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Progressive idiopathic juvenile osteoporosis in pregnancy: A case report of two successive pregnancies in the same woman

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ABSTRACT

A 33-year-old primiparous woman with progressive idiopathic juvenile osteoporosis (IJO) who had had multiple vertebral compressions and bilateral femoral neck fractures since the age of 15 years presented for perinatal management at 11 weeks of gestation. Her vertebral bone mass was 0.634 g/cm^2 before pregnancy. The target calcium intake was set at 800 mg/day. Cephalopelvic disproportion led to the patient having an elective cesarean section at 39 weeks 3 days of gestation and she delivered a female infant weighing 2785 g. After the delivery, her vertebral bone mass had increased to 0.700 g/cm^2. At 34 years of age, she conceived her second child. With similar perinatal management, she delivered a female infant weighing 2580 g at 38 weeks of gestation by elective cesarean section. Her vertebral bone mass had increased again after the second pregnancy. Few cases of pregnancy complicated by progressive IJO have been reported. However, an uneventful pregnancy course can be expected with proper management, and pregnancy can be a good opportunity to increase bone mass.

1. Introduction

Osteoporosis in young people may occur secondary to Cushing's syndrome, homocystinuria, hyperthyroidism, hyperparathyroidism, or steroid use. Idiopathic juvenile-onset osteoporosis differs from regressive osteoporosis in postmenopausal and elderly patients. Idiopathic juvenile osteoporosis (IJO) is a rare disease that develops in prepuberty and can typically result in fractures of the vertebral body due to bone mineral loss [1].

IJO typically develops in prepuberty in the vertebral body or femoral neck and may result in fractures due to bone mineral loss. Although IJO usually resolves in puberty, it can be progressive in some cases [2,3]. The first case of progressive IJO in Japan was reported in 1986 in a 31-year-old man who had developed the disease at 16 years of age [4]. Similar cases have been reported since then. In patients with prolonged or progressive IJO, bisphosphonates may be administered to minimize bone deformity, but the optimal treatment strategy has not been determined. Moreover, no definitive guideline has been established for the management of pregnant women with progressive IJO. Herein, we report the case of a patient with progressive IJO who gave birth to two offspring and discuss the management strategy used during pregnancy.

2. Case Presentation

A 33-year-old primigravida presented to the department of obstetrics and gynecology for perinatal management at 11 weeks of gestation. She had no significant family history of osteoporosis or metabolic disorders. She was known to have progressive idiopathic juvenile osteoporosis. Her first fracture-related symptoms were bilateral femoral neck and rib fractures caused by sneezing at the age of 15 years. She was referred for orthopedic evaluation. No underlying disease that could cause secondary osteoporosis could be identified, and a diagnosis of IJO was made. Throughout adolescence she experienced multiple vertebral compressions (Fig. 1). At the age of 18 years, she underwent a bilateral femoral neck fusion. Several medications, including bisphosphonates, elcatonin, and vitamin D derivatives, were prescribed for the treatment of osteoporosis. She was taking sodium alendronate when she conceived her first child. The vertebral (L2–L4) bone mass was maintained between 0.610 and 0.679 g/cm^2 pre-pregnancy. The patient was 136.4 cm tall and weighed 38.7 kg (39.0 kg before pregnancy) at her first antenatal visit. No abnormal findings were noted on haematological or biochemical assessment. Vertebral bone mass 1 year before pregnancy was 0.634 g/cm^2. Ultrasonography revealed that the gestational age of the fetus was appropriate. Alendronate therapy was discontinued and a calcium intake of 800 mg/day was achieved through milk and supplements. Vitamin D supplements were not given as she regularly consumed fish with high vitamin D levels. Fetal growth was appropriate during pregnancy. At the 19th week of gestation, the patient sustained a right femoral subtrochanteric fracture due to a fall and was admitted

