Int J Clin Exp Pathol 2026;19(7):352-359
www.ijcep.com /ISSN:1936-2625/IJCEP0171759

Case Report

The clinical recognition, diagnosis and treatment of osteogenesis imperfecta: a case report and literature review

Yifei Ma[1], Yanan Li[2], Ruolin Lv[2], Nailong Yang[2]

[1]Qingdao University, Qingdao 266000, Shandong, China; [2]Department of Endocrinology, The Affiliated Hospital of Qingdao University, Qingdao 266000, Shandong, China

Received January 29, 2026; Accepted June 23, 2026; Epub July 15, 2026; Published July 30, 2026

Abstract: Osteogenesis imperfecta (OI) is a rare congenital heterogeneous connective tissue disorder characterized by increased bone fragility, recurrent fractures, skeletal deformities, and short stature. Timely diagnosis and intervention can improve patients' quality of life and enhance their long-term prognosis. This study reports a case of a 26-year-old patient with OI who also had autoimmune diseases. Due to long-term treatment with glucocorticoids for autoimmune diseases, the OI was chronically missed. The typical clinical symptoms, skeletal imaging features, and genetic test results of this patient ultimately confirmed the diagnosis of osteogenesis imperfecta. At the same time, a multidisciplinary comprehensive individualized treatment plan was formulated and implemented for the patient, effectively alleviating clinical symptoms and improving the prognosis of the disease. This study reports a case of an adult patient with OI who also has an autoimmune disease. It emphasizes the need for clinicians to pay attention to the early identification and genetic diagnosis of OI in the context of co-morbidity. Multidisciplinary comprehensive treatment can significantly improve the patient's symptoms, providing a reference for the clinical diagnosis and treatment of rare hereditary bone diseases.

Keywords: Osteogenesis imperfecta, autoimmune diseases, *COL1A2*, rare diseases, genetic testing

Introduction

Osteogenesis imperfecta (OI) is a rare congenital connective tissue disorder. Its incidence is approximately 1/30,000 [1, 2]. The main feature of OI is abnormally fragile bones and repeated fractures. In addition, OI also involves non-bone systems, such as pale sclera, progressive hearing loss, poor tooth development, lax joint ligaments, and muscle weakness [3-5]. OI patients often develop the disease in childhood, with recurrent fractures after minor trauma. More severe cases may result in fetal or perinatal death [6]. OI is a hereditary disease that involves multiple genetic patterns, such as autosomal dominant, autosomal recessive, and X-linked [7, 8]. The pathogenesis of OI is attributed to mutations in the genes *COL1A1* or *COL1A2* that encode type I collagen, resulting in a deficiency of type I collagen. Specifically, the deletion of the *COL1A1* alleles usually leads to mild OI (Type I), while missense or splicing mutations in *COL1A1/COL1A2* usually result in more severe OI (Types II, III, or IV) [9-11].

At present, there is no clear international diagnostic standard for OI [12]. The diagnosis of this disease mainly follows the "Clinical Diagnosis and Treatment Guidelines for Osteogenesis Imperfecta" issued by the National Health Commission of China. It mainly relies on clinical and imaging findings, with genetic testing serving as a confirmation or auxiliary tool. In 1979, Sillence et al. classified OI into types I to IV based on clinical phenotypes [13]. Type I has the mildest symptoms, with only blue sclera and muscle and joint pain caused by joint laxity. Type II has severe symptoms, and children might die during the perinatal period. Type III, although not fatal, has the most severe symptoms among the survivors, with progressive skeletal deformities. Type IV has milder symptoms, with a severity level between type I and

https://doi.org/10.62347/GWJU3175

type III. Imaging examinations mainly involve X-ray of the bones and bone mineral density (BMD) measurements [14]. BMD values for lumbar spine and hip joints are below the normal range. The BMD Z-score is often less than -2.0. Genetic testing serves as an important auxiliary method, with a priority focus on pathogenic mutations of core disease-causing genes such as *COL1A1* and *COL1A2* [15]. However, the diagnosis of OI still faces significant challenges. The clinical manifestations of OI are complex and diverse, the individual differences in imaging findings are large, and there are no specific biochemical markers, which easily lead to missed diagnoses or misdiagnosis. Some patients with less typical symptoms may even be diagnosed with idiopathic scoliosis, osteogenic myositis, osteosarcoma, etc. [16, 17]. There are also limitations in BMD testing, determination of bone turnover biomarkers, and urine calcium metabolism testing. Although some OI patients with osteoporosis frequently suffer from fractures, their BMD and bone metabolism indicators remain within the normal range, which increases the possibility of being missed or misdiagnosed [18]. Due to the presence of multiple rare genetic variations in OI, and these variations being classified as variants of unknown significance (VUS), this has also led to delays in diagnosis [19].

