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Case Report

Multiple thoracolumbar compression fractures induced by glucocorticoid-induced osteoporosis and cachexia in a young adult female patient with systemic lupus erythematosus: a case report with a 5-year follow-up

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Abstract

Background: High doses of glucocorticoids and severe weight loss can cause osteoporosis. We present a case of glucocorticoid-induced osteoporosis and cachexia in an 18-year-old woman who experienced severe appetite loss leading to weight loss, amenorrhea, and multiple thoracolumbar compression fractures. Case presentation: The patient had been receiving high-dose glucocorticoid treatment for systemic lupus erythematosus since the age of 13 and developed unexplained appetite loss since the age of 16. She subsequently developed thoracolumbar compression fractures, which necessitated repeated hospitalization. Gradual glucocorticoid tapering using belimumab and weight regain were achieved through high-calorie nutrition administration via the central vein, which helped the patient overcome her cachexic state. Romosozumab administration increased bone mineral density. Conclusion: Long-term administration of glucocorticoids may lead to osteoporosis and cachexia, resulting in amenorrhea, especially in young adults. Approaches that taper glucocorticoids and promote weight regain may be helpful in the management of such patients.

Keywords: cachexia; compression fractures; glucocorticoids; osteoporosis; systemic lupus erythematosus

Introduction

Glucocorticoid-induced osteoporosis (GIOP) is a risk factor for multiple spinal compression fractures [1]. Severe weight loss due to reduced dietary intake causes hypothalamic amenorrhea and increases the risk of fragility vertebral fractures [2]. However, cases in which these conditions co-occur have not been reported. Here, we report the case of a young adult female patient with systemic lupus erythematosus (SLE), GIOP, and cachexia due to unexplained appetite loss who developed multiple thoracolumbar compression fractures.

Case report

An 18-year-old woman developed lower back pain after suffering minor trauma. She had been diagnosed with SLE at the age of 13 based on the following symptoms; malar rash, photosensitivity, antinuclear antibody positivity, anti-dsDNA antibody positivity, anti-Sm antibody positivity, hypocomplementemia, and lupus nephritis IV. SLE treatment was subsequently initiated with glucocorticoid pulse therapy, and the patient had been dependent on high-dose glucocorticoids (9–15 mg/day) since then as attempts at remission-induction therapy with cyclophosphamide or mycophenolate mofetil failed due to side effects of nausea. Alendronate was concurrently administered with the glucocorticoid treatment to prevent GIOP. However, the patient began experiencing unexplained appetite loss at the age of 16. Gastrointestinal endoscopy did not reveal any organic abnormalities; thus, she was diagnosed with functional dyspepsia. The patient subsequently lost a considerable amount of weight and developed amenorrhea.

At the first visit, her oral glucocorticoid dose was 13 mg/day. Her height, weight, and body mass index (BMI) were 150.4 cm, 33.6 kg, and 14.9 kg/m^2, respectively (Table 1, [1]). The patient had regular menstrual cycles until the onset of amenorrhea and did not have any gonadal disease or blood abnormalities that could lead to secondary osteoporosis, such as thyroid disease or diabetes. Radiography and magnetic resonance imaging revealed compression fractures of the L3 and L5 vertebrae (Fig. 1). Bone densitometry by dual-energy X-ray absorptiometry (DXA; Discovery: Hologic, Waltham, MA, USA) revealed low bone mineral density (BMD), and GIOP was diagnosed. Moreover, limb muscle

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Table 1. Patient status trends after the first fracture

	Period after the first fracture (months)	Height (cm)	Weight (kg)	BMI (kg/m^2)	Lumbar BMD (g/cm^2)	Lumbar Z-score	Femoral neck BMD (g/cm^2)	Femoral neck Z-score	Limb muscle mass (kg)	SMI (kg/m^2)
(1)	3	150.4	33.6	14.9	0.631	-	0.5	-	9.02	3.99
(2)	6	150.7	33.1	14.6	0.597	-	0.425	-	7.44	3.28
(3)	16	150.2	30.2	13.4	0.515	−4.7	0.331	−4.2	6.96	3.09
(4)	20	148.5	41.5	18.8	0.571	−4.1	0.384	−3.7	-	-
(5)	24	148.5	41.5	18.8	0.662	−3.3	0.497	−2.7	11.88	5.39
	29	149.0	46.0	20.7	0.695	−2.9	0.533	−2.3	11.39	5.13
(6)	38	150.0	45.0	20.0	0.770	−2.2	0.58	−1.9	10.98	4.88
	44	150.0	45.0	20.0	0.749	−2.4	0.548	−2.2	10.74	4.78
	50	150.0	45.0	20.0	0.752	−2.4	0.538	−2.3	12.26	5.45
	55	150.0	44.0	19.6	0.792	−1.9	0.558	−2.1	11.75	5.22
	60	150.0	44.0	19.6	0.776	−2.2	0.577	−1.9	11.43	5.08

