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Osteogenesis imperfecta and Rheumatoid arthritis: A coincidental association or a genetic overlap? A case report with literature review

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Case Report

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Abstract

Background: Osteogenesis imperfecta is a hereditary and rare disease characterized with frequent fractures, blue sclerae and hearing loss. Although musculoskeletal pain and deformities are common, persistent arthritis and inflammation are not a feature of the disease. Rheumatoid arthritis is a chronic autoimmune disease characterized by synovitis and progressive joint destruction. The coexistence of osteogenesis imperfecta and rheumatoid arthritis is exceptionally rare and poses diagnostic challenges

Case presentation: We report the case of a 25-year-old woman with a longstanding history of Osteogenesis Imperfecta diagnosed during adolescence with joint pain and deformity initially attributed to her disease. Rheumatoid arthritis that is positive for anti-cyclic citrullinated peptide auto anti bodies and rheumatoid factor was later on diagnosed and specific treatments helped to improve joint manifestations. As both Osteogenesis Imperfecta and Rheumatoid arthritis have skeletal deformities with different mechanisms, a possible pathogenic link was discussed and a literature review of cases with association was realized. Only four cases association cases have been reported so far.

Conclusions: The understanding of the putative pathogenic links between inflammatory arthritis and osteogenesis imperfecta may help in establishing new therapeutics.

Key Message

The presence of bony and skeletal deformities observed in a patient with osteogenesis imperfecta may be prone to misdiagnosis. An association with rheumatoid arthritis is possible and a shared pathogenic link may exist. Elucidating this link could provide valuable insights into the development of novel therapeutic strategies.

Introduction

Osteogenesis imperfecta (OI) is a genetic, rare connective tissuedisorder. Major clinical forms of OI represent quantitative and qualitative abnormalities of Type I collagen, the most abundant protein in bone [1]. It Is characterized by bone fragility and extra skeletal features such as blue sclerae, dentinogenesis imperfecta, hearing loss and ligamentous laxity [2]. However, inflammation was not a characteristic of the disease.

Rheumatoid arthritis (RA) is a chronic inflammatory disease affecting the joints, characterized by erosions and periarticular bone-resorption driven by proinflammatory cytokines [3]. Genetic predisposition and trigger factors like smoking or periodontitis are contributors to its development with the anti-citrullinated peptide antibodies (ACPA) and the rheumatoid factor (RF) serving as the key serologic biomarkers [4]. To date, the association of OI and RA was rarely described in the literature [5].

We report the rare case of a 25-year-old women, with OI and RA association. We describe her clinical, biological and radiological features, providing a review of literature.

Search strategy:

Publication search:

We performed a literature search in SCOPUS and PUBMED in English and French language using the following keywords chosen from the Medical Subject Headings (MeSH) of MEDLINE:

(“Rheumatoid arthritis” [Mesh]) AND (“Osteogenesis imperfect” [Mesh]).

The search included studies published from the database inception to September 2025

Three articles were selected in this review article [5, 6, 7].

Collection data:

Data of each case were collected: age at diagnosis of OI and RA, gender, genetic test of OI (if realized), RA serology, biology findings, and outcomes. The identified cases are shown in Table 1.

Case Presentation

Before the publication of the case details and accompanying images, written consent was obtained from the patient.

A 25- year-old woman presented to our rheumatology department with bilateral, symmetrical arthritis affecting mainly hands, knees and ankles. Her medical history was notable for OI, diagnosed since adolescence, based on a history of blue sclerae, recurrent fractures, hearing loss and osteopenia. The patient also reported a positive family history of recurrent fractures and blue sclera in her mother and brother.

The patient reported chronic articular pain and swelling of the knees and wrists over the last five years.

Her pain worsens at night and is accompanied with several episodes of morning stiffness. This subsequently affected her daily activities and limited her mobility. However, she denied systemic symptoms of fever, weight loss, or night sweats.

Physical examination revealed a BMI of 16.6 kg/m². She exhibited **blue sclerae** with normal vital signs and unremarkable neurological, cardiovascular and respiratory examinations. Musculoskeletal examination showed **bilateral, tender and swollen synovitis of the wrists, metacarpophalangeal and proximal interphalangeal joints**. She also had **bilateral knee arthritis with positive patellar tap** and bilateral painful ankle movement with no effusion.

Examination of the upper extremities unveiled a **Z-shaped deformity of the first phalanges** (Figure 1). Similarly, lower extremities showed deformities of the feet **with bilateral hallux valgus, triangular forefeet and claw toes** (Figure 2).

Laboratory investigations demonstrated elevated inflammatory biomarkers, with **erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) at 105 mm/h and 30 mg/L** respectively.

Complete blood count and liver enzymes were normal. Autoimmune screening revealed negative antinuclear antibodies (ANA), while **RF was positive at 300 IU/dL** (normal < 8 IU/dL).