The treatment strategies for OI are relatively complex [20]. The clinical diagnosis and treatment guidelines for OI advocate a comprehensive treatment approach, with the core objective being to increase the patient's BMD, reduce the incidence of fractures, and improve skeletal deformities [21, 22]. In clinical practice, bisphosphonate drugs are commonly used to improve BMD and reduce the incidence of fractures. When patients have severe deformities, they need to wear orthotic braces or undergo corrective surgeries. In daily life, patients improve their motor functions through rehabilitation training, and at the same time, strengthen their nutritional intake and take other measures to improve their quality of life and delay the progression of their condition. However, due to the lack of long-term tracking and monitoring of BMD and related complications, it is difficult to implement standardized and systematic treatment plans [23]. Against this backdrop, our study based on relevant literature, analyzed cases of adult osteogenesis imperfecta. This study not only enriches the phenotypic and mutational spectrum of osteogenesis imperfecta, but also provides reference evidence for the diagnosis and individualized treatment of OI.

Case presentation

A 26-year-old Han Chinese woman presented for the first time in 2022, complaining of "a 9-month history of weight gain and 6-month history of generalized arthralgia". Since the age of 3, this patient has experienced recurrent fractures that were not caused by trauma. Previous physical examinations revealed slate-gray sclera, which raised clinical suspicion of OI, but a specific treatment was deferred. Nine months prior, she was diagnosed with connective tissue disease, idiopathic thrombocytopenic purpura, and antiphospholipid syndrome, and subsequently treated with glucocorticoids. During the treatment process, her weight increased by a total of 15 kg. At the same time, she suffered from chronic urticaria for a period of 3 months and had irregular menstrual cycles. The patient is the only child in her family. She was born via full-term natural delivery. Her parents did not marry within close kinship. There is no history of hereditary bone diseases in the family, and no relatives have a history of nontraumatic fractures.

Further physical examination revealed that the patient was 155 cm tall and weighed 113.6 kg, with a body mass index of 47.28 kg/m^2. This patient has a round face, excessive body hair, black desquamative dermatosis on the neck, and purplish-red stripes distributed on the chest, back and limbs. We suspect that these symptoms are related to the patient's long-term use of hormones. Therefore, we conducted an oral glucose tolerance test (OGTT). The results showed that the patient had fasting hypoglycemia, hyperinsulinemia and delayed peak insulin secretion (**Table 1**). The results of the hypothalamic-pituitary-adrenal axis and daytime cortisol rhythm examination were disordered (**Table 2**), and further differentiation of Cushing's syndrome was needed. The low-dose dexamethasone suppression test (LDDST) results showed that the levels of adrenocorticotropic hormone (ACTH, 1.50 pg/mL) and cortisol (27.20 nmol/L) after suppression were

Table 1. The patient's OGTT results

Index	0 min	60 min	120 min	180 min
C-peptide (ng/mL)	3.10	14.80	11.40	9.09
Insulin (uIU/mL)	21.20	175.00	92.10	60.60
Blood glucose (mmol/L)	3.51	7.96	6.12	5.18

Note: OGTT, oral glucose tolerance test.

Table 2. The diurnal rhythm of ACTH and cortisol of the patient

Index	8:00	16:00	0:00
ACTH (pg/mL)	13.50	30.60	26.80
Cortisol (nmol/L)	190	118	232

Note: Reference ranges; ACTH, adrenocorticotropic hormone. ACTH: 7:00 AM-10:00 AM: 7.2-63.3 pg/mL; 12:00 PM: < 20 pg/mL. Cortisol: 6:00 AM-10:00 AM: 172-497 nmol/L; 4:00 PM-8:00 PM: 71.1-286 nmol/L.

within a reasonable range, which excluded endogenous Cushing's syndrome. Finally, it was clearly determined that the patient's obesity was caused by hormones.