BMI, body mass index; BMD, bone mineral density; SMI, skeletal muscle mass index.

mass was measured using DXA. The skeletal muscle mass index (limb muscle mass (kg)/height (m)^2) was lower (3.99 kg/m^2) than the cut-off value (5.46 kg/m^2) for Japanese women [3], indicating sarcopenia (Table 1, [1]). Conservative treatment was initially initiated using a lumbar corset. The osteoporosis treatment was changed to intravenous zoledronate 5 mg. However, she developed subsequent thoracolumbar compression fractures, which occurred following nontraumatic activities of daily living. She developed T10, T11 and L1, T12, and L2 fractures 2, 5, 6, and 9 months after the first fracture, respectively, and required repeated hospitalizations (Fig. 2). Despite treatment with zoledronate, her BMD decreased (Table 1, [2]). Treatment with Romosozumab (210 mg subcutaneous (SC) once a month for 12 months) was started 9 months after the first fracture. To enable tapering of glucocorticoids, belimumab (10 mg per kilogram of body weight) was added 12 months after the first fracture. However, BMD did not increase 16 months after the first fracture (Table 1, [3]). To correct weight loss, high-calorie nutrition administered via the central vein was supplemented in addition to an oral intake of 1800 kcal. This was increased by 50 kcal per day, until finally reaching 3000 kcal per day, and was administered 17 months after the first fracture for a total of 2 months. During this period, the patient's weight and appetite gradually increased, her blood data gradually improved, and no further treatment was required thereafter (Fig. 3a). As a result, twenty months after the first fracture, the patient's weight and BMD improved (Table 1, [4]) (Fig. 3b). After the patient regained weight, her appetite improved, and her menstruation resumed for the first time in 3 years. By using belimumab, the glucocorticoid dose was reduced without major side effects. Twelve months after treatment, romosozumab was switched to denosumab (60 mg SC once every 6 months). Subsequently, the patient maintained her weight, and her BMD further increased (Table 1, [5]). Thirty-eight months after the first fracture, the glucocorticoid dosage was reduced to 2 mg/day; therefore, denosumab was discontinued after the fourth dose every 6 months. Her BMD did not decrease after discontinuing sequential treatment (Table 1, [6]). Radiography 55 months after the first fracture showed recovery of the vertebral body height and ossification of the endplates (Fig. 4). The timeline and scheme of SLE treatment in this patient were illustrated in Fig. 5.

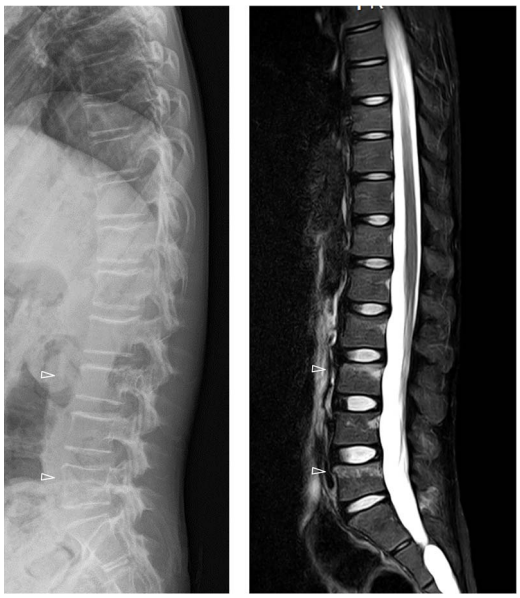

Figure 1. Initial fractures of the thoracolumbar spine. Radiography and short TI inversion recovery (STIR) images of magnetic resonance imaging showing compression fractures of the L3 and L5 vertebrae.

