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Does Celiac Cause Acro-Osteolysis: A Case Report Study

Mohammad Eshagh Hosseini [1], Mohammad Heidary [1], Seyed Mahmoud Eshagh Hosseini [2], Samira Alesaedi [2, 3, *] and Iraj Salehi Abari [2, 3]

[1] Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran
[2] Amir Alam Research Center, Tehran University of Medical Sciences, Tehran, Iran
[3] Rheumatology Research Center, Tehran University of Medical Sciences, Tehran, Iran

[*] *Corresponding author*: Rheumatology Research Center, Tehran University of Medical Sciences, Tehran, Iran. Email: dr.saedi62@yahoo.com

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Abstract

Introduction: Acro-osteolysis is characterized by resorption of distal phalanges of fingers and toes. Plain radiography is the best imaging technique for the detection of acro-osteolysis.
Case Presentation: Our report describes a 38-year- old man with a history of rheumatoid arthritis and celiac disease, who presented with shortness of distal phalanges. Roentgenograms disclosed terminal phalangeal resorption in the fingers.
Conclusions: All work-ups were normal from tests and surveys for secondary causes. According to longstanding and poor-controlled celiac disease, after excluding secondary causes, we presume that celiac disease is the leading cause of acro-osteolysis in this patient.

Keywords: Acro-Osteolysis, Digital Clubbing, Celiac, Rheumatoid Arthritis, Resorption

1. Introduction

Acro-osteolysis is characterized by resorption of distal phalanges of fingers and toes. Acro-osteolysis possesses two patterns of resorption in adults: diffuse and band-like (1). Differential diagnosis includes primary and secondary. Secondary causes are more common, including pyknodysostosis, collagen vascular disease, vasculitis, Raynaud's, trauma, epidermolysis bullosa, psoriasis, psoriatic arthritis, frostbite, sarcoidosis, and hypertrophic osteoarthropathy (2).

Characteristic of digital clubbing is that the terminal segments of the fingers and toes get enlarged because connective tissue between the nail matrix and the distal phalanx gets proliferated (2). It increases the front, back, and sideway diameter of the nails. Clubbed fingers are also called as Hippocratic fingers/nails, watch-glass nails, and drumstick fingers. For the first time, it was described by Hippocrates almost two and half millennia ago in a patient with empyema (2). Subsequently, it was diagnosed that it is associated with different clinical conditions consisting of lung cancer, liver cirrhosis, bronchiectasis, etc.

In spite of the fact that clubbed fingers are mainly symptomless, which often demonstrates the existence of outrageous internal sickness as idiopathic pulmonary fibrosis, lung cancer, or underlying supportive conditions (2).

Pseudo-clubbing (PC) is regarded as an unusual manifestation of clubbing, distinguished clinically through unsymmetrical inclusion of the fingers, and radiographically via re-absorption of the closing tufts (acro-osteolysis).

Celiac disease is a genetic autoimmune disorder. It is also called gluten-sensitive enteropathy and non-tropical sprue. The precise relationship between celiac disease and excess bone loss is still unrevealed; nevertheless, there are diverse possible reasons for the relationship, such as Vitamin D deficiency, calcium, and magnesium malabsorption, and persistent inflammation (3).

Rheumatoid arthritis (RA) is a systemic illness distinguished by inflammation of the synovial tissues interlining the joints.

The multiplication of synovial lining cells and penetration of inflammatory cells into the joint tissues leads to the emergence of "pannus" tissue covering the surfaces of articular cartilage and bone producing proinflammatory factors that result in the demolition of both bone matrix and cartilage.

To the best of our knowledge, there is no published literature revealing the incidence of celiac involving acro-osteolysis. Acro-osteolysis can be associated with a wide selection of systemic and localized malformations, plus acquired and congenital.

Based on the past literature, celiac disease could be a rare and unknown cause of acro-osteolysis. In this study, we aimed to examine the role of celiac in the incidence of acro-osteolysis.

2. Case Presentation

A 38-year-old man who resided in the city of Tehran, Iran, and previously shoemaker presented with shortness of multiple distal phalanges from three months ago. He was a known case of rheumatoid arthritis and celiac disease in the last four years ago (Table 1).

