of cardiac abnormalities and congenital heart disease in individuals with OI. Collagen is imperative to wound healing, and this process can be impaired in individuals with OI. [16]. Kyphoscoliosis and severe chest wall deformities may lead to cardiorespiratory complications. [17].

Up to 35% of those with OI will have hypertension, and a small case series found a 20% rate of pre-eclampsia in pregnant women with OI. Due to immobility women with OI are more likely to develop

venous thrombosis during the hyper-coagulable state of pregnancy. This complication occurred in our described case during the postpartum period. Severe back and musculoskeletal pain is common in pregnancies affected by maternal OI with 13% having pain severe enough to disrupt their daily lives. Pregnancy does not increase the risk of fractures for individuals with OI. [18].

Many women with Osteogenesis Imperfecta (OI) have children without any significant problems in pregnancy. But there are a few things to consider, and planning can make things much easier. The main things to consider are: the best time for you to become pregnant, how your body will manage to carry a baby, what the best delivery options are and whether your baby will have OI type 1. 2. 3. 4. 5.

In general, decisions about the best mode of delivery i.e. vaginal vs. cesarean should be made on an individual basis. There is no definitive research data showing that cesarean delivery is safer than vaginal delivery in women with OI who have normal pelvic dimensions, nor no other significant complications. A recent study (Cubert) found evidence that cesarean delivery did not decrease fracture rates at birth in infants with non-lethal forms of OI nor did it prolong survival for those with more severe forms.

Some physicians believe it is appropriate to assess the degree of mineralization of the baby's skull when planning the mode of delivery. Theoretically, there is an increased risk of central nervous system injury with vaginal delivery when the baby's skull is poorly mineralized. Most cesarean deliveries in a recent study were done for the usual obstetric indications. [19].

Some physicians might consider a planned cesarean section if a woman has a history of pelvic fractures or contracted pelvis, if the woman has a severe form of OI, or if other significant complications are present. Some of the complications that have been reported during delivery include a birth canal that is too small to permit birth, uterine rupture and hemorrhage.

Women at greatest risk for bleeding are those with a history of recurrent nosebleeds, easy bruising, or excessive bleeding following previous surgical procedures. Though uterine rupture has been reported to occur (Carlson), it does not appear to be a frequent complication. Because some people with OI may be at increased risk for hyperthermia i.e. an increase in body temperature in response to anesthesia some physicians might consider spinal or epidural anesthesia to be the safest approach.

Also, it has been shown that by checking the values of calcium, phosphate, vitamin D, parathyroid hormone, LDH,CK, CRP, kidney and liver function tests by a 3-month laboratory analysis would help the management of treatment.[4]

Bisphosphonates and Pregnancy

Bisphosphonate therapy remains the mainstay of medical treatment in OI and has been shown to decrease bone pain, enhance well-being, improve muscle strength and mobility plus a decrease in the incidence of fractures.

In pregnancy bisphosphonates should not be used and women should not become pregnant while they are taking Bisphosphonates. Babies can be born with bone problems or low calcium levels.

There is no good evidence to decide which Bisphosphonate is better to use in women who might want to have a baby soon i.e. Pamidronate, Zoledronate and Risedronate. Ideally patient should stop Bisphosphonates about a year before becoming pregnant. Unplanned pregnancies happen, and problems are very rare.

Conclusion

The pregnancy of a patient with a diagnosis of osteogenesis imperfecta is a complicated process physically and psychologically. It carries an elevated risk to both mother and child, and should be managed by a multidisciplinary team.

Optimal management of OI requires a multidisciplinary approach involving a pediatrician, endocrinologist, rehabilitation specialist, orthopedic surgeon, dentist, geneticist, social worker/psychologist, physiotherapist and occupational therapist.

The concern of transferring defective genetic structures to the next generation are the problems that can be seen during the pregnancy of an OI patient i.e. difficulty of carrying pregnancy due to anatomic deformity, frequent gestational complications such as antepartum bleeding, abruptio placentae, preterm labor, intrauterine growth restriction, frequent labor complications such as bleeding, uterine atony, stress fractures, thromboembolism and anesthesia risks.

Due to advances in neonatal care, prenatal diagnostics and artificial reproductive techniques women affected by skeletal disorders now survive into their reproductive years, desire fertility and become pregnant.

The successful outcome of this high-risk pregnancy and delivery can be attributed to a collaboration between different specialty teams and planning for the known complications that may affect pregnancy and delivery in women with these genetic skeletal disorders.

