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Case Report

# Radiological insights into mandibuloacral dysplasia: A case report ☆

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ABSTRACT

Mandibulo-acral dysplasia was first described by Young et al in 1971. It is a rare, autosomal genetic disorder describing characteristic general, craniofacial, and oral manifestations. However, the detailed characteristics of this multisystemic disease have not yet been clarified due to its rarity and the limited number of cases described. Through a clinical case, we have tried to expose some of the most common clinical and radiological signs especially in their bucco-facial location, some modalities of management and the importance of an early diagnosis which turns out to be a real challenge especially for dentists in their daily practice.



## Introduction

Mandibulo-acral dysplasia (MAD) is a rare autosomal genetic disorder characterized by growth retardation, skeletal abnormality with progressive osteolysis of the distal phalanges and clavicles, craniofacial anomalies with mandibular hypoplasia, lipodystrophy, mottled cutaneous pigmentation, late closure of the cranial sutures, a thin, beak-shaped nose, prominent eyes, and postnatal growth retardation [1].

Two main types of MAD have been differentiated on the basis of body fat distribution patterns: type A, characterized by a partial form of lipodystrophy MADA, and type B, with generalized lipodystrophy MADB [2].

But, due to the rarity of this disease and the limited number of cases described, the detailed characteristics of this multisystem disease have not been fully elucidated.

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The aim of this study was to highlight unusual clinical and radiological features of the MADA, namely sinus hypoplasia and arthrosis of the temporomandibular joint through a case of a MADA patient with a severe mouth opening limitation. A clinical case of a Tunisian patient followed for 8 years was reported.

## Case report

The patient was born in 2004 to healthy parents. The family's country of origin is Tunisia, and within its lineage, 2 brothers and their sister are diagnosed with MADA. The parents are first cousin. Extensive investigations revealed that the family has lost 2 brothers from acute heart failure. At his first consultation, the patient, who is the eldest brother, was 12-year-old. It was stated that his sister and his brother had a physical appearance similar to the patient's. He was referred to the radiology department for appropriate radiological examinations to uncover the various manifestations of this condition. The patient presented with craniofacial dysmorphia, namely mandibular hypoplasia resulting in anterior dental crowding, significant dento-maxillary disharmony and labial incompetence with the prominence of the zygomatic bones and orbital arches. He had prominent eyes, a beaked nose, and a small mouth. The patient showed no abnormalities during the perinatal period. Functionally, he had a severe limitation of mouth opening (18 mm) with signs on osteoarthritis of the left temporomandibular joint (TMJ). At the trunk level, a decrease in biacromial distance as a result of clavicular hypoplasia was observed. At the limb level, the child presented contractures at the interphalangeal joints of the hands with flexion deformity of the fingers. Mottled pigmentation was noted all over the body, sparing the face and palmoplantar skin. Moreover, he had a growth hormone (GH) deficiency. Psychomotor, vocal and cognitive development were normal. This patient presented type A acral lipodystrophy.

A full radiological work-up was requested. Lateral and frontal radiographs (Fig. 1) showed delayed closure of the metopic and lambdoid sutures, slight mandibular hypoplasia with antegonial depression and dental crowding in the anterior region. The panoramic radiograph (Fig. 2) showed a mandibular antegonial depression and flattened mandibular condyles. For a better visualization of the TMJ and to have a clear idea about this condition, a computed tomography (CT) scan was performed. Multiple subchondral microgeodes, cortical erosion, and pinching of the joint space were revealed at the level of both condylar heads in Fig. 3A, with local temporomandibular bone ankylosis more pronounced on the left side. Axial CT and coronal CT scans (Figs. 3B and C) revealed maxillary right sinus hypoplasia associated with a depression of anterior surface of the maxilla. Wormian bones were revealed in Fig. 3D. The open lambdoid cranial suture can be seen in para-sagittal CT scan section (Fig. 3E).