Table 1. The Variables of Underlying Diseases of the Case[a]

Clinical Parameters	Measures (Normal Value)
Rheumatoid	
Chronic polyarthritis	Small and large joints of lower and upper limbs. (> 10)
Rheumatoid factor (RF)	32 (15)
Anti-CCP	6.2 (5.2)
ESR	35
CRP	2+
Celiac	
Duodenal biopsy	Inflamed mucosa, crypt hyperplasia, intraepithelial lymphocytes, and villous atrophy
weight loss and diarrhea	Significant
Anti-gliadin Ab IgG	52 (12)
Anti-gliadin Ab IgA	93.1 (12)

[a]Values are expressed as No. (%).

The patient fulfilled RA criteria with chronic polyarthritis accompanying, positive RF (32 > 15) and Anti-CCP (6.2 > 5.2), elevated ESR (35), and CRP (2+). Celiac disease was also confirmed by the history of weight loss and diarrhea, positive Anti-Gliadin Ab IgG (52 > 12), and anti-gliadin Ab IgA (93.1 > 12) with characteristic biopsy view of the duodenum, which indicated inflamed mucosa, crypt hyperplasia, intraepithelial lymphocytes, and villous atrophy.

The patient was on the gluten-free regimen for a while, and he did not show any symptoms at that time. The medications included prednisolone 5 mg daily and methotrexate 15 mg weekly.

His family history was negative for any autoimmune disease or similar symptoms. He drank alcohol occasionally and did not mention any drug addiction. He also denied using any vibrating tool, having any trauma, and thermal injury.

In physical examinations, acro-osteolysis of distal phalanges of fingers in the patient during first visit and diagnosis in 2014 was presented (Figure 1). It was observed that multiple distal phalanges were shortened, and no other abnormality was detected.

There was no malformation of long bones, including craniofacial dysmorphism and serpentine fibula. The patient was admitted to the rheumatology ward for further evaluation. Acro-osteolysis of distal phalanges of fingers in the patient during the last visit in 2018 was presented (Figure 2). Acro-osteolysis was confirmed with plain radiography. Multiple lysis in the distal phalanges were evident.

According to the family history, celiac and RA flames should be kept in mind. ESR, CRP, and CBC all were normal. Anti-CCP was not high. There was no evidence of arthritis and arthralgia. The patient also did not mention any recent weight loss and diarrhea. Moreover, 24-hour stool did not suggest steatorrhea, and endoscopy was normal.

He did not report any sweating, weight loss, hair loss, irritability, palpitation, and tremor. While examination, thyroid gland palpation was normal, with no nodules. TSH, T3, and T4 were also normal, which hyperthyroidism ruled out. There was no complaint of abdominal pain or bone pain. Bone marrow density (BMD) was done, which demonstrated osteopenia with T-score of -1.49. In addition, Ca, P, PTH, and 25-OHD were normal as well. The parathyroid scan did not report hyperactivity in the glands. He also did not have other radiological manifestations of hyperparathyroidism, such as a brown tumor, subperiosteal resorption, or soft tissue calcifications.

The osteopenia could be explained with corticosteroid consumption chronically by the patient in the last four years. Neuropathy was less likely because of no sensory or motor disturbances, as well as a negative family history for neurological problems. There were no signs or symptoms of other underlying diseases such as diabetes, vitamins, and mineral deficiencies. Normal EMG-NCV excluded whole causes of neuropathy, vasculitis, and dermatomyositis.

Scleroderma may cause acro-osteolysis besides other manifestations, like Raynaud phenomenon, skin stiffness, limb gangrene, etc. No evidence of Raynaud and skin changes were detected in our patient, and the related autoantibodies were shown to be negative.

Reactive arthritis can cause acro-osteolysis in rare conditions. The patient did not explain recent gastrointestinal (GI) or urogenital infections recently, and arthritis in axial joints was not detected in physical examinations.

We believe that celiac disease is a leading cause of acro-osteolysis in this case.

The gluten-free regimen was taught to the patient more accurately and was suggested to visit the doctor every three months.

