

A Patient With Turner Syndrome Received the Percutaneous Vertebroplasty Seven Times: a Case Report and Literature Review

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Case report

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Abstract

Background Turner syndrome (TS) is characterized as the complete or partial absence of one X chromosome and is an extremely rare disease affecting approximately 1:2,500 live female births. Though the prevalence of osteoporosis among women with TS is estimated to be around 55-64% and they suffer more frequently from fractures than normal, few reports concerning TS patients with osteoporosis are able to be seen due to tiny number of patients.

Case presentation Here we report a rare case of TS with osteoporosis, who has undergone percutaneous vertebroplasty (PVP) seven times because of several vertebral compression fractures (VCFs). G-banded karyotype analysis was performed and the result was 45,X[43]/47,XXX[17], indicating that the patient was a mosaicism of TS karyotype and Trisomy X syndrome karyotype. TS is the underlying cause of low level of estrogen for this patient. The interaction of aging, estrogen deficiency and intestinal dysbacteriosis leads to her severe osteoporosis and multi-segmental VCFs. The aim of this report is to provide recommendations regarding the management of TS patients with osteoporosis by reviewing the clinical presentation of TS, the influence of estrogen deficiency in osteoporosis, etc.

Conclusions Early diagnosis and hormone replacement treatment are essential to prevent osteoporosis and reduce the risk of fractures. This is a rare case report describing TS patient with severe osteoporosis and VCFs.

Introduction

Turner syndrome (TS) is characterized as the complete or partial absence of one X chromosome and is an extremely rare disease affecting approximately 1:2,500 live female births. The most common karyotype causing TS is 45,X, found in 45% of live births. The incidence of 45,X/47,XXX mosaicism among patients with TS is less than 5% [1]. It is estimated that the incidence of osteoporosis among TS patients is about 55–64%. Women with TS have a higher fracture risk than healthy individuals because there is a cortical density reduction among these patients [2].

Herein, we report the case of a patient who was diagnosed as severe osteoporosis with TS and received the percutaneous vertebroplasty seven times due to vertebral compression fractures (VCF).

Case Presentation

Our patient was a 65-year-old woman who was enrolled in the orthopaedics department of this hospital because of lumbar and back pain after seven times of percutaneous vertebroplasty (PVP).

The patient had been healthy until September 2019, when she got a fall carelessly and suffered from badly lumbago. She was evaluated in a local hospital because the pain was not alleviated after a rest. The lumbar spine X-ray showed the VCF at L1 and L4. She underwent the first PVP to stabilize the fractured vertebral bodies and relief the symptom.

The patient had a severe backache again because of falling down from the bed in July 2020. According to the X-ray, the patient underwent the PVP for the second time due to a new VCF at T11. One month later, she felt low back pain again after bending forward to pick up a potted flower. X-ray showed that there was an obvious VCF at T9 and the patient had another PVP. Though the lumbar and back pain has been relieved after three times surgeries, she took the 600mg calcium and 125 IU vitamin D daily since then.

In September 2020 the patient felt lumbar pain again without any recognizable precipitating factors. Bone mineral density (BMD) was measured with ultrasound BMD analyzer and the Speed of Sound (SOS) was 4016m/s, indicating that T-score of the patient was - 1.5. VCF at L2 could be seen clearly by X-ray and magnetic resonance imaging (MRI). Owing to this, she underwent a PVP for L2 immediately. After two months the low back pain became worse without any clear reasons. A new VCF at L3 was found and another PVP for L3 was administered. Additionally, the patient underwent another PVP at T12 ten days later because of the aggravation of pain after bending from the waist. Unfortunately, the situation of the patient was not improved this time.

Apart from that, her general past medical history was remarkable. The patient was amenorrhea all the time, which means menarche had not happened ever and the lifelong absence of menses.

The patient underwent cholecystectomy ten years ago because of gallbladder stones. Chronic superficial gastritis also confused her for almost eight years and she had the resection of gastric polyp in January 2021. Coronary heart disease (CHD) was diagnosed five years ago and stent was implanted in the stenosed artery. Doctors decided to implant another scaffold for the exacerbation of chest pain in January 2021. However, the operation was canceled after assessing and concluding that the patient could not bear the surgery due to her poor health.