The 3-dimensional (3D) CT scan reconstruction in profile view (Fig. 4A) confirmed the antegonial bone depression observed in the 2-dimensional imaging. The 3D CT scan reconstruction in frontal view (Fig. 4B) revealed dental crowding. In terms of clinical and radiological examination, this patient presented with significant dento-maxillary disharmony with severe limitation of mouth opening, left temporomandibular ankylosis, and hypoplasia of the right maxillary sinus. The patient was referred for a possible left condyloplasty to address the joint ankylosis. After assessing the benefits-to-risks ratio of this surgery, the decision to proceed with the intervention was made. The release of the joint improved mouth opening from 18 to 35 mm. The patient underwent replacement therapy with somatotropin (GH). This patient was under observation for the last 8 years. At the age of 18, in 2022, he received an orthodontic treatment to correct the dental crowding. The

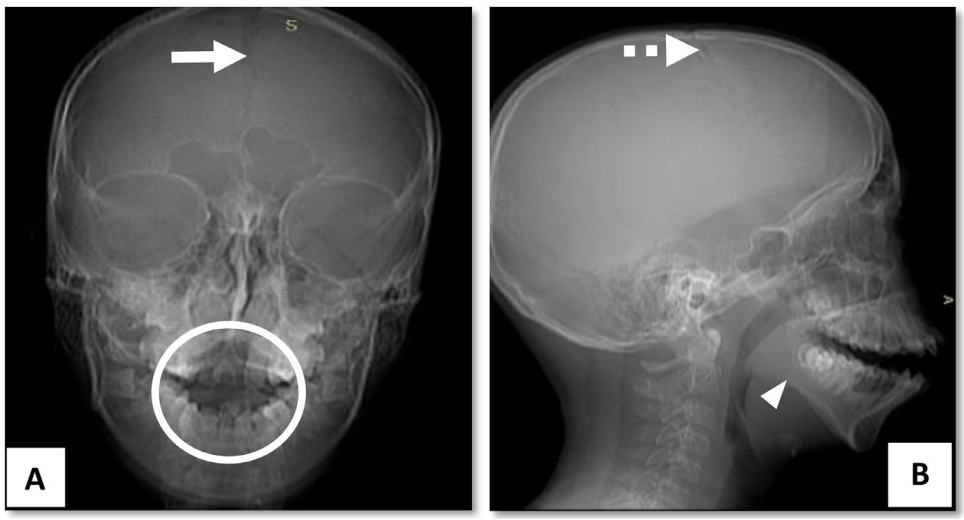


**Fig. 1 – (A) Frontal radiograph of the skull revealing dental crowding in the anterior region (circle) and open cranial metopic suture (white arrow). (B) Lateral radiograph of the skull showing hypoplasia of the mandible with preangular depression (arrowhead) and open cranial lambdoid suture (dashed white arrow).**

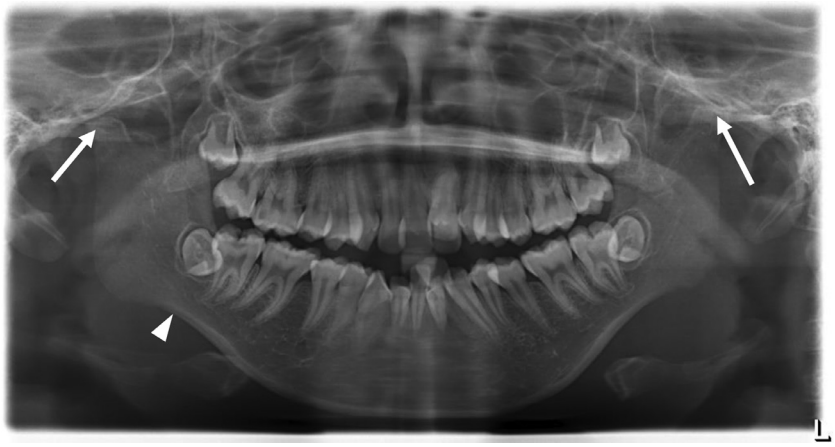

**Fig. 2 – Panoramic radiograph: Mandibular antegonial depression (arrowhead) and flattened mandibular condyles (white arrow).**