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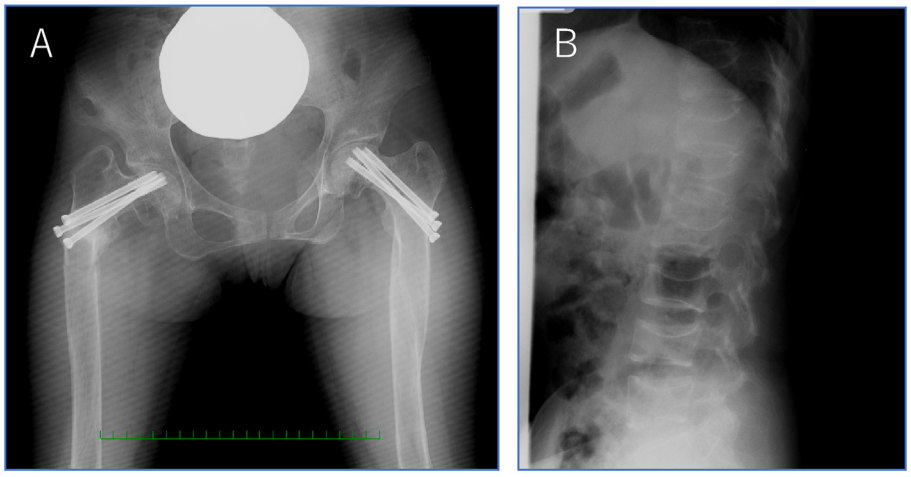

Fig. 1. Plain radiographs of the patient before pregnancy. A) Posteroanterior view of the pelvis. B) Sagittal view of the spine. Bilateral femoral neck (A) and multiple previous vertebral compression fractures (B) are also shown.

to a nearby orthopedic hospital until the 27th week of gestation. The urinary cross-linked N-telopeptide of type I collagen (uNTx) value during pregnancy ranged from 17.7 to 52.7 nmol bone collagen equivalents/creatinine (BCE/Cr), indicating that she had maintained a lower uNTx value than normal during the second trimester (m = 166 nmol BCE/Cr, m − 1.5SD = 44.5 nmol BCE/Cr) [5].

The patient underwent an elective cesarean section at 39 weeks 3 days of gestation because of cephalopelvic disproportion. This was determined on the basis of positive Seitz's method findings, short stature, and limitation of hip abduction due to bilateral femoral neck fractures. She delivered a female infant weighing 2785 g, with Apgar scores of 8 at 1 min and 9 at 5 min. The baby showed no notable abnormalities.

Breastfeeding was discontinued 2 weeks after delivery and replaced with formula in accordance with prior consent, and menstruation resumed around 2 months after delivery. The vertebral (L2–L4) bone mass at 1 month postpartum was 0.700 g/cm^2, which was higher than the value before pregnancy by 0.066 g/cm^2, but decreased to 0.642 g/cm^2 at 4 months postpartum, and bisphosphonate administration was resumed (Fig. 2).

The second pregnancy was achieved in a natural cycle, 6 months postpartum after the first pregnancy. Her first antenatal visit was at 5 weeks 5 days of gestation. Bisphosphonate administration was discontinued, and the same nutritional guidance was given as for the first pregnancy. During the second pregnancy, the uNTx values remained low, as in the first pregnancy. She had an unremarkable pregnancy course and delivered a female infant weighing 2580 g at 38 weeks 0 day of pregnancy by elective cesarean section. The vertebral bone mass was 0.671 g/cm^2 at 1 week postpartum, which was higher than the value before pregnancy (0.642 g/cm^2). After the second delivery, bisphosphonate administration was resumed, and the patient was followed up by the department of orthopedics. Her vertebral bone mass showed a slight decrease to 0.664, 0.660, and 0.651 g/cm^2 at 6, 10, and 22 months postpartum, respectively. Thus, a higher level than that before the first pregnancy was still maintained.

3. Discussion

A meta-analysis by Karlsson et al. indicated that, in healthy women, vertebral and femoral neck bone mineral contents decrease by approximately 5% after pregnancy compared with before pregnancy [6], but the effect of pregnancy on bone mass is complex. During pregnancy, an additional 320-mg/day calcium is required for loss due to fetal calcium supply and increased urine output compared with the non-pregnant state. However, the intestinal calcium absorption increases from approximately 25% in non-pregnancy to 50% during pregnancy [7], so calcium can be supplied to the fetus and the calcium loss can be compensated owing to the increased renal blood flow with adequate calcium intake. Estrogen derived from the placenta and adipose tissue, and the load on the bones due to the increase in the weight of the mother are also factors that increase bone mass during pregnancy.