References:

1. Sillence D. O., Senn, A., & Danks, D. M. (1979). Genetic heterogeneity in osteogenesis imperfecta. Journal of medical genetics, 16(2), 101–116. https://doi.org/10.1136/jmg.16.2.101
2. Lyra TG, Pinto VA, Ivo FA, Nascimento J dos S. Osteogenesis imperfecta in pregnancy. Case report. Rev Bras Anestesiol. 2010 May-Jun; 60(3):321-4, doi: 10.1016/S0034-7094(10)70040-4. PMID: 20682164.
3. Shulman, Rachel & Ellis, Jane & Shore, Eileen & Kaplan, Frederick & Badell, Martina. (2015). Maternal Genetic Skeletal Disorders: Lessons Learned From Cases of Maternal Osteogenesis Imperfecta and Fibrodysplasia Ossificans Progressiva. Journal of Clinical Gynecology and Obstetrics. 4. 184-187. 10.14740/jcgo306w.
4. Kumar V, Abbas A, Aster J. 9th ed., Philadelphia, PA: Elsevier; 2015. Robbins and Cotran pathologic basis of disease. p. 1203. p. ISBN 978-1-4557-2613-4.
5. Chamunyonga F, Masendeke KL, Mateveke B. Osteogenesis imperfecta and pregnancy: a case report. J Med Case Rep. 2019 Dec 11;13(1):363. doi: 10.1186/s13256-019-2296-0. PMID: 31822291; PMCID: PMC6905103.
6. Ruiter-Ligeti J, Czuzoj-Shulman N, Spence AR, Tulandi T, Abenhaim HA. Pregnancy outcomes in women with osteogenesis imperfecta: a retrospective cohort study. J Perinatol. 2016 Oct;36(10):828-31. doi: 10.1038/jp.2016.111. Epub 2016 Jul 21. PMID: 27442154.
7. Cunningham F, & Leveno K.J., & Bloom S.L., & Dashe J.S., & Hoffman B.L., & Casey B.M., & Spong C.Y.(Eds.), (2018). Williams Obstetrics, 25e. McGraw Hill. https://accessmedicine.mhmedical.com/content.aspx?bookid=1918&sectionid=185041518.
8. McCarthy E. F. (2011). Genetic diseases of bones and joints. Seminars in diagnostic pathology, 28(1), 26–36. https://doi.org/10.1053/j.semdp.2011.01.004.
9. Chetty, S. P., Shaffer, B. L., & Norton, M. E. (2011). Management of pregnancy in women with genetic disorders, Part 1: Disorders of the connective tissue, muscle, vascular, and skeletal systems. Obstetrical & gynecological survey, 66(11), 699–709. https://doi.org/10.1097/OGX.0b013e31823cdd50.
10. Biggin, A., & Munns, C. F. (2014). Osteogenesis imperfecta: diagnosis and treatment. Current osteoporosis reports, 12(3), 279–288. https://doi.org/10.1007/s11914-014-0225-0.
11. Murray, S., Shamsuddin, W., & Russell, R. (2010). Sequential combined spinal-epidural for caesarean delivery in osteogenesis imperfecta. International journal of obstetric anesthesia, 19(1), 127–128. https://doi.org/10.1016/j.ijoa.2009.07.009.

12. Cozzolino, M., Perelli, F., Maggio, L., Coccia, M. E., Quaranta, M., Gizzo, S., & Mecacci, F. (2016). Management of osteogenesis imperfecta type I in pregnancy; a review of literature applied to clinical practice. Archives of gynecology and obstetrics, 293(6), 1153–1159. https://doi.org/10.1007/s00404-016-4012-2.
13. Ruiter-Ligeti, J., Czuzoj-Shulman, N., Spence, A. R., Tulandi, T., & Abenhaim, H. A. (2016). Pregnancy outcomes in women with osteogenesis imperfecta: a retrospective cohort study. Journal of Perinatology, 36(10), 828-831.
14. McCarthy E. F. (2011). Genetic diseases of bones and joints. Seminars in diagnostic pathology, 28(1), 26–36. https://doi.org/10.1053/j.semdp.2011.01.004.
15. Parasuraman, R., Taylor, M. J., Liversedge, H., & Gilg, J. (2007). Pregnancy management in type III maternal osteogenesis imperfecta. Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology, 27(6),619–621. https://doi.org/10.1080/01443610701546292.
16. Zhao, X., & Yan, S. G. (2011). Recent progress in osteogenesis imperfecta. Orthopaedic surgery, 3(2), 127–130. https://doi.org/10.1111/j.1757-7861.2011.00128.x
17. Parasuraman, R., Taylor, M. J., Liversedge, H., & Gilg, J. (2007). Pregnancy management in type III maternal osteogenesis imperfecta. Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology, 27(6), 619–621. https://doi.org/10.1080/01443610701546292.
18. Litos, M., Michala, S., & Brown, R. (2008). Osteogenesis imperfecta and pregnancy. European journal of obstetrics, gynecology, and reproductive biology, 136(1), 126–127. https://doi.org/10.1016/j.ejogrb.2006.09.003.
19. Cubert, R., Cheng, E. Y., Mack, S., Pepin, M. G., & Byers, P. H. (2001). Osteogenesis imperfecta: mode of delivery and neonatal outcome. Obstetrics and gynecology, 97(1), 66–69. https://doi.org/10.1016/s0029-7844(00)01100-5.