

## Case Report

# A case of acrodysostosis: a rare primary bone dysplasia

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### ABSTRACT

Acrodysostosis is a rare skeletal dysplasia characterized by brachydactyly, facial dysostosis and nasal hypoplasia. Diagnostic approach to this disorder is based on clinical, radiological and hormonal assays. We present a case of 11-year-old female child who presented with the complaint of short stubby hands and feet since birth and facial dysmorphism. Her skeletal survey revealed typical radiographic features of acrodysostosis. Hormonal assays did not reveal any significant abnormality. In this case report, we would like to highlight the clinical and radiological features of this disorder which could be helpful in diagnosis of this rare disease.

**Keywords:** Acrodysostosis, Brachydactyly, Nasal hypoplasia, Radiology, V-shaped epiphysis

### INTRODUCTION

Acrodysostosis, also known as maroteaux-malamut syndrome, is a rare skeletal dysplasia characterized by distinctive facial features, severe brachydactyly and nasal hypoplasia.<sup>1</sup> Some affected individual may show varying degree of intellectual disability, while in others intelligence may remain unaffected. The aetiology and prevalence of this disorder are still unknown. Recently, mutations in the PRKARIA and PDE4D genes were found to be the cause of acrodysostosis.<sup>2</sup> Most cases are sporadic, although some cases have occurred in families suggesting autosomal dominant inheritance.

Typical radiographic features of this disorder includes severe shortening of metacarpals, phalanges and metatarsals, hypoplastic nasal bones, cone shaped epiphysis of phalanges.<sup>3</sup> Relative sparing or hyperplasia of 1st toe have been reported in some of the cases.<sup>4,5</sup> Additional radiographic features include lack of normal caudal widening of lumbar interpedicular distance.<sup>4,6</sup> Reported paediatric and adolescent cases have revealed

advanced bone age or premature fusion of epiphysis as a constant feature.<sup>5,7</sup>

It can be differentiated from the related disorders like pseudohypoparathyroidism (PHP1a) and pseudopseudohypoparathyroidism (PPHP) by the absence of endocrinal abnormalities, more generalized osseous abnormalities and a characteristic facial appearance. Here we demonstrate a case of an 11-year-old girl who presented to our hospital with distinctive features of acrodysostosis.

### CASE REPORT

An 11-year-old girl presented to the paediatric department with the complaint of short and stubby hands and feet since birth and facial dysmorphism (Figure 1). On physical examination her height was 136cm (5.4cm above 3<sup>rd</sup> percentile) and weight was 45.6kgs (10. kgs above 10<sup>th</sup> percentile). Craniofacial features revealed hypertelorism, epicanthal folds, depressed nasal bridge and thick lips (Figure 2 and 3). Extremity examination

revealed short and broad hands and feet with stubby fingers and toes (Figure 4).



**Figure 1: An 11-year-old girl with typical features of acrodysostosis (short stature, facial dysostosis, short stubby hands and feet).**



**Figure 2: Broad face with mid facial hypoplasia, widely spaced eyes, thick lips and depressed nasal bridge.**

There was relative sparing of 1<sup>st</sup> toe on both sides. The patient had well developed secondary sexual characters with sexual maturity Tanner stage 4. IQ assessment revealed her IQ to be in range of 75-80. Lab investigations including, serum electrolytes, ALP and hemogram were normal. Serum PTH level was normal, 62.7pg/ml (normal range: 15-68.3pg/ml). Serum calcium level was 9.77mg/dl (normal range: 8.6-10.3mg/dl). Serum phosphorous level was 2.99mg/dl (normal range: 4-7mg/dl). Serum TSH was found to be mildly elevated 6.07mIU/ml (normal range: 0.6-5.5mIU/ml).

Skeletal survey revealed premature fusion of epiphysis with her bone age being more than 20 years. Radiographs of hands and feet showed short metacarpals and metatarsals with cone shaped epiphysis in phalanges (Figure 5).