The patient was transferred to this hospital for further evaluation and treatment after seven PVPs. BMD was measured again with dual-energy X-ray absorptiometry (DEXA) and the T-score was - 4.1. The whole spine erect lateral projection radiograph displayed seven vertebral bodies injected bone cement clearly (Fig. 1a).

Physical examination for this patient demonstrated short stature, short neck, and no breast development. Since amenorrhea is one of the most significant clinical manifestations of this patient, a three-dimensional transvaginal ultrasound examination was considered for differential diagnosis. The result indicated suspected congenital infantile uterus and the structure of bilateral ovaries was not observed. The levels of six serum sex hormones were measured and the result suggested low levels of estrogen and testosterone (Table 1). However, other etiologies could not be distinguished by the examinations that already had done for the reason that aging may affect all these results, especially the levels of sex hormone. Owing to this, G-banded karyotype analysis was performed and the result was 45,X[43]/47,XXX[17], indicating that the patient was a mosaicism of TS karyotype and Trisomy X syndrome karyotype (Fig. 1b).

Discussion

G-banded karyotype analyses showed that the karyotype of this patient was 45,X[43]/47,XXX[17], meaning that 60 cells were randomly selected totally, and 43 cells and 17 cells displayed a 45,X karyotype and 47,XXX karyotype, respectively. This result indicated that the patient was a mosaicism and Turner karyotype was in the overwhelming majority. Previous reports have demonstrated that this mosaicism have a lower likelihood of cardiovascular and skeletal anomalies compared with common TS patients [3]. The presence of XXX cells makes it more likely to retain the ovarian function and fertility [4]. Unfortunately, though the patient in this case was a typical 45,X/47,XXX mosaicism, she still suffered from primary amenorrhea, cardiac disease and severe osteoporosis for the reason that cells which had 47,XXX karyotype were in a decided minority.

It has been confirmed that it is intrinsic bone abnormalities and hormonal imbalance together that result in the increase of skeletal fragility in women with TS [2]. According to the result of ultrasound examination, it was highly likely that the patient had no ovaries and her uterus was in the primitive state combined with clinical history. This patient had decreased level of estrogen and testosterone compared with normal references. Estrogen deficiency plays an important role in the pathophysiology of osteoporosis. The relevant mechanisms include affecting bone metabolism via releasing the bone-active cytokines, stimulating the proliferation and differentiation of regulatory T (T-reg) cells to be anti-osteoclastogenic, etc.[5, 6]

Aging of the patient was another cause of her severe osteoporosis. Therefore, only the level of estrogen being considered is not comprehensive. It is believed that the substantial majority of trabecular bone loss during the life is age-related and estrogen-independent [7]. Increased oxidative stress (OS) caused by advancing age is a fundamental mechanism of the loss of bone mass and strength. It is excessive accumulation of reactive oxygen species (ROS) that leads to age-related changes including osteopenia. However, a close association is also recognized between aging and estrogen. Estrogen deficiency decreases the defence of body against OS and may aggravate adverse effects of aging on both bone and lipid metabolism [8]. This is able to explain why the patient suffered from both osteoporosis and CHD to some extent.

Chronic superficial gastritis of the patient influenced her gut microbiome. Fecal samples were collected and undergone the gut microbiota test, indicating that the kinds of beneficial bacteria was rare though the diversity of gut microbiota kept at a high level (340 kinds of bacteria were found). Besides, several kinds of bacteria which had the ability to produce Short-chain fatty acids (SCFAs) accounted for less than 8% of all tested bacteria. Researches has confirmed that gut microbiome is relevant to osteoporosis extremely [9]. SCFAs produced by intestinal flora through fermenting dietary fibers have the ability to inhibit bone resorption without affecting bone formation [10]. Additionally, intestinal microbes can regulate the differentiation and apoptosis of osteoclast by controlling the dynamic balance of Th-17/T-reg cell [11, 12].

It is reported that hormone replacement therapy used in the treatment of patients with TS at younger ages may provide benefit for bone quality and decreased fragility fractures in the future [13]. Considering the age of this patient, no particular treatment for TS is needed for the reason that she had no demand and indeed for fertility. Estrogen replacement therapy is not the key point of her management.

