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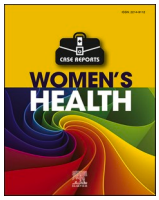

Postpartum multiple vertebral fractures in a patient with osteogenesis imperfecta type I: A case report and literature review

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ABSTRACT

A 39-year-old woman with type I osteogenesis imperfecta reported experiencing back pain at 35 weeks of gestation. Two days following an elective cesarean section, the patient developed a Th12 vertebral compression fracture; 3 weeks postoperatively, she sustained an L3 vertebral compression fracture. The patient displayed a lumbar spine *Z*-score of −1.7; she subsequently discontinued breastfeeding, and treatment with active vitamin D was initiated. Genetic testing confirmed a diagnosis of osteogenesis imperfecta.

1. Introduction

Osteogenesis imperfecta (OI) is an inherited disorder of the skeletal system characterized by connective tissue abnormalities and generalized bone fragility, including fractures and bone deformities. Approximately 85–90 % of patients with OI have heterozygous mutations in the genes encoding type I collagen, namely COL1A1 or COL1A2, which correspond to the α1(I) and α2(I) chains of type I collagen, respectively. The remaining 10–15 % have recessive mutations, primarily in various other genes, and, to date, more than 24 genes have been identified as causes of OI [1]. As type I collagen is the major structural protein (94 %) of the pre-calcified bone matrix, the abnormal synthesis of type I collagen reduces bone mass and increases susceptibility to fractures [1]. Other clinical features of OI may involve extra-skeletal tissues and organs, such as blue sclera, dentin dysplasia, and post-pubertal deafness [2].

Pregnancy- and lactation-associated osteoporosis (PLO) is a rare condition that presents with back pain and multiple vertebral fractures during late pregnancy or the early postpartum period. This phenomenon was first described by Nordin and Roper (1955). The incidence of PLO is estimated to be about 0.4 to 0.5 per 100,000 women [3]. PLO is associated with a high risk of osteoporosis during the postpartum period; however, the pathophysiology of this disorder remains unknown [3]. The contributing factors reportedly include increased bone metabolism to meet fetal calcium requirements, elevated serum parathyroid hormone-related peptide (PTHrP), relative hypoestrogenemia, high prolactin levels during lactation, and genetic predisposition [4]. The risk factors for postpartum osteoporosis include amenorrhea, oral contraceptive use, suppressive levothyroxine treatment, anorexia nervosa, and corticosteroid therapy [4]. Patients with OI have a reduced bone mineral density (BMD) [5], which is considered a risk factor for PLO [4]. There are few reports of PLO in patients with OI, and little is known about the risk factors for fractures and their management during pregnancy or the postpartum period. Herein, we report the case of a patient with type I OI who developed multiple spinal fractures during the postpartum period.

2. Case Presentation

A 39-year-old woman (gravida 3, para 0) had a successful pregnancy following in vitro fertilization–embryo transfer. She had experienced 10 fractures during childhood, had blue sclera and deafness, and was clinically diagnosed with OI (Sillence type I) characterized by these specific features. The patient's mother was also suspected of having OI but declined genetic testing. The patient's height, weight, and body mass index prior to pregnancy were 151 cm, 54 kg, and 23.6 kg/m^2, respectively. She had no history of smoking, alcohol consumption, or steroid medication use.

The course of pregnancy was uneventful but the patient had been experiencing back pain since 35 weeks of gestation, although this is a common complaint among pregnant women. To avoid injury to both mother and child during delivery, an elective cesarean section was performed at 38 weeks and 4 days of gestation. She delivered a female baby weighing 3152 g, with Apgar scores of 8/9 and an umbilical artery