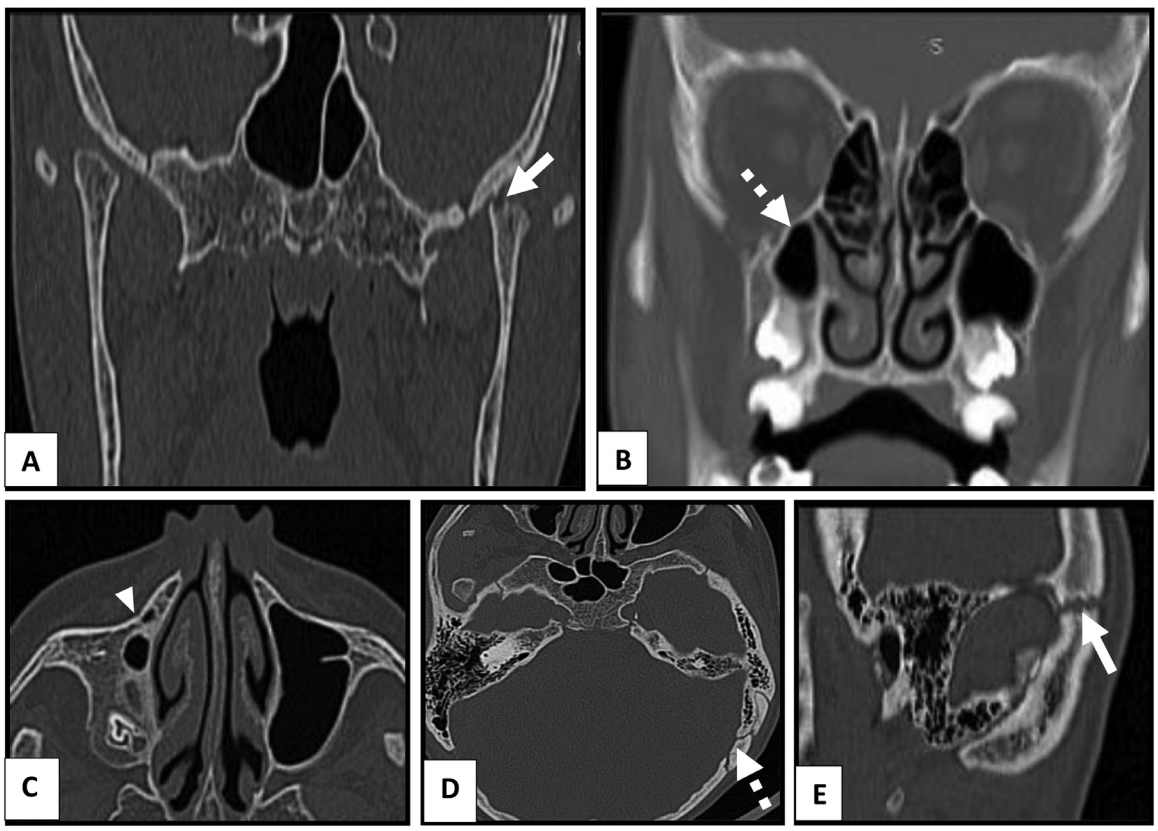


**Fig. 3 – (A) Frontal section wide window CT scan through the mandibular branches and condylar heads revealing bicondylar shape anomaly with flattening of the articular surfaces and the presence of osteophytes, more pronounced on the left side (white arrow). (B) Frontal section wide window CT scan through the molar region revealing maxillary right sinus hypoplasia (dashed white arrow). (C) Axial section wide window CT scan of the maxillary sinuses revealing depression of the anterior surface of the right maxillary bone (arrowhead). (D) Axial section wide window CT scan revealing wormian bones (dashed white arrow). (E) Parasagittal section wide window CT scan revealing open lambdoid cranial suture (white arrow).**