In addition, the patient presented with grayish-black sclera. She had hearing impairment in her left ear and complete deafness in her right ear. Her teeth were malformed. The patient could not walk normally. Musculoskeletal examination identified bilateral lower limb deformities, as well as spinal kyphosis with mild scoliosis. Given the patient's history of non-traumatic recurrent fractures and abnormal bone lesions in the spine and lower limbs, we conducted a series of specialized examinations. The patient's bone metabolism showed that the urine calcium excretion was 4.26 mmol/L (reference range: 2.11-2.52 mmol/L), and 24-hour urinary phosphorus excretion was 23.25 mmol/L (reference range: 0.85-1.51 mmol/L). All four bone turnover markers were within the normal range. Further imaging studies demonstrated normal BMD at the lumbar spine (L1-4 T-score: -0.3, Z-score: -0.3, BMD: 1.083 g/cm^2) and left femoral neck (T-score: 1.6, Z-score: 1.6, BMD: 1.123 g/cm^2). However, the Digital Radiography (DR) identified irregular morphology of the left femoral shaft (**Figure 1**). Based on the patient's clinical manifestations, medical history and the results of auxiliary examinations, we had a high suspicion that the patient was suffering from a rare genetic disorder. In order to further clarify the diagnosis, peripheral blood samples were collected from the patient and her parents for whole-exome sequencing (WES). The Verita Trekker variant detection system and the Enliven variant annotation system were used for data analysis. In accordance with the guidelines of the American College of Medical Genetics and Genomics (ACMG), as well as the HPO, OMIM and GHR databases, we screened gene variants associated with the patient's clinical phenotype. The results showed that no definite pathogenic variants were detected, but we identified 3 other variations. Among them, the variation in the *COL1A2* gene deserves particular attention. According to public databases, *COL1A2* mutations are associated with osteogenesis imperfecta (types II, III, and IV). We found a heterozygous missense variant c.1000G>A:p.Gly334Ser in the exon19 subregion of the gene. This variation has not been included in the "Shenzhou Genome Data Cloud Project", "Exome Aggregation Consortium (ExAC)", "1000 Genomes Project (1000G)", and "Genome Aggregation Database (gnomAD)" databases. It is a rare mutation. However, this variation has been detected in 2 to 5 cases of OI patients. The pathogenicity analysis revealed that the Rare Exon Variant Ensemble Learner (REVEL) predicted that this mutation would impair the gene or its encoded product. The Human Gene Mutation Database (HGMD) also mentioned it as disease-causing mutation (DM) based on peer-reviewed literature, further supporting its potential pathogenic role. According to the current information, there is still insufficient evidence to prove that the variation of *COL1A2* has pathogenicity, which this variation was ultimately classified as VUS. To further explore the genetic pattern of this variation, we conducted phenotypic observations and genetic testing on the patient's parents. The results demonstrated that neither parent manifested abnormal symptoms related to OI nor presented skeletal lesions typical of OI. Her father carried the same heterozygous variant in the *COL1A2* gene, whereas her mother did not (**Figure 2**).

Integrating the patient's medical history, clinical manifestations, familial genetic profile, imaging findings and genetic sequencing results, the patient was ultimately diagnosed with OI.

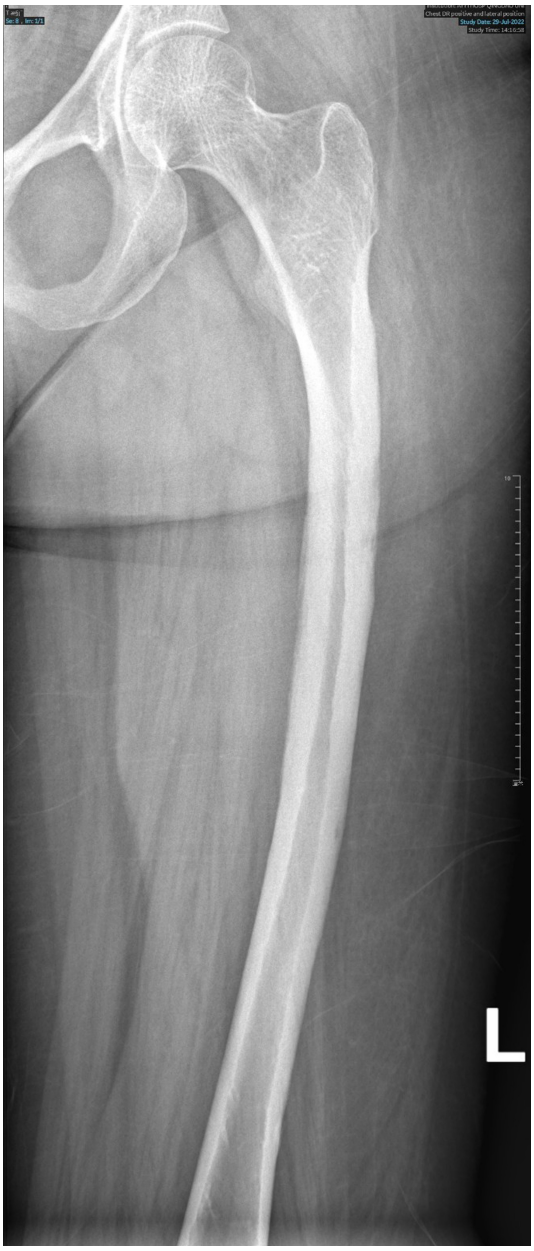

Figure 1. The patient's digital radiograph of the left femoral shaft.