PVP has been widely used around the world for treating painful VCFs during the last two decades. It is believed as a safe and effective technique to release pain and improve functional status [14]. Although some authors declare that the incidence of new fractures in adjacent vertebrae may increase for the patients who were treated by PVP previously, it seems that it is osteoporosis rather than PVP that leads to new adjacent VCFs [15]. Considering the patient had undergone seven PVP, anti-osteoporosis therapy is the most important and appropriate management for this patient.

Conclusions

TS is the underlying cause of low level of estrogen for this patient. The interaction of aging, estrogen deficiency and intestinal dysbacteriosis leads to her severe osteoporosis and multi-segmental VCFs. Hormone replacement therapy is not suitable for her owing to aging. Anti-osteoporosis therapy is the most appropriate management for her in the long run. For patients with TS, early diagnosis and early hormone replacement treatment are essential to prevent osteoporosis and reduce the risk of fractures.

Abbreviations

TS = Turner syndrome

PVP = percutaneous vertebroplasty

VCF = vertebral compression fractures

BMD = Bone mineral density

SOS = Speed of Sound

MRI = magnetic resonance imaging

CHD = Coronary heart disease

DEXA = dual-energy X-ray absorptiometry

T-reg = regulatory T

OS = Increased oxidative stress

ROS = reactive oxygen species

SCFAs = Short-chain fatty acids

Declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the Bioethics Committee of Zhengzhou University.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editors-in-Chief of this journal.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

LY L and YF S prepared the first draft of the paper. NZ, ZPL, ZZ, ZMS, SLZ and MHY was responsible for statistical analysis of the data. ZKL, SF C, GW S, HW K and HJ L were involved in the diagnosis and clinical management of the patient. HJ L is guarantor. All authors read and approved the final manuscript.

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References

1. Lim HH, Kil HR, Koo SH (2017) Incidence, puberty, and fertility in 45,X/47,XXX mosaicism: Report of a patient and a literature review. Am J Med Genet A 173:1961-1964

2. Augoulea A, Zachou G, Lambrinoudaki I (2019) Turner syndrome and osteoporosis. *Maturitas* 130:41-49
3. Hanew K, Tanaka T, Horikawa R, Hasegawa T, Yokoya S (2018) Prevalence of diverse complications and its association with karyotypes in Japanese adult women with Turner syndrome-a questionnaire survey by the Foundation for Growth Science. *Endocr J* 65:509-519
4. Sybert VP (2002) Phenotypic effects of mosaicism for a 47,XXX cell line in Turner syndrome. *J Med Genet* 39:217-220
5. Foger-Samwald U, Dovjak P, Azizi-Semrad U, Kerschan-Schindl K, Pietschmann P (2020) Osteoporosis: Pathophysiology and therapeutic options. *EXCLI J* 19:1017-1037
6. Bhattacharai HK, Shrestha S, Rokka K, Shakya R (2020) Vitamin D, Calcium, Parathyroid Hormone, and Sex Steroids in Bone Health and Effects of Aging. *J Osteoporos* 2020:9324505
7. Manolagas SC, O'Brien CA, Almeida M (2013) The role of estrogen and androgen receptors in bone health and disease. *Nat Rev Endocrinol* 9:699-712
8. Manolagas SC (2010) From estrogen-centric to aging and oxidative stress: a revised perspective of the pathogenesis of osteoporosis. *Endocr Rev* 31:266-300
9. Ding K, Hua F, Ding W (2020) Gut Microbiome and Osteoporosis. *Aging Dis* 11:438-447
10. Lucas S, Omata Y, Hofmann J, Bottcher M, Iljazovic A, Sarter K, Albrecht O, Schulz O, Krishnacoumar B, Kronke G, Herrmann M, Mougiakakos D, Strowig T, Schett G, Zaiss MM (2018) Short-chain fatty acids regulate systemic bone mass and protect from pathological bone loss. *Nat Commun* 9:55
11. Dar HY, Pal S, Shukla P, Mishra PK, Tomar GB, Chattopadhyay N, Srivastava RK (2018) *Bacillus clausii* inhibits bone loss by skewing Treg-Th17 cell equilibrium in postmenopausal osteoporotic mice model. *Nutrition* 54:118-128
12. Cooney OD, Nagareddy PR, Murphy AJ, Lee MKS (2020) Healthy Gut, Healthy Bones: Targeting the Gut Microbiome to Promote Bone Health. *Front Endocrinol (Lausanne)* 11:620466
13. Acosta AM, Steinman SE, White KK (2019) Orthopaedic Manifestations in Turner Syndrome. *J Am Acad Orthop Surg* 27:e1021-e1028
14. Zuo XH, Zhu XP, Bao HG, Xu CJ, Chen H, Gao XZ, Zhang QX (2018) Network meta-analysis of percutaneous vertebroplasty, percutaneous kyphoplasty, nerve block, and conservative treatment for nonsurgery options of acute/subacute and chronic osteoporotic vertebral compression fractures (OVCFs) in short-term and long-term effects. *Medicine (Baltimore)* 97:e11544
15. Yang W, Yang J, Liang M (2019) Percutaneous Vertebroplasty Does Not Increase the Incidence of New Fractures in Adjacent and Nonadjacent Vertebral Bodies. *Clin Spine Surg* 32:E99-E106