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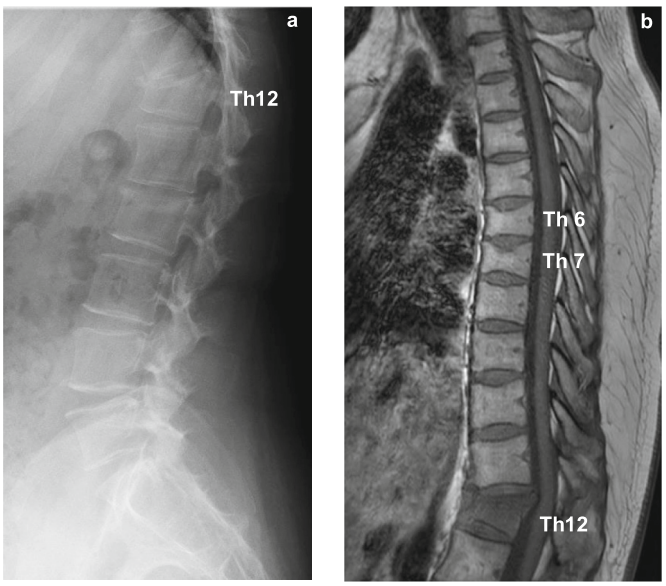

Fig. 1. Vertebral fracture imaging. (a) Lateral radiograph of the lumbar spine showing a fracture of the Th12 vertebra. (b) T1-weighted magnetic resonance image showing the presence of a compression fracture at Th12, along with pre-existing fractures of Th6 and Th7.

Table 1
Laboratory findings at the time of diagnosis.

	Results	Reference Ranges
Calcium	9.0	8.8–10.1 mg/dL
Phosphorus	4.3	2.7–4.6 mg/dL
Albumin	3.2	4.1–5.1 g/dL
Parathyroid hormone	29	10–65 pg/mL
25-hydroxy vitamin D	18.2	>20 ng/mL
Thyrotrophin	1.625	0.35–4.94 μIU/mL
Free triiodothyronine	2.38	1.68–3.67 pg/mL
Free thyroxine	0.96	0.70–1.48 ng/dL

blood pH of 7.33.

On the second postoperative day, the patient suddenly developed severe back pain. Lumbar spine radiography revealed a fresh compression fracture of Th12 (Fig. 1), and magnetic resonance imaging revealed pre-existing fractures of Th6 and Th7 (Fig. 1). Blood tests indicated normal levels of parathyroid hormone-C and intact parathyroid hormone, thyroid stimulating hormone, free T4, and calcium, though 25-hydroxy vitamin D was mildly low (18.2 ng/mL) (Table 1). Considering the risk of further fractures, the patient chose to discontinue breastfeeding. Both the mother and the baby were discharged on the seventh postoperative day. Dual-energy X-ray absorptiometry (DXA) revealed a lumbar spine *Z*-score of −1.7. Three weeks after delivery, the patient experienced back pain while caring for her child and was diagnosed with a new compression fracture of L2 via lumbar spine radiography. Genetic counseling and subsequent genetic testing revealed a pathological variant of COL1A1. Vitamin D supplementation was initiated for the patient.

3. Discussion

OI is an inherited disorder of the skeletal system, characterized by connective tissue symptoms, fractures due to generalized bone fragility, and bone deformities. Sillence classified OI into four types, ranging from mild to fatal, based on clinical and radiographic features [6]. Type I OI, the mildest form, is associated with quantitative defects in structurally normal collagen. In contrast, the lethal (type II), severe (type III), and moderate (type IV) forms involve mutations that alter collagen structure [6,7].

The incidence of deliveries by patients with OI is low, at approximately 1 in 25,000 deliveries [8], with most cases attributed to type I OI [2]. Pregnant women with OI are reported to have nearly double the incidence of antepartum hemorrhage, premature placental abruption, preterm delivery, and fetal growth restriction compared to those without OI [8]. Infants with non-fatal OI are also commonly reported to sustain fractures at birth, which can increase the incidence of neonatal complications and the need for specialized neonatal care [9]. OI is also a risk factor for PLO owing to its association with low BMD and increased bone fragility [10,11]. However, because of the low frequency of the disease, little is known about the risk factors and treatment of PLO in patients with OI.