We have developed a comprehensive multidisciplinary treatment plan for this patient. For this OI patient, we recommend intravenous injection of zoledronic acid, intramuscular injection of vitamin D_2, oral administration of calcium carbonate D_3 and oral administration of alfacalcidol to improve BMD. By optimizing the diet structure, increasing sun exposure time and performing appropriate rehabilitation exercises, the strength of the bones can be enhanced. For autoimmune diseases, we recommend that this patient switch to hydroxychloroquine to regulate her immune system, and use aspirin to prevent the risk of thrombosis secondary to autoimmune diseases. At the same time, we also recommend that this patient start subcutaneous injection of dulaglutide to control weight, take febuxostat orally to lower uric acid, and undergo regular dental examinations to monitor the condition of tooth decay. The follow-up results showed that the patient's joint pain was significantly relieved, and she was able to stand independently and walk with the aid of assistive devices. No new non-traumatic fractures were detected during the observation period. In 2023, the patient was admitted to the hospital for a second intravenous injection of zoledronic acid. Physical examination revealed that the acanthosis nigricans on the posterior side of the patient's neck had improved, and the patient had lost 10.8 kg in weight since the initial visit. BMD assessment showed normal spine bone mass (L1-4 T-score: 1.4, Z-score: 1.4, BMD: 1.279 g/cm^2), but there was still osteoporosis in the left femoral neck (L1-4 T-score: -1.3, Z-score: -1.3, BMD: 0.771 g/cm^2).

Discussion

OI is a rare genetic connective tissue disorder characterized by defects in the synthesis, processing and regulation of collagen [24]. Type I collagen is the core pathogenic material basis of OI. Pathogenic mutations in the genes *COL1A1* or *COL1A2* encoding type I collagen account for approximately 90% of OI cases [25, 26]. The deletion alleles in *COL1A1* are usually associated with a reduction in the production of type I collagen, leading to mild OI (Type I), while missense mutations or splicing mutations in *COL1A1* or *COL1A2* often result in more severe forms, namely Type II, Type III, or Type IV OI [27-29]. However, due to the diversity of clinical manifestations, different genetic characteristics, diverse imaging manifestations, and the lack of specific biochemical markers, OI is often missed or misdiagnosed in clinical practice.

The typical symptoms of OI include recurrent non-traumatic fractures, scleral discoloration, progressive hearing loss, dental maldevelopment, spinal and lower limb deformities, etc.