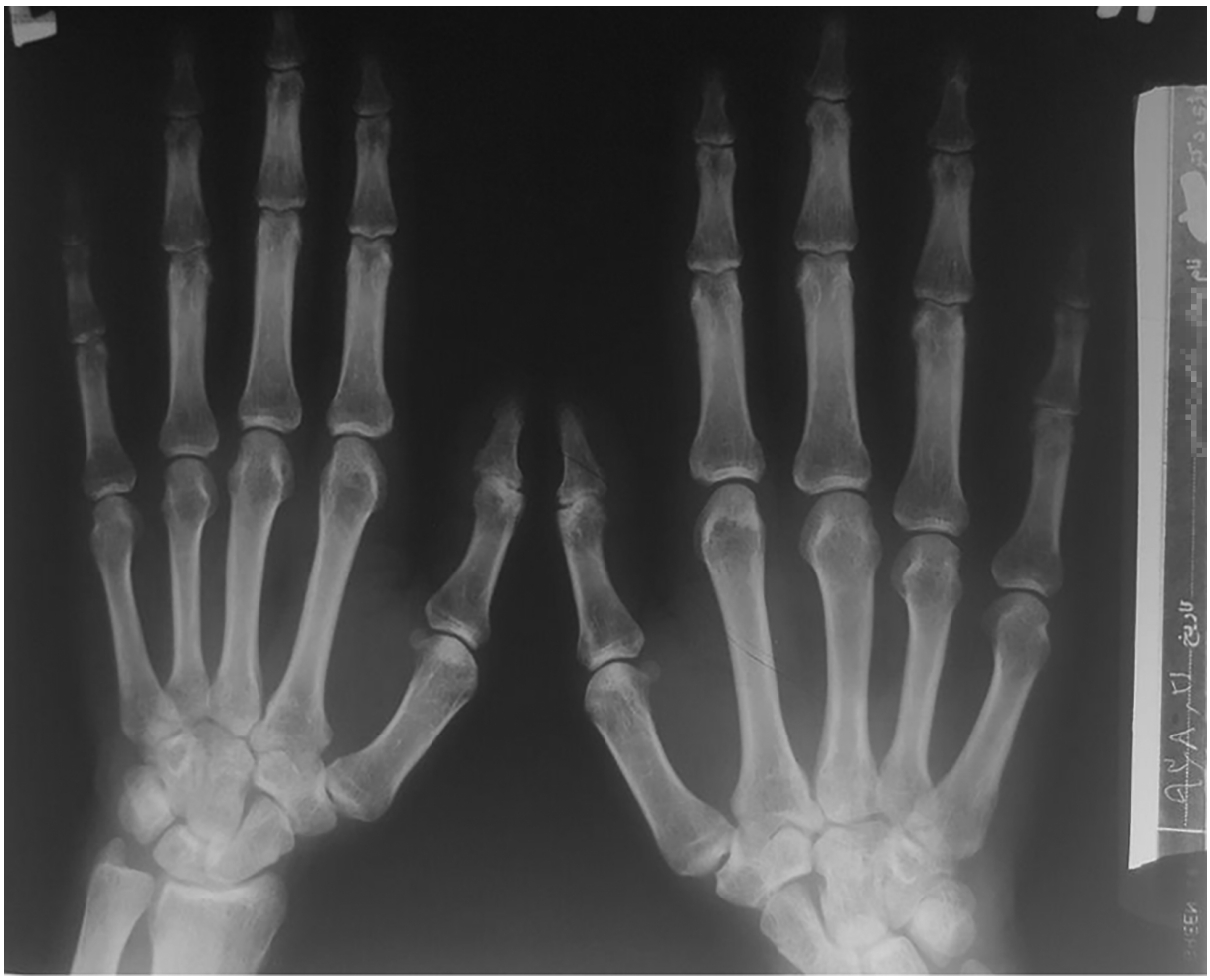

Figure 1. Acro-osteolysis of distal phalanges of fingers in the patient during first visit and diagnosis in 2014

3. Discussion

Pseudo-clubbing (PC) is regarded as an unusual introduction of clubbing, distinguished clinically through unsymmetrical inclusion of the fingers, and radiographically via re-absorption of the closing tufts (acro-osteolysis). It has been reported in chronic renal failure, subungual hemangioma, systemic sclerosis, acrometastases, etc. The precise mechanism is not clear, but it could be the consequence of soft-tissue collapse because of distal phalangeal osteolysis (4).

Mittermayer et al. suggested the following features that may help in differentiating PC from clubbing. In PC, profile sign is usually normal, and there is usually asymmetrical nail involvement. Acro-osteolysis is classically present instead of soft tissue swelling of the nail bed in clubbing. Acro-osteolysis may also be present in Hypertrophic Osteoarthropathy (HOA), but unlike HOA, there are no signs of periostitis or synovial effusion (4).