Table

Table 1

Laboratory results

Variable	Evaluation at our center	Reference Range
Six serum sex hormones ^a		
Follicle stimulating hormone (mIU/mL)	56.54	25.80-134.80
Luteinizing hormone (mIU/mL)	23.79	7.70-58.50
Prolactin (ng/mL)	12.69	4.79-23.30
Estrogen (pg/mL)	5.00	5.00-138.00
Progesterone (ng/mL)	0.09	0.05-0.126
Testosterone (ng/mL)	0.025	0.029-0.408
Parathormone (pg/mL)	31.70	15.00-65.00
25-hydroxyvitamin D (ng/mL)	27.59	18.00
Serum calcium (mmol/L)	2.23	2.00-2.70
Serum phosphorus (mmol/L)	1.42	0.81-1.90
Alkaline phosphatase (U/L)	62	35-105

^aThe ranges of six serum sex hormones are for postmenopausal women. They may therefore not be appropriate for all patients.

Figures

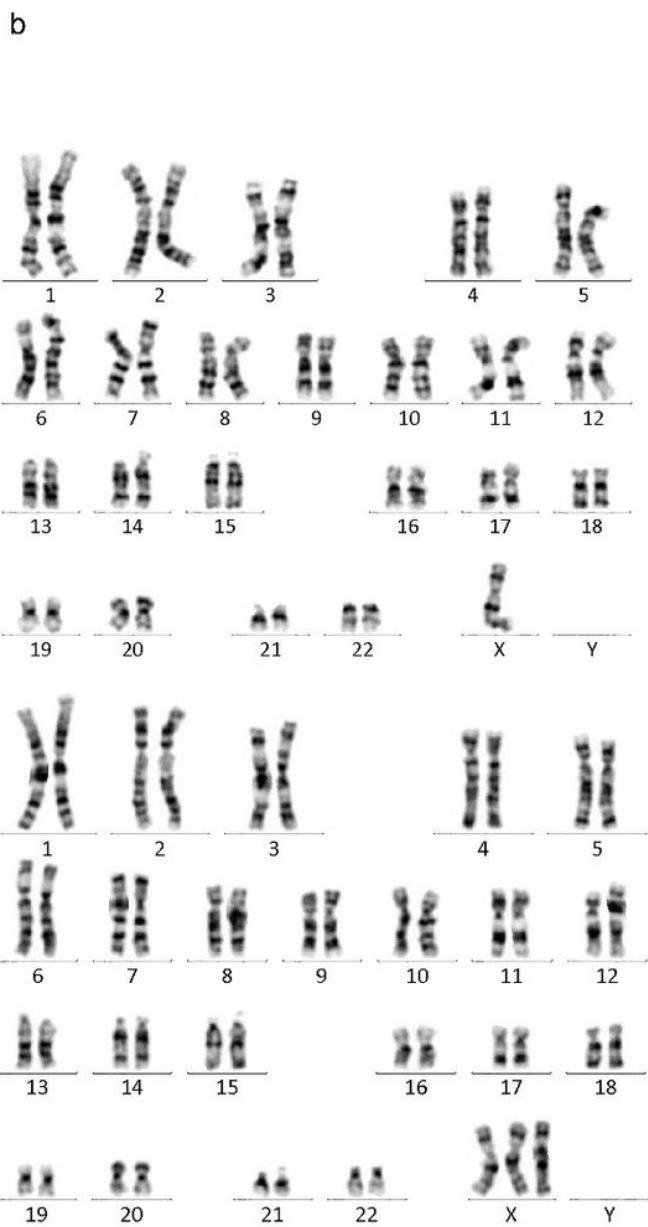
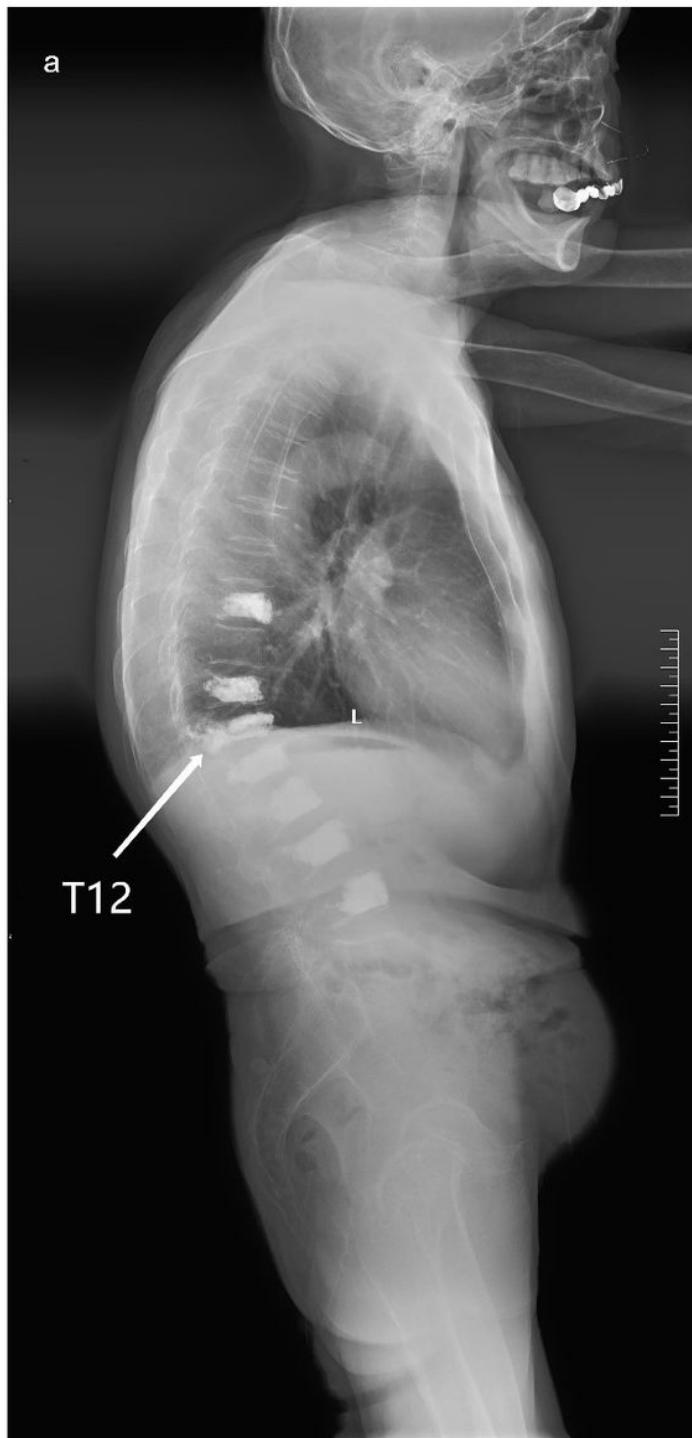


Figure 1

Imaging studies and karyotype analysis a The whole spine erect lateral projection shows the patient had received seven times of PVPs at T9, T11-L4. The minimum scale of the ruler in this radiograph represents 5mm. b The result of G-banded karyotype analysis shows the karyotype of this patient is 45,X[43]/47,XXX[17].