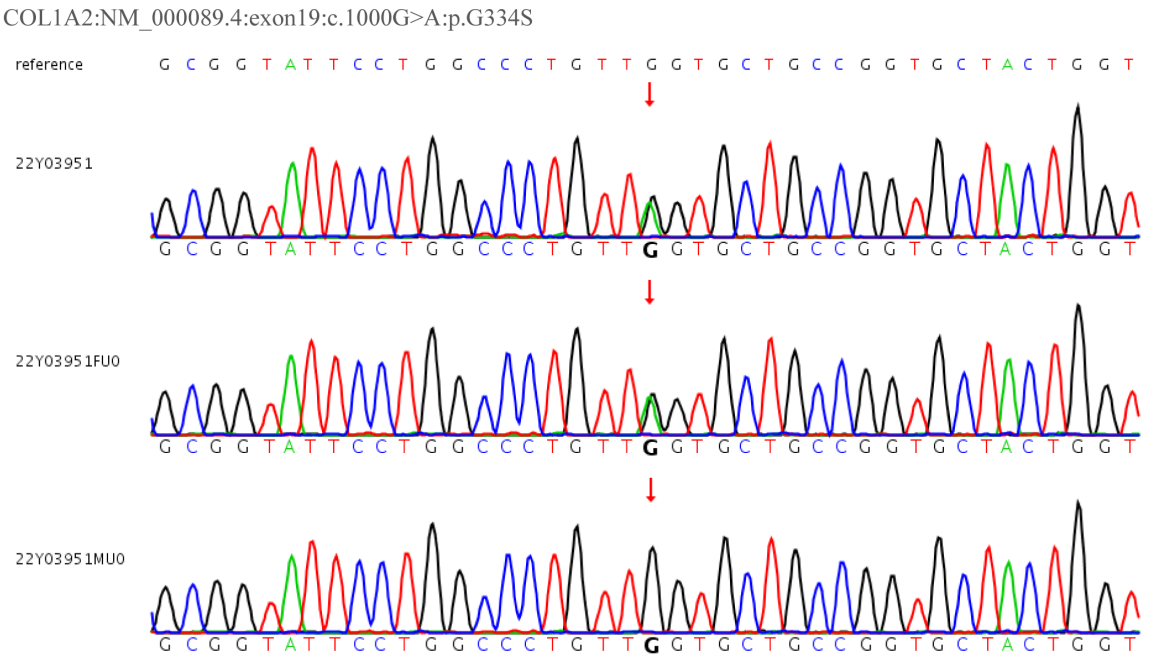

Figure 2. Single nucleotide variant (SNV) and insertion and deletion (InDel) sequencing results. 22Y03951: Proband; 22Y03951FU0: Patient's father; 22Y03951MU0: Patient's mother. The annotated arrow marks the *COL1A2*: NM_000089.4:exon19: c.1000G>A:p.Gly334Ser variant of uncertain significance (VUS), which was detected in both the proband and her father but absent in the mother according to genetic testing.

[30, 31]. This patient had a history of recurrent non-traumatic fractures before admission. Physical examination revealed that the patient also presented with abnormal sclera, hearing impairment, dental maldevelopment, and spinal and lower limb deformities. Subsequently, we measured the patient's bone mineral density, and the results showed that the bone mineral density of the patient's lumbar spine and left femoral neck was normal. Studies on bone mineral density values for patients with different types of OI have shown that some patients have BMD within the normal range or even slightly above the normal level, but their bones remain very fragile [32, 33]. Taking into account the patient's clinical manifestations, we collected a blood sample for sequencing analysis. Whole exome sequencing identified a heterozygous missense variant *COL1A2* c.1000G>A (p.Gly334Ser). This variation lacks sufficient evidence to prove its pathogenicity, and thus is classified as VUS. Further genetic testing showed that her father carried the same heterozygous variant. Missense mutations in the *COL1A2* gene have also been identified in other patients with OI. Muñoz-Miro et al. reported a case of adolescent OI with *COL1A2* c.964G>A (p.Gly322Ser) presenting with delayed spontaneous femoral fractures as the initial symptom [34]. Intarak et al. detected a novel missense variant c.752C>T (p.Ser251Phe) and c.758G>T (p.Gly253Val) in OI patients, with destruction of dentin structure and disordered collagen fiber arrangement in the patient [35]. Mehta et al. sequenced 3 patients with OI and found that a heterozygous c.838G>A mutation occurred in the *COL1A2* gene of all the patients, resulting in a p.Gly280Ser substitution [36].

It is worth noting that research has found that *COL1A2* also plays an important role in autoimmune diseases [37]. Existing studies have confirmed that OI is closely related to autoimmune diseases [38, 39]. This patient suffers from connective tissue diseases, idiopathic thrombocytopenic purpura, and antiphospholipid syndrome, among other autoimmune diseases. This OI coexists with multiple autoimmune diseases, presenting significant challenges in comprehensive treatment. The patient has been using hormones for the treatment of autoimmune diseases for a long time, resulting in excessive obesity and metabolic disorders, which also increases the risk of frac-

tures. For OI patients with autoimmune diseases, the use of hormones should be minimized, and alternative immunomodulatory agents such as hydroxychloroquine should be preferred to reduce metabolic adverse reactions [40]. At the same time, we recommend that the patient use dulaglutide to lower blood sugar and reduce weight. Considering that the patient has antiphospholipid syndrome, we recommend that the patient use aspirin for antithrombotic prevention to prevent the occurrence of thrombotic events.