In a large study of 205 pregnancies and deliveries in Danish women with OI, there was no increased risk of fracture after pregnancy compared with before pregnancy. However, this study did not include data on BMD or calcium levels [12]. In a retrospective study of 50 women with OI and 83 pregnancies, Koumakis et al. found that 12 patients experienced fractures during pregnancy or within 6 months postpartum and all of these patients had low pre-pregnancy BMD. Nearly all fractures during pregnancy and in the postpartum period in women with type I OI were associated with reduced BMD (Table 2).

Most of these fractures occur during the postpartum period and are associated with breastfeeding. Vertebrae are the most common fracture sites, with scattered cases of multiple fractures. This differs from the most frequent fracture sites during pregnancy, the proximal femur (25 %) and pelvis (25 %) [2]. Currently, there are no reliable predictors of fractures during pregnancy or the postpartum period in women with OI. However, low lumbar spine BMD before pregnancy may serve as a marker for predicting vertebral fractures during this period. Since pre-pregnancy BMD values were not measured in most cases, it is unclear whether the BMD decline was pre-existing or was pregnancy induced. Additionally, it is important to note that assessing osteoporosis in patients with OI using DXA has certain limitations [13,14]. Given that most fractures occur during the third trimester and postpartum period [3], lifestyle guidance to prevent fractures, such as avoiding load-bearing activities, may also be crucial. When lower back pain is reported during pregnancy and the postpartum period, as in the present case, the possibility of a vertebral fracture should be considered, and a radiological examination should be performed to assess the presence of a fracture.

It is still unclear whether pharmacotherapy for PLO is superior to conservative management, because of the lack of controlled comparisons [15,16]. It is suggested that pharmacological therapy for PLO should be reserved for severe cases with multiple vertebral fractures, persistent disabling pain, or in patients who do not show satisfactory recovery of BMD after adequate calcium and vitamin D supplementation [3,15]. The discontinuation or avoidance of breastfeeding should be encouraged to prevent further bone loss and allow for natural recovery [15].

Bisphosphonates are the standard therapy for controlling bone resorption in patients with moderate or severe OI [1], although they are generally contraindicated for women of reproductive age. Administration of pamidronate before pregnancy may alter fetal bone formation and reduce the amount of resorbable bone calcium available to the fetus during late pregnancy [17]. However, recent studies have suggested that women with OI (type I or IV) who received pamidronate before pregnancy showed no adverse maternal or fetal effects [17] [18]. Teriparatide, a 1–34 fragment of the parathyroid hormone, has been reported to have anabolic and fracture-preventive effects in osteoporotic patients [13] and may produce superior BMD increases compared with calcium and vitamin D alone [19]. Teriparatide shows a positive skeletal effect in patients with type I OI and so may be an attractive treatment option, especially in cases of high vertebral fracture risk or bisphosphonate intolerance [13]. However, it shows no benefit in patients with the more severe types III and IV OI [13].

Table 2
Cases of type I OI with fractures during pregnancy and postpartum, or diagnosed with osteoporosis.