During pregnancy, bone turnover is high, providing a favorable opportunity to increase bone mass with proper management. The average recommended daily calcium intake for adult pregnant and lactating women is 1000 mg [7]. However, women of reproductive age in Japan have a calcium intake of only 428–446 mg/day [8], indicative of chronic calcium deficiency. In this case, the patient was managed with calcium intake of approximately 800 mg/day from milk and supplements aside from meals.

The patient in this case regularly consumed fish with high levels of vitamin D. During the management of her pregnancy, 25-hydroxyvitamin D [25-(OH) D] blood concentration measurement was

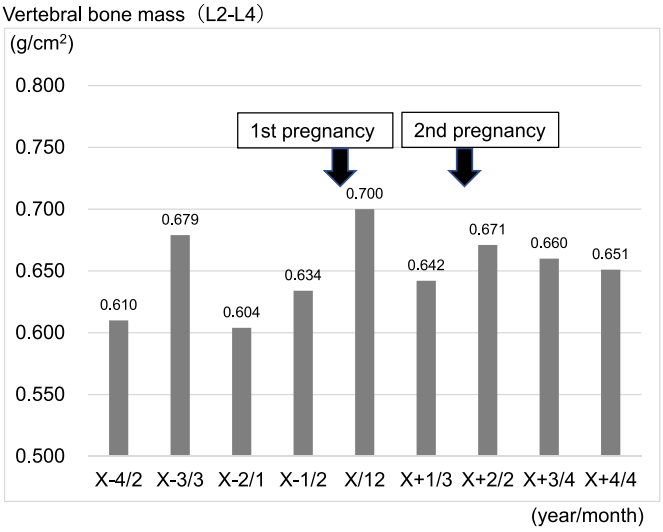

Fig. 2. Vertebral (L2–L4) bone mineral mass before and after the first and second pregnancies. The unit of the horizontal axis is year/month, where X/0 indicates the time of the patient's presentation to the department of obstetrics and gynecology for perinatal management at 11 weeks of gestation.

not covered by public insurance, so we refrained from continuous vitamin D product administration. Prescribing vitamin D derivatives might be useful for pregnant women with osteoporosis while monitoring maternal serum 25-(OH) D levels.

Lactation is known to be associated with decreased bone volume. The amount of bone mineral in breastfeeding women decreases by approximately 5% at 6 months after delivery [9] and tends to recover with resumption of menstruation, returning to the pre-pregnancy state 6 to 18 months after delivery [10]. In this case, the physician in charge discussed breastfeeding with the couple during pregnancy and decided to restrict breastfeeding to only the first 2 weeks, although the optimal term of lactation and time to resumption of menstruation for women with osteoporosis need further study.

Few cases of pregnancy have been reported among patients with IJO; some of these cases showed 25% decreased post-pregnancy vertebral bone mass [11]. The safety of pregnancy and delivery are not clear, and no management guidelines have been established. The patient had received various medications for osteoporosis prior to conception, but without significant results.

Although bisphosphonates are one of the most effective class of drugs for osteoporosis, they are not generally administered to young or infertile women. In this case, alendronate was administered until conception because the patient did not wish for a baby and alendronate has relatively few side-effects. The medication was stopped immediately after the patient noticed conception, and she was not given the widely used medications for the treatment of osteoporosis, such as bisphosphonate or denosumab, during pregnancy because they are contraindicated for pregnant women. In spite of the expected risk of bone loss, increased bone mass was observed during pregnancy owing to the physiological effect of pregnancy, adequate calcium intake, and minimized lactation.

In conclusion, our patient with progressive IJO was successfully managed during two pregnancies. Although pregnancy-induced bone volume loss is a concern in women with osteoporosis, the present case suggests that pregnancy is not necessarily a risk factor for bone loss in patients with IJO but, rather, provides an opportunity for increased bone mass with proper management.

Contributors

Kaori Kishimoto contributed to interpretation of data and drafting of the manuscript.

Chisato Kodera contributed to critical revision for important intellectual content.

Fumitaka Saito contributed to critical revision for important intellectual content.

Takashi Ohba was the patient's attending physician, contributed to conceptualization and design of the study, and critical revision for important intellectual content.

Hidetaka Katabuchi provided critical assessment and final approval of the version to be submitted.

Conflict of Interest

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

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Patient Consent

Obtained.

Provenance and Peer Review

This case report was peer reviewed.

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