In clinical diagnosis and treatment, the combination of bisphosphonates with calcium supplements and active vitamin D can effectively improve bone metabolism and reduce the risk of fractures in patients with osteoporosis and hereditary bone diseases [41]. Vitamin D is a key factor in regulating the homeostasis of bone metabolism, and vitamin D deficiency is common among patients with osteoporosis [42]. Studies have confirmed that zoledronic acid has good tolerance and low incidence of adverse reactions in patients with abnormal bone metabolism, and can significantly increase bone density and effectively reduce the occurrence of fragility fractures [43]. Based on this, this study formulates individualized intervention plans for patients, providing regular intravenous infusion of zoledronic acid, while combining oral administration of vitamin D_2, calcium D_3 and alfacalcidol to synergistically enhance bone density and improve bone matrix mineralization. In addition, regular bone imaging observations and monitoring of bone density are also essential for dynamic adjustment of the treatment plan. As of 2023, the patient has received regular injections of zoledronic acid and vitamin D_2, and has persisted in taking alfacalcidol and vitamin D_3 orally. Follow-up evaluations have shown that the patient's clinical symptoms have significantly improved, including no new non-traumatic fractures, significant relief of joint pain, the ability to stand intermittently independently, and the ability to walk with assistance. A comprehensive review of the treatment process of this patient indicates that fully considering the patient's clinical condition and formulating a comprehensive treatment strategy plays an important role in improving the patient's condition. In addition, we have provided the patient with personalized psychological support to promote the patient's active participation in rehabilitation training.

These findings indicate that for the complex condition of this type of OI accompanied by autoimmune diseases, its clinical diagnosis and treatment require a comprehensive analysis of multiple factors. The diagnosis and treatment of the disease should be advanced through the joint efforts of clinical manifestations, past medical history, family history, imaging examinations, and genetic testing. Currently, for the clinical treatment of OI, we advocate the use of a multidisciplinary collaborative approach, aiming to provide coordinated care among various specialties such as endocrinology and metabolism, orthopedics, and rehabilitation medicine. The plan is based on the patient's symptoms and complication status. The goal is to alleviate pain, reduce the risk of fractures, improve growth and movement functions, and delay the progression of potential severe complications through early intervention of potential serious injuries.

Conclusion

This patient is suffering from both OI and an autoimmune disease. When OI is combined with autoimmune diseases and long-term hormone use, it is prone to be missed in diagnosis. Through bone density tests alone this disease cannot be ruled out. A comprehensive diagnosis requires a combination of medical history, physical examination, bone imaging, and genetic testing. For such patients with complex comorbidities, individualized comprehensive intervention plans based on multidisciplinary collaboration can effectively reduce the risk of brittle fractures and improve the patient's motor function. This can provide practical references for the clinical diagnosis and treatment of patients with rare hereditary bone diseases combined with autoimmune comorbidities.

Disclosure of conflict of interest

None.

Address correspondence to: Nailong Yang, Department of Endocrinology, The Affiliated Hospital of Qingdao University, No. 16, Jiangsu Road, Shinan District, Qingdao 266000, Shandong, China. Tel: +86-0532-82911847; Fax: +86-0532-82911847; E-mail: 17852834875@163.com

References

[1] Lindahl K, Åström E, Rubin CJ, Grigelioniene G, Malmgren B, Ljunggren Ö and Kindmark A. Genetic epidemiology, prevalence, and genotype-phenotype correlations in the Swedish population with osteogenesis imperfecta. Eur J Hum Genet 2015; 23: 1042-1050.

[2] Barba AAA, Meza PVM and Abarca-Barriga HH. Osteogenesis imperfecta in Peruvian children: phenotypic and therapeutic insights from a pediatric hospital. Intractable Rare Dis Res 2024; 13: 236-244.

[3] Treurniet S, Burger P, Ghyczy EAE, Verbraak FD, Curro-Tafili KR, Micha D, Bravenboer N, Ralston SH, de Vries R, Moll AC and Eekhoff EMW. Ocular characteristics and complications in patients with osteogenesis imperfecta: a systematic review. Acta Ophthalmol 2022; 100: e16-e28.

[4] Joseph JK and Maharaj SH. Osteogenesis Imperfecta and hearing loss in the paediatric population. Int J Pediatr Otorhinolaryngol 2021; 150: 110914.

[5] Zaripova AR and Khusainova RI. Modern classification and molecular-genetic aspects of osteogenesis imperfecta. Vavilovskii Zhurnal Genet Selektsii 2020; 24: 219-227.

[6] Sillence D. Six at Sixty. Commentary on osteogenesis imperfecta 1975-2025. J Med Genet 2025; 62: 422-426.

[7] Marini JC, Forlino A, Bachinger HP, Bishop NJ, Byers PH, Paepe A, Fassier F, Fratzl-Zelman N, Kozloff KM, Krakow D, Montpetit K and Semler O. Osteogenesis imperfecta. Nat Rev Dis Primers 2017; 3: 17052.

[8] Giuca MR. Rare diseases: a challenge in paediatric dentistry. Eur J Paediatr Dent 2024; 25: 171.