In an approach to acro-osteolysis, at first, we should confirm it with radiology, and the plain X-ray is the most accessible and beneficial image technique. Trauma, electrical devices, and thermal injuries should be kept in mind if the acro-osteolysis is in the single phalanx. Taking history with complete details could help to rule out or rule in these possible diagnoses.

Epidermal inclusion cyst, in rare cases, happens in bones with a single acro-osteolysis presentation. It is mostly manifest inflammatory symptoms such as erythema, edema, and tenderness, in the bones or nails. The biopsy of the lesion is helpful. Glomus tumors can cause acro-osteolysis of a finger in the terminal phase, as it is placed in glomus body rich spots of skin, such as subungual regions. It has a purple appearance and presents as a

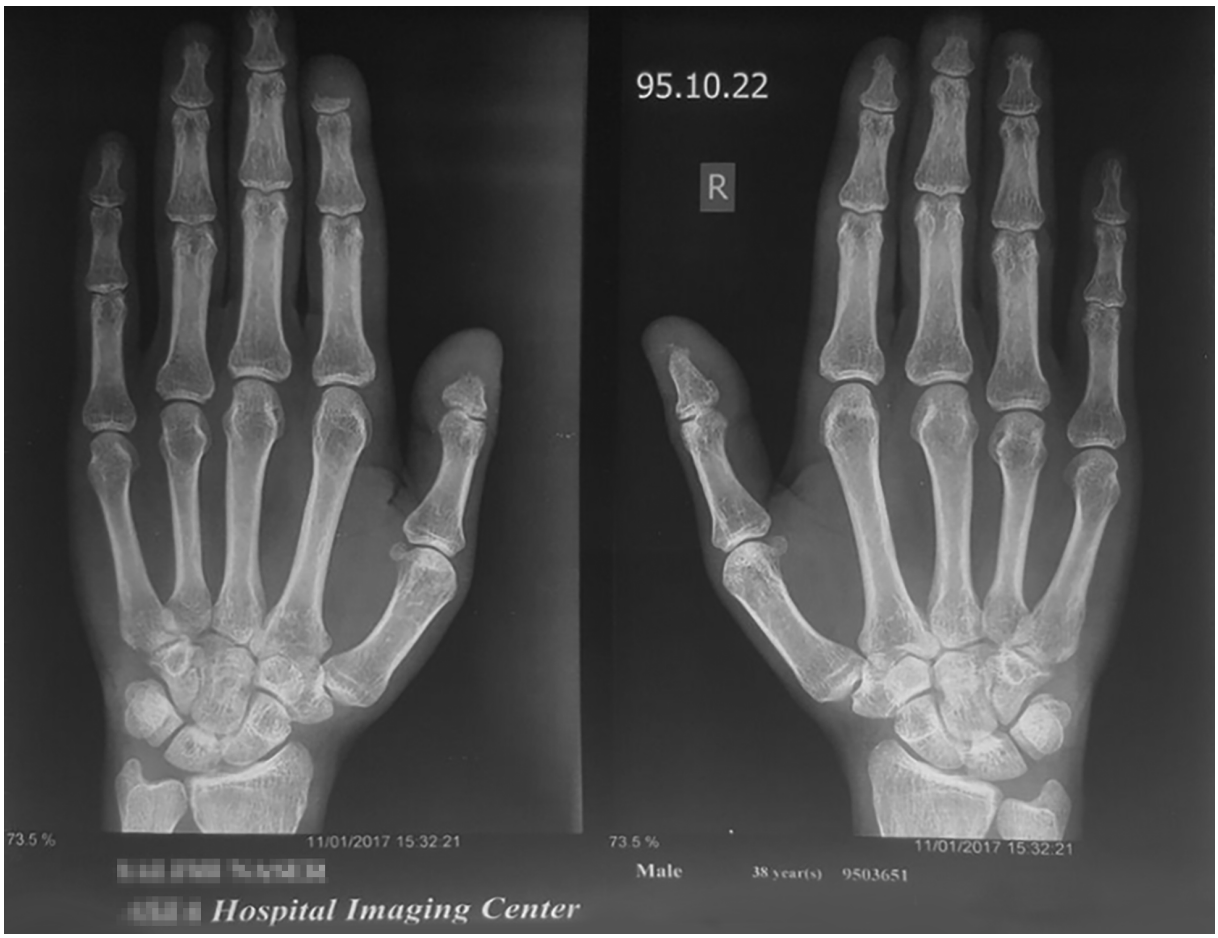

Figure 2. Acro-osteolysis of distal phalanges of fingers in the patient during last visit in 2018

painful nodule. A biopsy is confirming.