Report	Age	Bone densitometry (*Z*-score)	Term of fracture/ osteoporosis	Fracture/osteoporosis localization	Breastfeeding (months)	Risk factors for osteoporosis	Treatment
[7]	21	N/A	33 weeks	Ankle	N/A	No	N/A
[15]	25	Spine −4.0	Back pain began in the 3rd trimester	Old fractures (ribs, lumbar vertebras)	3	No	Intranasal calcitonin, alendronate, elementary calcium, and vitamin D
[10]	32	N/A	3rd trimester (pain in right hip)	Hips (Transient osteoporosis)	3	No	Bisphosphonate (pamidronate), calcium and vitamin D
[2] P2.1	32	Spine −2 Hip −1.1	3rd trimester	Sacrum	1	Anorexia, poor calcium intake	N/A
[2] P3	36	Spine-2 hip-1.2	Pregnancy term	Ribs	No	smoking	N/A
[2] P4	26	Spine-0.4 hip-1	30 weeks	Femoral head, trochanter in post-partum	6	No	N/A
[2] P5	36	Spine-3.3 hip-2.6	3rd trimester	Femoral neck	4	No	N/A
[2] P7.1	39	Spine-3.7 hip-2.7	2 M post -partum	Th10	18	No	N/A
[2] P8	29	NA	1.5 M post- partum	T8	1.5	Smoking	N/A
[2] P11	31	Spine-3	6 M post- partum	Femoral head	6	No	N/A
[2] P12	31	Spine-5.5	6w post- partum	Th11 Th2 L1	1.5	AS	N/A
[11]	32	BMD 52 %	2 M post- partum	Th11, 12, L1, L2, L3	5	No	Bisphosphonate, calcium, vitamin D
[19] Case 3	19	Spine −7.8 Femoral neck −4.1 hip −4.4	4 M post-partum	T6, T8	4	Ex-smoker, low vitamin D, BMI 18.5	Risedronate
Present case	39	Spine −1.7, Femoral neck −1.7	2 days post- partum	Th12, L2	N/A	No	Vitamin D

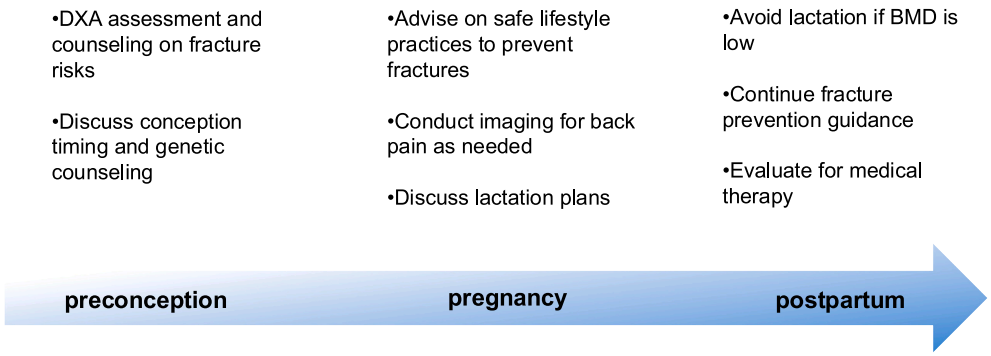

Fig. 2. Management of women with type I OI during the preconception, pregnancy, and postpartum periods.

In cases of PLO, a decrease in BMD is typically reversible, and BMD recovery can be expected upon discontinuation of breastfeeding. However, women with a genetic predisposition may face a risk of recurrent fractures in subsequent pregnancies [20]. For patients with type I OI considering another pregnancy, it is essential to confirm that adequate BMD recovery has occurred and to ensure they are fully informed of the risk of fractures during pregnancy.

Pregnancies in patients with OI are still underreported, and knowledge of perinatal management is limited. However, with advancements in pediatric care, the life expectancy of patients with OI is increasing [2], and the number of pregnancies and childbirths in women with OI is expected to rise. Preventing fractures during pregnancy and the postpartum period is crucial because such fractures can significantly reduce quality of life (Fig. 2). Patients with OI who wish to become pregnant should undergo BMD measurement before conception. If BMD is low, careful perinatal management is necessary to reduce the risk of fractures during late pregnancy and the postpartum period.

Contributors

Yumiko Miyazaki contributed to conception of the case report, acquiring and interpreting the data, drafting the manuscript and undertaking the literature review.

Mizuki Hosokawa and Sho Kudo contributed to patient care and revising the article critically for important intellectual content.

Toshimichi Onuma and Makoto Orisaka contributed to patient care, conception of the case report, and revising the article critically for important intellectual content.

Yoshio Yoshida contributed to conception of the case report, and revising the article critically for important intellectual content.

All authors approved the final submitted manuscript.

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Patient consent

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Provenance and peer review

This article was not commissioned and was peer reviewed.

Conflict of interest statement

The authors declare that they have no conflict of interest regarding the publication of this case report.

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