[9] He D, Luo Y, Wei S, Wang Y, Zhang C, Chen S, Ban B, Zhang M and Li Y. A novel splice-altering frameshift variant in the COL1A1 gene underlies osteogenesis imperfecta type I: molecular characterization of a four-generation Chinese pedigree and literature review. Hum Genomics 2025; 19: 103.

[10] Ben Amor M, Rauch F, Monti E and Antoniazzi F. Osteogenesis imperfecta. Pediatr Endocrinol Rev 2013; 10 Suppl 2: 397-405.

[11] Niyibizi C, Wang S, Mi Z and Robbins PD. Gene therapy approaches for osteogenesis imperfecta. Gene Ther 2004; 11: 408-416.

[12] Hidalgo Perea S and Green DW. Osteogenesis imperfecta: treatment and surgical management. Curr Opin Pediatr 2021; 33: 74-78.

[13] Yang H, Zhu W, Li B, Wang H, Xing C, Xiong Y, Ren X and Ning G. Height prediction of individuals with osteogenesis imperfecta by machine learning. Orphanet J Rare Dis 2024; 19: 420.

[14] Wen H, Zhou M, Niu H and Xia H. Non-linear associations between UHR and bone mineral density in US adults: NHANES 2017-2018. Eur J Med Res 2025; 30: 1091.

[15] Glorieux FH, Langdahl B, Chapurlat R, De Beur SJ, Sutton VR, Poole KES, Dahir KM, Orwoll ES, Willie BM, Mikolajewicz N, Zimmermann E, Hosseinitabatabaei S, Ominsky MS, Saville C, Clancy J, MacKinnon A, Mistry A and Javaid MK. Setrusumab for the treatment of osteogenesis imperfecta: 12-month results from the phase 2b asteroid study. J Bone Miner Res 2024; 39: 1215-1228.

[16] Deng Y, Huo Y and Li J. Case report: hyperplastic callus of the femur mimicking osteosarcoma in osteogenesis imperfecta type V. Front Endocrinol (Lausanne) 2021; 12: 622674.

[17] Ferreira DG, Spranger A, Almeida P, Presa D, Fernandes I and Soares do Brito J. Telangiectatic osteosarcoma arising in osteogenesis imperfecta. Acta Reumatol Port 2021; 46: 171-176.

[18] Sait H, Adarsha N, Moirangthem A, Saxena D, Sharma L, Dabadgao P, Gupta A and Phadke SR. Molecular and clinical landscape of osteogenesis imperfecta: unraveling autosomal recessive forms, therapeutic outcomes, and bone mineral density in carriers. Clin Genet 2025; 108: 684-695.

[19] Cannalire G, Biasucci G, Bertolini L, Patianna V, Petraroli M, Pilloni S, Esposito S and Street ME. Osteoporosis and bone fragility in children: diagnostic and treatment strategies. J Clin Med 2024; 13: 4951.

[20] Yang EC, Ciğeroğlu O, Gupta RN, Shen Y, Sader S, Byers HM, Jain M and Franzone JM. Real-world data of fracture rates and musculoskeletal disorders for patients living with osteogenesis imperfecta. JBMR Plus 2025; 9: ziaf124.

[21] Bala MM and Bala KA. Severe cases of osteogenesis imperfecta type VIII due to a homozygous mutation in P3H1 (LEPRE1) and review of the literature. Adv Clin Exp Med 2021; 30: 1233-1238.

[22] Marom R, Rabenhorst BM and Morello R. Osteogenesis imperfecta: an update on clinical features and therapies. Eur J Endocrinol 2020; 183: R95-R106.

[23] Nowicki JK and Jakubowska-Pietkiewicz E. Serum osteocalcin in pediatric osteogenesis imperfecta: impact of disease type and bisphosphonate therapy. Int J Mol Sci 2025; 26: 7953.

[24] Deguchi M, Tsuji S, Katsura D, Kasahara K, Kimura F and Murakami T. Current overview of osteogenesis imperfecta. Medicina (Kaunas) 2021; 57: 464.