**Figure 3: Side photograph of face denoting severe nasal hypoplasia.**



**Figure 4: Photograph of hands and feet showing stubby hands and feet with relative sparing of 1<sup>st</sup> toe on either side.**



**Figure 5: Radiographs of hands and feet representing severe shortening of metacarpals, metatarsals and phalanges with relative sparing of 1<sup>st</sup> toe (Note: V-shaped epiphysis of phalanges).**

There was relative sparing of great toe on either side. Lateral view of skull showed hypoplastic nasal bone (Figure 6). In the dorsolumbar spine, vertebrae were of normal height. There was loss of normal caudal widening of lumbar interpedicular distance without any sign of spinal canal stenosis (Figure 7).



**Figure 6: Radiographic lateral view of skull showing severe hypoplastic nasal bone.**



**Figure 7: X ray LS spine AP and lateral view denoting absence of normal caudal widening of interpedicular distance in lumbar vertebrae.**

The chest x-ray and long bones of the upper and lower limbs appeared unremarkable. On eliciting family history, paternal age at the time of her birth was 34 years. The patient had 2 siblings, an elder brother and sister, none of them had similar complaints. In view of clinical, radiological and laboratory investigations a presumptive diagnosis of acrodysostosis syndrome was made.

## DISCUSSION

Acrodysostosis is a rare congenital disorder, which may not be apparent for few years after birth. Recently autosomal dominant pattern of inheritance have been observed in some cases.<sup>7,8</sup> Genetic factors responsible for

this disorder are thought to be mutation in PRKAR1A and PDE4D genes, as reported in several studies. Two types have been described based on the some recent studies-type 1 (ADOHR) caused by mutation in PRKAR1A gene and type 2 (ADOP4) caused by mutation in PDE4D gene.<sup>2</sup> Advance paternal age is one more factor found to be associated with this disorder.<sup>9</sup>

The classical clinical features of this syndrome includes short and stubby hands and feet, short stature, broad face, widely space eyes and depressed nasal bridge, all of which were present in our case. Intellectual disability have been reported in some cases, however it can be normal in variable numbers of patients. Patient with ADOHR (type 1) does not show mental retardation, although some degree of behavioural abnormality may be present, while most of the ADOP4 cases (type 2) demonstrates mental retardation.<sup>1,2</sup> Patient in this case had normal IQ, ranging between 75 and 80. Some additional reported features include bilateral cryptorchidism in males and pigmented skin spots.<sup>2</sup>

Some patients with acrodysostosis may exhibit resistance to certain hormones like TSH or PTH, while others may not. Hormonal resistance have been reported to be associated with mutation in PRKAR1A gene. Patient with PDE4D gene mutation does not show hormonal resistance.<sup>2</sup> Some disorders may simulate the clinical and radiological features of acrodysostosis, which includes pseudohypoparathyroidism (PHP1a) and pseudopseudohypoparathyroidism (PPHP). Patient with PHP1a and PPHP presents with round face, nasal hypoplasia and brachydactyly. They also demonstrate hormonal resistance to certain hormones. Certain features which can help to differentiate this disorder include presence of more generalized osseous abnormality in case of acrodysostosis as compared to PHP where brachydactyly is limited to 4<sup>th</sup> and 5<sup>th</sup> metacarpals.<sup>10</sup>

Also an upturned nose and V-shaped epiphysis of phalanges have been reported as the predominant feature of acrodysostosis which may help to differentiate it from PHP1a and PPHP.<sup>3</sup> Subcutaneous ossification is not reported in acrodysostosis which is a well-recognized feature of PPHP.<sup>5,10</sup> Absence of GNAS mutation favours the diagnosis of acrodysostosis, which is present in PHP1a.<sup>1</sup> Complications associated with this disorder includes spinal canal stenosis, arthritic complications and progressive restriction of movements of hand, elbow and spine.<sup>4,11</sup> Treatment of the patient with acrodysostosis is directed to treat the specific symptoms. There is no standardized protocol or guidelines for the affected individuals.

## Learning points

- In a patient presenting with short stubby hands and feet, distinctive facial features and nasal hypoplasia possibility of acrodysostosis should be considered.

- Early diagnosis in the course of the disease can prevent the complications, like spinal canal stenosis and can help to manage neurological complications.
- Presence of more generalized and typical osseous abnormalities, characteristic facial appearance and absence of endocrinal abnormalities can aid to differentiate it from the related treatable disorders like PHP1a and PPHP.

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