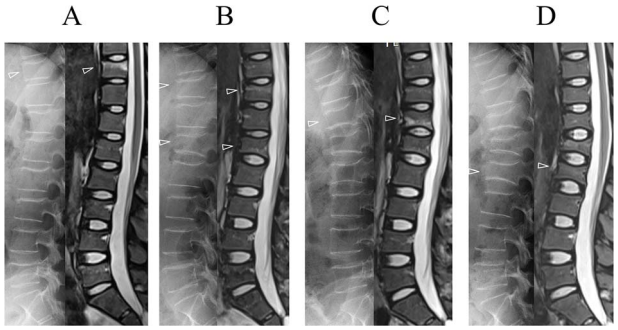

Figure 2. Time of each fracture following the initial fracture of the thoracolumbar spine. (**A**) 2 months. (**B**) 5 months. (**C**) 6 months. (**D**) 9 months.

Discussion

The current case highlights the following two points; First, multiple thoracolumbar compression fractures were caused by GIOP and severe weight loss in a young adult female patient. In patients with GIOP, the duration of glucocorticoid administration, low BMI, and low BMD are risk factors for vertebral fractures [1]. Furthermore, hypothalamic amenorrhea due to weight loss causes further BMD loss. In SLE, some patients develop neuropsychiatric

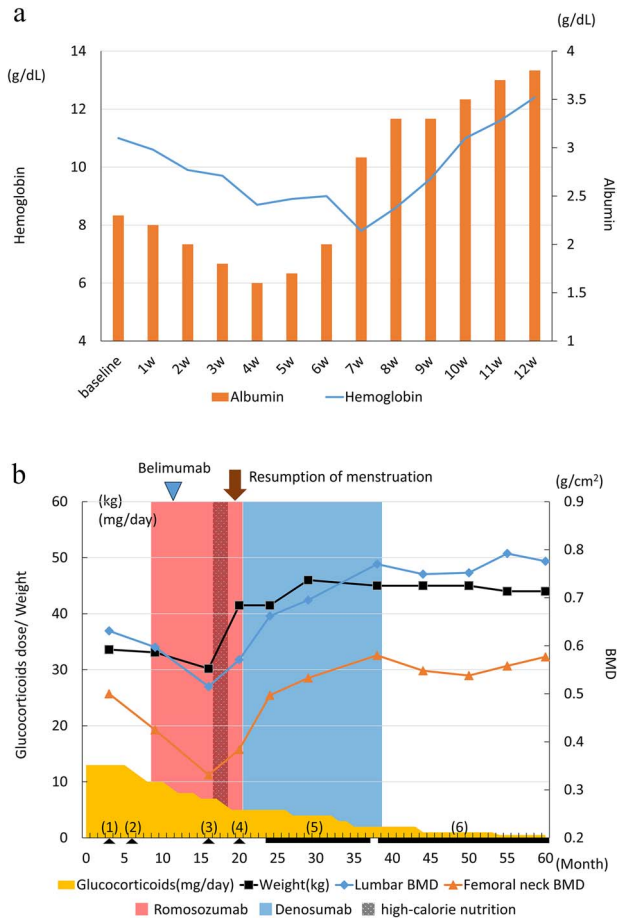

Figure 3. (**a**) Changes in blood test data (albumin: bar graph, hemoglobin: line graph) after the initiation of hypercaloric nutritional therapy. (**b**) Changes in body weight, lumbar spine and femoral neck bone mineral density (BMD), and glucocorticoid dosage since the first fracture. The period of romosozumab administration (first band), denosumab administration (second band), and hypercaloric nutrition (mosaic pattern). The times of menstruation resumption (arrow) and the start of belimumab administration (arrowhead). The points or periods (1) through (6) in the figure correspond to points or periods (1) through (6) in Table 1.

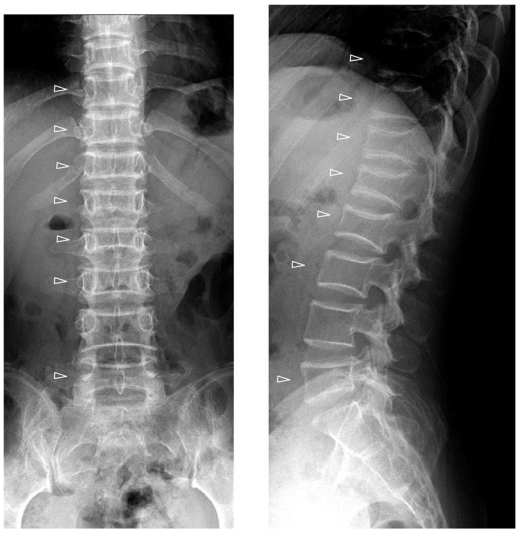

Figure 4. Radiography images obtained 55 months after the first fracture. Radiography shows recovery of the collapsed vertebral body height and ossification of the endplates.