[25] Jovanovic M and Marini JC. Update on the genetics of osteogenesis imperfecta. Calcif Tissue Int 2024; 115: 891-914.
[26] Pan TT, Han L, Zheng HW, Xing ZM, Yu LS and Liu YJ. A novel mutation in COL1A1 causing osteogenesis imperfecta/hearing loss. Braz J Otorhinolaryngol 2023; 89: 101312.
[27] Rodriguez Celin M, Steiner RD and Basel D. *COL_1A_1*- and *COL_1A_2*-related osteogenesis imperfecta. In: Adam MP, Bick S, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, editors. GeneReviews((R)) [Internet]. Seattle (WA): University of Washington, Seattle; 1993.
[28] Batkovskyte D, Swolin-Eide D, Hammarsjo A, Sæther KB, Thunstrom S, Lundin J, Eisfeldt J, Lindstrand A, Nordgren A, Åström E and Grigelioniene G. Structural variants in COL_1A_1 and COL_1A_2 in osteogenesis imperfecta. Am J Med Genet A 2025; 197: e63935.
[29] Robinson ME, Rauch D, Glorieux FH and Rauch F. Pubertal growth in osteogenesis imperfecta caused by pathogenic variants in COL_1A_1/COL_1A_2. Genet Med 2022; 24: 1920-1926.
[30] Costache A, Riza AL, Popescu M, Șerban RC, Mituț-Velișcu AM and Streață I. Diagnostic challenges in bone fragility: osteogenesis imperfecta case series. Biomedicines 2025; 13: 865.
[31] Ciancia S, Högler W, Sakkers RJB, Appelman-Dijkstra NM, Boot AM, Sas TCJ and Renes JS. Osteoporosis in children and adolescents: how to treat and monitor? Eur J Pediatr 2023; 182: 501-511.
[32] Mäkitie RE, Henning P, Jiu Y, Kämpe A, Kogan K, Costantini A, Välimäki VV, Medina-Gomez C, Pekkinen M, Salusky IB, Schalin-Jäntti C, Haanpää MK, Rivadeneira F, Bassett JHD, Williams GR, Lerner UH, Pereira RC, Lappalainen P and Mäkitie O. An *$ARHGAP_{25}$* variant links aberrant Rac_1 function to early-onset skeletal fragility. JBMR Plus 2021; 5: e10509.
[33] Marr C, Seasman A and Bishop N. Managing the patient with osteogenesis imperfecta: a multidisciplinary approach. J Multidiscip Healthc 2017; 10: 145-155.
[34] Muñoz-Miro H, Lugo E, Carlo S and Ramírez N. COL1A2 (p.Gly322Ser) mutation causes late-onset osteogenesis imperfecta: a case report. Cureus 2022; 14: e30172.
[35] Intarak N, Budsamongkol T, Theerapanon T, Chanamuangkon T, Srijunbarl A, Boonprakong L, Porntaveetus T and Shotelersuk V. Tooth ultrastructure of a novel COL_1A_2 mutation expanding its genotypic and phenotypic spectra. Oral Dis 2021; 27: 1257-1267.
[36] Mehta P, Vishvkarma R, Gupta S, Chattopadhyay N and Rajender S. Exome sequencing identified mutations in the WNT_1 and COL_1A_2 genes in osteogenesis imperfecta cases. Mol Biol Rep 2024; 51: 449.
[37] Zhou X, Zhang Y and Wang N. Systematic identification of key extracellular proteins as the potential biomarkers in lupus nephritis. Front Immunol 2022; 13: 915784.
[38] Goddard JF, Mehrotra S and Mehrotra M. Osteogenesis imperfecta: exploring an autoimmune and immunotherapy perspective. JBMR Plus 2025; 9: ziaf053.
[39] Damian LO, Miclea D, Vulturar R and Craciun A. Osteogenesis imperfecta and rheumatoid arthritis: connective issues. Osteoporos Int 2022; 33: 2237-2239.
[40] Zora HK, Aydin T, Uzun Bektas A, Sahin S, Kasapcopur O and Kilic SS. A rare association of osteogenesis imperfecta and juvenile idiopathic arthritis: case reports and literature review. Turk J Pediatr 2025; 67: 273-281.
[41] Botor M, Fus-Kujawa A, Uroczynska M, Stepien KL, Galicka A, Gawron K and Sieron AL. Osteogenesis imperfecta: current and prospective therapies. Biomolecules 2021; 11: 1493.
[42] Jiang Y, Mei Y, Tian Y, Shen L, Xu S, Zhang H and Zhang Z. The vitamin D status in a Chinese osteogenesis imperfecta population and its correlation with bone metabolic markers and bone density. Front Nutr 2024; 11: 1390668.
[43] Riaz M, Hafeez S, Ibrahim MN, Khoso ZA, Laghari Br TM and Raza SJ. Safety and efficacy of zoledronic acid in children with osteogenesis imperfecta. J Coll Physicians Surg Pak 2022; 32: 1165-1169.