Radiographic evaluation further supported the diagnosis of inflammatory arthritis. Hand X-rays showed **bilateral carpal joint inflammation**, **joint space narrowing** and **marginal erosions of metacarpophalangeal joints** (Figure 3). Similarly, feet radiographs showed **bilateral hallux valgus, joint space narrowing** and **periarticular erosion of metatarsophalangeal joints** (Figure 3). Additionally, pelvic radiographs demonstrated **bilateral coxitis**.

Musculoskeletal ultrasound was performed and demonstrated **active bilateral synovitis of both wrists,** along with **tenosynovitis of the carpal ulnar extensor tendons**, supporting the diagnosis of inflammatory arthritis.

Bone densitometry measurement revealed osteopenia with **T-scores of – 2.3 at the lumbar spine** and **– 2.0 at the left hip**, consistent with her OI history.

Taking all of the clinical, biological and radiographic information into consideration, we reached the diagnostic conclusion an active RA in a patient with pre-existing OI and she was initially treated with sulfasalazine (2g/day) and methotrexate (20mg/week). However, despite optimal adherence, the patient's symptoms persisted, prompting the initiation of a biological treatment. Consequently, infliximab at the dose of 3 mg/kg every two months was prescribed, leading to a marked clinical and biological improvement, achieving a persistent low disease activity on follow-ups (DAS28-ESR=2.6).

Discussion and review of the literature:

Our case is of interest because it highlights the exceptional co-existence of OI, a genetic bone disease, and RA, a chronic inflammatory rheumatism.

OI is rare, with an estimated prevalence of 1 in 15, 000 to 20, 000 people [8, 9]. Its diagnosis is clinical, based on skeletal and extra-skeletal manifestations [2]. Genetic study is not essential for diagnosis. Nevertheless, it is usually offered to the parents as part of genetic counselling, if a pregnancy is desired.

The extent of OI ranges from mild to extremely severe [10]. It is characterized by congenital bone fragility that results in pathological fractures responsible for the high morbidity and mortality of the disease.

The occurrence of multiple fractures is variably linked to deformities in long bones, the spine, pelvis, and thorax. This is accompanied by ligament hyperlaxity leading to deformities in fingers or toes. Other features include reduced stature, blue sclera, dentinogenesis imperfecta, hyperlaxity of the skin, and hearing impairment [11].

In our case report, we describe a patient with OI who was also diagnosed with RA, complicated with joint deformities of the hands and feet. While the OI disease itself can cause arthralgias, ligamentous laxity, tendon rupture and reversible contractures leading to deformities like swan neck fingers, it does not typically present with inflammatory arthritis, synovitis, or erosive radiographic changes [12,13]. Therefore, the coexistence of RA and OI may be considered as either an incidental finding or a particular phenotype, induced by specific mutations.

More than 90% of OI cases stem from mutations in the COL1A1 and COL1A2 genes, which encode the alpha-1 and alpha-2 chains of type I collagen. These variant impairments result in deficiencies in the quantity and/or quality of type 1 collagen [14,15].

Beyond reducing collagen production, COL1A1 mutations can also alter post-translational processing, extracellular matrix interactions, and receptor-mediated signaling pathways [16,17]. Several key ligands that bind to collagen, including cytokines, cell adhesion molecules, matrix metalloproteinases, proteoglycans, and other molecules, are known targets of autoimmunity and contribute to the pathogenesis of RA [18].

In addition, endoplasmic reticulum stress has been observed in both RA and OI, likely resulting from protein misfolding or excess. This promotes apoptosis and the generation of autoantigens, subsequently triggering inflammatory response. [19].

Another hypothesis was suggested by Okamoto K et al. [3], states that the structural abnormalities and repeated trauma in OI, such as fractures, could locally activate the innate immunity and precipitate arthritis, similar to post-traumatic arthritis. Notably, systemic inflammation, a hallmark of RA, has occasionally been described in OI [1].

Through our literature review, we came across four previously reported cases of OI and RA association (Table 1). The patients were all female aged 25 to 75 years (mean 47.4 years) with OI generally diagnosed since childhood or adolescence. Type 1 OI was the most commonly reported. Recurrent fractures, blue sclera and osteoporosis were the most commonly reported symptoms. Genetic testing was performed in three patients [5, 6, 7].

Damian's case revealed a previously unreported deletion in the COL1A1 gene (c.3399del, p.Ala1134Profs*105). This deletion, absent in population databases, results in a premature translational stop signal in the COL1A1 gene, within the major ligand binding region 3 of collagen 1 [5].

Similarly, Mormile et al. identified a pathogenic heterozygous missense variant in COL1A1 p.(Gly257Arg), affecting the presumed ligand binding site for interleukin-2 and α2β1 integrin [7].