Further, any lying diseases should be surveyed as the leading cause. Flare-up indices in the underlying diseases must be rechecked. Also, CBC, ESR, and CRP, as inflammatory markers, are recommended in autoimmune diseases.

According to which phalanges involve, the differential diagnosis may be different.

Multiple distal phalanges involvements are the most common and vague ones. Hyperparathyroidism causes various types of bone involvements. Subperiosteal bone resorption, Brown tumor, soft tissue calcification, and acro-osteolysis are some of the reported radiographic features. On the occasions, which hyperparathyroidism has caused acro-osteolysis, generalized osteopenia is not improbable. Hyperparathyroidism can lead to mid-shaft resorption as well (5). Hyperthyroidism can be assessed with thyroid examination and Thyroid Function test (TFT) evaluation in the case that symptoms of hyperthyroidism are present.

Scleroderma by the related vasculopathy can cause terminal shaft resorption. It should be remembered that in these patients, other symptoms of vascular involvements, such as Raynaud phenomenon, pitting ulcer, and gangrene are present. Anti-nuclear antibodies (ANA), anti-scl-70, and anti RNA polymerase are highly specific in diagnosis (6).

Vascular occlusion by thrombosis or emboli may cause the exact symptoms to happen in scleroderma. The patient mostly has a history of atherosclerosis or valvular disease (7).

Psoriatic arthritis is another rare condition of terminal acro-osteolysis. Psoriatic skin changes or pitting nails are detected in physical examination, or a patient mentions the history (8).

Reactive arthritis in the patient with GI or GU infection in the last several weeks can be another answer. The arthritis is chronic and asymptomatic. All serum indices were

negative; however, HLA-B27 is positive and helpful in half of the cases. In severe cases with bone resorption, skin manifestations like keratoderma and ulcers are confirmative (9).

Leprosy, due to the neuropathy, can cause acro-osteolysis as well. The patient has a history of traveling to the endemic area, and painless skin lesions, which demonstrate *Mycobacterium leprae* in acid-fast culture (10).

Tuberculosis, as a thousand faces infection, should be highly considered in every patient with no explained acro-osteolysis. Tuberculosis mostly invades to one finger and associates with discharge or wound and systemic presentations, whereas all the symptoms can be absent. Special caution must be taken in endemic regions.

Metabolic bone disease is common in celiac disease. Osteopenia, osteoporosis, and osteomalacia are sometimes seen (10). A higher prevalence of osteoarthritis is also described in celiac disease (10).

In this study, we did not find any published literature confirming the association between celiac disease and acro-osteolysis.

3.1. Conclusions

Acro-osteolysis can be associated with a wide selection of systemic and localized malformation, as well as acquired and congenital. Differential diagnosis includes primary and secondary causes. The primary is rare, while secondary causes are more common. Of special importance are the collagen-vasculature disorders, hyperparathyroidism, scleroderma, job-related causes, injury, psoriatic arthritis, and genetic syndromes (e.g., HadjuCheney syndrome). Clinical features, laboratory data, and other investigations should be connected to reaching the correct diagnosis in most cases.

Celiac disease could be a rare and unknown cause of acro-osteolysis. We believe that celiac disease as a leading cause of acro-osteolysis in this case. After excluding all the other causes, according to past medical history, uncontrolled celiac disease, acro-osteolysis due to celiac disease is the most possible one.

3.2. Weakness and Strength of the Study

The weakness of this study is that as this is a case report; therefore, there is a need for further studies in order to conclude that celiac disease could cause acro-osteolysis in general.

The strength point of our study is the thorough and deep examinations and work-ups done by the authors for excluding all the possible differential diagnoses of acro-osteolysis. As a result, the authors believe that celiac disease is a leading cause of acro-osteolysis in this case.

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Footnotes

Authors' Contribution: ME drafted the initial manuscript, was involved in the care of the patient and edited, and approved the final manuscript. SA made the pathological diagnosis and provided the figures for the manuscript and reviewed and revised the manuscript and approved the final manuscript. All authors read and approved the final manuscript.

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Informed Consent: Written informed consent was obtained from the patient for publication of this case report, and any accompanying images and a copy of the consent form was uploaded to review.

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