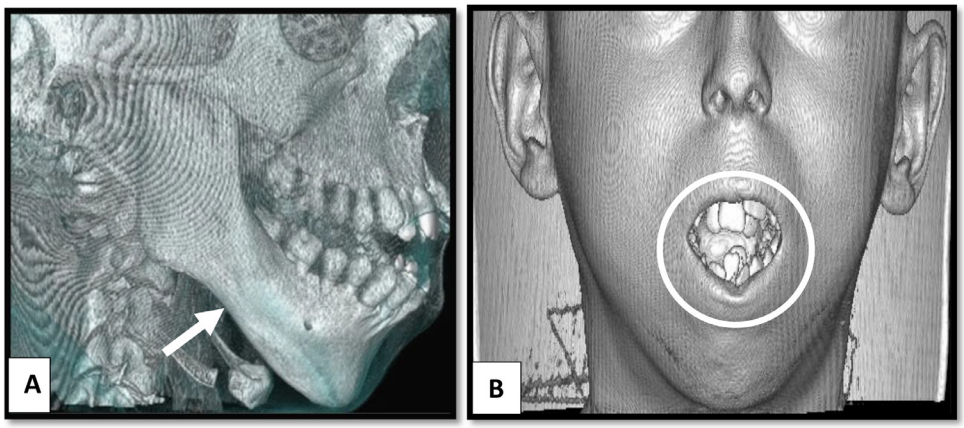


**Fig. 4 – (A) 3D CT scan reconstruction in profile view revealing antegonial bone depression (white arrow). (B) 3D CT scan reconstruction in frontal view revealing dental crowding and labial incompetence (circle).**

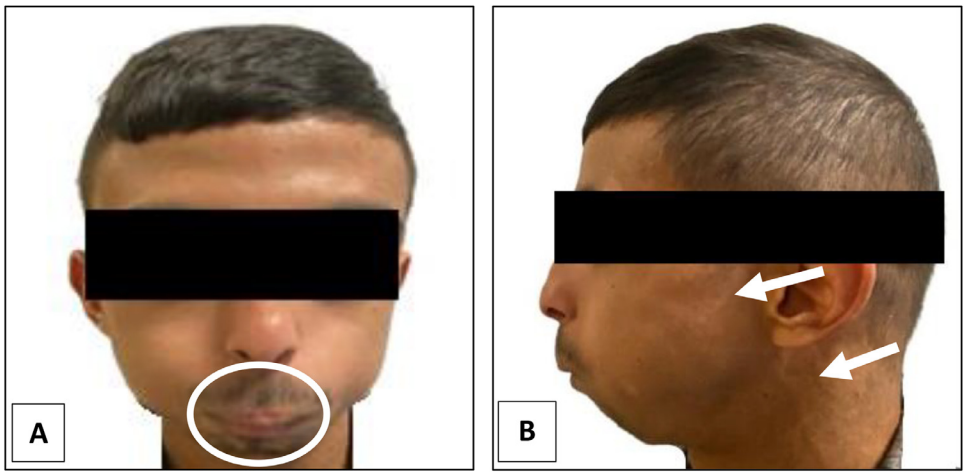


**Fig. 5 – Facial appearance after orthodontic treatment: Small mouth, puffy cheeks, beaked nose, retromicrognathia and mottled pigmentation on the neck and on the cheek (white arrows). Labial incompetence has been rectified (circle), (A): Front view; (B): Lateral view.**

reevaluation in January 2024 (Fig. 5) highlighted an improvement in dental crowding and labial incompetence. Clinical and radiological control (Fig. 6) revealed an advanced acroosteolysis of the distal phalanges of both hands.

At this stage of treatment, a mandibular advancement surgery is also scheduled.

## Discussion

Patients with MAD have a distinctive facial appearance, mostly characterized by prominent scalp veins, exophthalmos, a thin beaked nose, slow and progressive osteolysis of the mandible, phalanges, and clavicles, microstomia with dental overlapping and malocclusion. Delayed closure of cranial sutures is common. Intelligence is normal [3,4]. These characteristics, evident in the literature review, are present in our case. In addition to the phenotypic changes, these patients may present certain metabolic abnormalities. These include hypertriglyceridemia, insulin resistance, and even diabetes mellitus [5]. Although our patient has a GH deficiency, no correlation between GH deficiency and MADA has been well described in the literature. Our patient is the first documented case in the literature of MADA with maxillary sinus hypoplasia. Indeed, the diagnosis of this hypoplasia relies primarily on CT scans. However, based on the literature concerning MADA, only 3 case reports [6–8] have utilized CT scans. This might explain why this manifestation often goes unnoticed.