RA onset average age in these cases was 39 years and all were immunopositive.

Regarding therapy, patients were treated mainly with conventional synthetic disease-modifying antirheumatic drugs (methotrexate, sulfasalazine, leflunomide) with a general improvement in symptoms. Biologic therapy with anti-TNF agents (Infliximab, Adalimumab) was used in the treatment of our case and in Mormile's achieving favorable results.

The key insight from our case report is to underline the importance of considering alternative osteoarticular pathologies in patients followed for OI rather than systematically attributing all skeletal or extra-skeletal manifestation to OI itself. Clinicians should further investigate any severe joint deformities or destructive arthritis in extremities of patients with long-standingOI**.**

Further investigation of potential pathophysiological links between OI and inflammatory arthritis, as suggested by Mormile et al, can deepen our understanding of their shared pathways and guide new therapeutic approaches.

Limitations

Although musculoskeletal ultrasound was performed and confirmed active bilateral synovitis and tenosynovitis, ultrasound images were not available for inclusion, as the examination was performed as part of routine clinical care and images were not archived for research or publication purposes.

Despite these limitations, the diagnosis of rheumatoid arthritis was supported by the combination of clinical features, serological findings, ultrasound results, and available radiographic data. This case highlights a rare clinical association and underscores the need for further studies to explore potential shared mechanisms between osteogenesis imperfecta and inflammatory rheumatic diseases.

Conclusions

The coexistence of Osteogenesis Imperfecta and Rheumatoid Arthritis is rarely described in literature. Further investigations are needed to understand the pathogenesis underlying this association. Raising awareness regarding a possible association may facilitate early recognition and management, ultimately improving quality of life in affected patients.

Abbreviations

Anti-citrullinated peptide antibodies (ACPA)

C-reactive protein (CRP)

Erythrocyte sedimentation rate (ESR)

Rheumatoid arthritis (RA)

Rheumatoid factor (RF)

Osteogenesis imperfecta (OI)

Declarations

Funding: No external funding from public, commercial or non-profit organizations was received to support the work presented in this article.

Consent of participation: Informed consent from the patient was obtained to carry our research.

Consent for publication: Informed consent for publication of this case report and any accompanying images or data from the medical file was obtained from the subject. All identifying information has been removed to protect patient anonymity.

Ethics approval: Our locally appointed hospital ethics' committee has approved the research protocol.

Data availability statement: All data from our research is available upon reasonable request.

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Tables

Table1: Cases of co-existence of Osteogenesis imperfecta and rheumatoid arthritis reported in literature

Authors	Age /gender	Age of diagnosic of OI	Genetic test/ Type of OI	Symptoms of OI	Age of diagnosis of RA	Biology	Treatment	Evolution
Bica et al (2013) **[6]**	53/F	Childhood	Not done	Recurrent fractures Blue sclera Osteoporosis Bone deformities	15	-ESR:72 mm/h -positive FR	Gold salts	Not described
Damian et al (2020) [5]	46/F	Adolescence	A COL1A1 heterozygous pathogenic variant, c.3399del, p.Ala1134Profs*105) Type 1 of OI	Recurrent fractures Blue sclera osteoporosis	46	-ESR:43 mm/h, -CRP:24 mg/L -RF:28 IU/dL -ACPA: 224 IU/ml	Sulfasalazine Methotrexate Leflunomide	Good clinical and biological evolution with Leflunomide
	70/F	Adolescence	A COL1A1 heterozygous pathogenic variant, c.3399del, p.Ala1134Profs*105) Type 1 of OI	Recurrent fractures Blue sclera Osteoporosis Bone deformities Hearing loss	70	-ESR: 34 mm/h -CRP: 12 mg/ -RF: 32 IU/mL ACPA: 218 IU/mL	Methotrexate Leflunomide	Good clinical and biological evolution with Leflunomide
Mormile et al **(2022)** **[7]**	43/F	Infancy	A pathogenic heterozygous missence variant in COL1A1 gene, NM_000088:c.769 G>A, p.(Gly257Arg) (rs72645321; HGMD ID: CM960320).	Recurrent fractures	43	Not specified	Adalimumab	Not specified
Our case	**25/F**	Adolescence	Not done	Recurrent fracture Blue sclera Osteopenia Hearing loss	25	-ESR:105 mm/h CRP:30mg/L FR:300UI/l	Sulfasalazine Methotrexate Infliximab	Good clinical and biological evolution wih Infliximab.

Figures



Figure 1

Photographs of the patient's hands



Figure 2

Photograph of the patient's feet



Figure 3

a: Hand radiography: bilateral carpitis, joint space narrowing and marginal erosion of metacarpophalangeal joints.

b: Feet radiography: bilateral hallux valgus and marginal erosion of metatarsophalangeal joints.