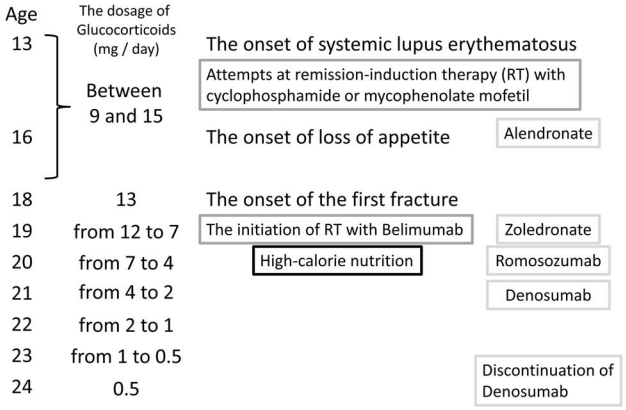

Figure 5. The timeline and scheme of systemic lupus erythematosus treatment in this patient.

symptoms such as anorexia nervosa or nonspecific gastrointestinal symptoms [4, 5]. However, both tend to respond well to drug treatment with glucocorticoids and immunosuppressants. Conversely, administering glucocorticoids to SLE patients can be a risk factor for cachexia. In this case, appetite loss occurred due to long-term glucocorticoid administration despite the improvement in SLE symptoms, therefore, it was considered cachexia. Cachexia can result from glucocorticoid administration [6]. A combination of GIOP and cachexia led to multiple vertebral fractures.

Second, a drastic increase in BMD was observed after tapering glucocorticoids, restoring body weight, and administering romosozumab. Moreover, discontinuation of sequential therapy was made possible by maintaining body weight and regular menstrual cycles.

There is still no optimal treatment for osteoporosis in premenopausal women, especially young adults. Weight gain and the resumption of regular menstruation are necessary in cases of underweight patients [2]. Teriparatide is effective in premenopausal women with osteoporosis, but it can only be used for two years in a lifetime [7]. Romosozumab is also effective in premenopausal women with pregnancy- and lactation-associated osteoporosis [8], and in those with anorexia nervosa [9].

Generally, teriparatide and romosozumab require sequential therapy with antiresorptive drugs to prevent post-treatment bone loss even in premenopausal women [10], however, it should ideally be discontinued in women of childbearing age, as its safety during pregnancy is uncertain [11].

In recent years, advances in treatment for SLE made remission maintenance therapy possible [12]. Glucocorticoids should preferably be kept at a maintenance dose of 5 mg/day or lower, and preferably discontinued if possible [13]. In this case, belimumab therapy and weight gain supported by high-calorie intravenous fluids enabled the patient to overcome cachexia by reducing glucocorticoids. She was also able to resume and maintain regular menstrual cycles.

In conclusion, long-term administration of glucocorticoids may lead to osteoporosis as well as cachexia, which can result in amenorrhea, especially in young adult women, and finally multiple thoracolumbar compression fractures. Tapering glucocorticoids and gaining body weight are important for recovery from cachexia. Maintaining body weight can enable discontinuation of treatment and prevent new fractures. This strategy is beneficial with the combination of glucocorticoid-induced osteoporosis and

cachexia in premenopausal (especially young adult) women. However, these findings are based on single case reports, and longer-term follow-up is necessary.

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Author contributions

Kazuki Fujimoto: Conceptualization, Writing–Original draft preparation. Taro Akiyama, Kohei Kakinuma, Narumi Maki, Daisuke Hashiba, Toshifumi Maeyama, and Ryosuke Nakagawa: Writing–Reviewing and editing. Toshikazu Kano, Hajime Arai, and Seiji Ohtori: Supervision. All authors have read and agreed to the manuscript.

Conflict of interest

No conflicts of interest.

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Ethical approval

The study was conducted in accordance with the Declaration of Helsinki and its later amendments.

Consent

The patient was informed that her data and images would be submitted for this case report, and consent was obtained.

Guarantor

Kazuki Fujimoto.

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