Mandibular hypoplasia is considered a major diagnostic criterion. Its underdevelopment gives the appearance of a receding chin. This mandibular hypoplasia can lead to respiratory and feeding difficulties. Dental anomalies, such as dental crowding, especially in the anterior region, enamel hypoplasia, and premature loss of mandibular teeth, have been observed to varying degrees in cases of MADA [7,3,9]. Unlike case reports mentioning that the majority of patients had premature loss of mandibular teeth with an edentulous

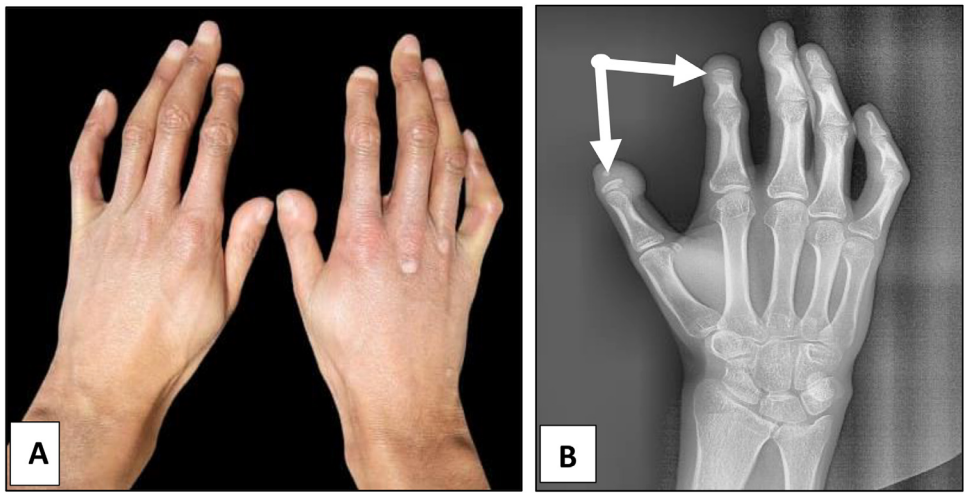


**Fig. 6 – (A) Left and right Hands with short and round tipped terminal finger phalanges; (B) Left hand X-ray showing short terminal fingers phalanges with acroosteolysis (white arrows).**

mandible [10–12], our patient had no dental loss. However, he did have slight mandibular hypoplasia with antegonial depression, dental crowding in the anterior region, and cortical erosion of the left condylar head. This arthritic involvement, not previously described, explains the limited mouth opening of our patient, which was the major reason for his consultation.

There is a scarcity of published data regarding conservative and preventive strategies for individuals with (MADA), particularly in rehabilitating maxillo-mandibular and dental problems. Besides being such a rare disorder, the present case is important in which dental and maxillofacial problems are reported on, rehabilitated, and discussed.

Regarding differential diagnosis, despite the distinctive features of this syndrome, MADA is frequently misdiagnosed and confused especially with progeroid syndromes. There are striking clinical and radiological similarities between MADA and Hutchinson-Gilford progeria syndrome (HGPS). However, the HGPS is characterized by early onset and faster progression [13]. As for juvenile scleroderma, it can be distinguished from MAD by the presence of the Raynaud phenomenon, widespread skin involvement, and visceral impairment [14]. Werner syndrome, unlike MADA, is characterized by late onset (after 20 years) [15], while acrogeria is differentiated by the absence of clavicle hypoplasia and pronounced osteolysis in the phalanges [16]. Therefore, the diagnosis of MADA relies on identifying characteristic symptoms, a detailed patient history, thorough clinical evaluation, and specialized genetic testing. Radiological assessment, including standard and sectional imaging, remains crucial, strongly guiding the diagnosis and appropriate therapeutic approach.

To conclude, MADA is a debilitating condition, with the most severe handicaps stemming from bone disorders and accelerated aging of the organism. Psychological aspects associated with changes in body shape are also relevant. Detecting oral and maxillofacial anomalies might be the initial manifestation of this disease. In such cases, practitioners should inform the patient and refer them to a geneticist not only to confirm the diagnosis but also to raise awareness among patients and their parents about the presence of MADA in a sibling context, as well as options for prenatal diagnosis for potential future births.

## Patient consent

The consent was obtained from the parent for the case report.

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