Acromesomelic dysplasia (Marotaeux type) associated with craniovertebral junction anomaly: A report of a rare case and review of literature

Jayesh C. Sardhara, Kumar Ashish, Anant Mehotra, Arun K. Srivastava, Kuntal K. Das
Department of Neurosurgery, Sanjay Gandhi Post Graduate Institute of Medical Science, Lucknow, India

ABSTRACT

Acromesomelic dysplasia Maroteaux type (AMDM) is a rare autosomal recessive osteochondrodysplasia. The responsible gene, AMDM gene, in human beings, has been mapped on 9p13-q12 chromosome by homozygous mapping and pathogenic mutation was later identified in natriuretic receptor B (NPR-B) which has been implicated in the regulation of skeletal growth. Till now, around 40 to 50 cases of AMDM have been described in the world literature. Association of the congenital craniovertebral (CV) junction anomaly has not been reported. Here we are presenting a case of AMDM, with CV junction anomaly. A 10-year boy presented with short stature (122 cm) with short distal limbs, symptomatic for thoracic kyphoscoliosis with back pain. On examination there were no neurological deficits. On radiological investigation, he was found to have short and broad phalanges and toes, thoracic kyphoscoliosis, abnormal pelvic ring, mild ventriculomegaly, cervical syringomyelia and tonsillar descent below foramen magnum, hydrocephalus, os odontoideum with Klippel-Feil anomaly. This was diagnosed as AMDM with congenital os odontoideum, Klippel-Feil anomaly with Arnold-Chiari malformation (ACM) type-1. The patient underwent posterior fossa decompression by removal of foramen magnum ring along with C1 arch for ACM type-1. Kyphosis was left for conservative treatment till further observation and required orthopedic correction in his further age. To the best of our knowledge this is a very rare entity of AMDM with congenital CV junction anomaly.

Key words: Acromesomyelia, craniovertebral junction, marotaeux variant, surgery

INTRODUCTION

Acromesomyelic dysplasia Maroteaux (AMDM) type is a rare autosomal recessive osteochondrodysplasia belonging to the group of acromesomelic dysplasias (AMDs). The other varieties are Hunter-Thompson and Grebe type.[1] AMDM was first described in 1971 by P. Maroteaux. It is characterized clinically by severe dwarfism with shortening of middle and distal segment of limbs and radiologically by short broad fingers, shortening of long bones with bowed radius, and vertebral abnormalities. The facial appearance and intellegence are normal. Recently, an AMDM gene has been mapped to human chromosome 9p13-q12.[1-6]

Access this article online	
Quick Response Code:	Website: www.ijns.in
	DOI: 10.4103/2277-9167.138919

The prevelance of AMDM remains unknown.[1] AMDM is listed as a "rare disease" by the Office of Rare Diseases (ORD) of the National Institutes of Health (NIH) [affects less than 200,000 people in the US population]. It is the most commom form of the autosomal recessive AMDs. Only 40 to 50 cases have been reported till date.[1]

We are reporting a case of acromesomyelic dwarfism, kyphoscoliosis, Arnold-Chiari malformation (ACM) type-1, and Klippel-feil syndrome (KFS). To the best of authors knowledge this is the first reported case of AMDM associated with syringomyelia, hydrocephalus, and tonsillar descent with ACM type-1 with KFS.

CASE REPORT

A 10-year boy, weighing 30 kg, height 122 cm, presented with short stature and stooping posture with back pain on prolonged sitting or walking without any weakness noticed for the past 3 year. Pain was localized on the upper thoracic region of spine and was radiating to the suboccipital region. There was history of trivial trauma due

Address for correspondence: Dr. Arun K. Srivastava,
Department of Neurosurgery, Sanjay Gandhi Post Graduate Institute of Medical Science, Rae Bareli Road, Lucknow, Uttar Pradesh, India.
E-mail: doctorarunsrivastava@gmail.com

to fall down from height 1-year back. He was the second child, born out of a non-consanguineous marriage, by full-term normal vaginal delivery and the antenatal period was uneventful. The birth weight was 2.8 kg. Parents were normal and though his father was of short stature, family history of dwarfism was absent. Since birth, weight gain was normal and his mental function and intellectual development appeared normal. He was doing well in studies as compared to other children of the same age.

Examination revealed normal higher mental function. Sensory and motor examination revealed no sensory or motor deficits. He had broad forehead, with small flat nose, short neck with low hair line, and normal head circumference. He had a stooped posture [Figure 1a], short and broad fingers and toes (toes were slight curved) with no polydactyly [Figure 1b and c]. There was no disproportionate shortening of thigh to legs and arms to forearms. Passive movements of shoulder were normal, however mild restriction of 20 degree on flexion at elbow on both sides, and 20 degree restriction on flexion and extension was noted at wrist joint on both the sides. There was multiple café–au-lait spot on both legs approximately 5 × 2 cm on left leg medial aspect and small two spots on left lower legs [Figure 1d].

On radiograph X-ray, skull and chest x-rays appear normal [Figure 2d]. X-rays of the upper limbs revealed short and broad phalanges and metacarpals, arms and forearm bones normal [Figure 2b]. In lower limbs, the proximal bones were normal but in foot, metatarsal and toes were short and broad, great toe metatarsal bone appeared larger than other corresponding metatarsals [Figure 2c]. Lower thoracic kypho-scoliosis, wedge-shaped thoracic and lumbar vertebrae (T11, T12, L1) [Figure 2a] and congenital odontoid process anomaly without atlanto axial dislocation (Atlanto dental interval on CT scan: 2 mm) were observed on radiology [Figure 3a]. X-ray pelvis revealed hypoplastic lilac ring. MRI of the brain revealed mild hydrocephalus with ventriculomegaly [Figure 3b], small posterior fossa with crowding of structures, tonsillar descent below foramen magnum with canal size at foramen magnum (19 mm) [Figure 3c]. In addition, 3 mm size dilatation of the central canal of upper cervical cord noted in MRI [syringomyelia] at the level of C2 and T6 to T8 level [Figure 3d].

There was complete congenital fusion of anterior cervical vertebral body of 2nd and 3rd cervical vertebrae along with partial fusion of posterior elements of same vertebrae [Figure 4]. Genetic evaluation was not possible.

He underwent foramen magnum decompression and excision of C1 posterior arch and C2 lamina for ACM type-1. Intraoperative finding included tonsillar descent till 1st cervical vertebral ring, fibrous adhesions between dura, arachnoids, and tonsils with occlusion of foramina of Luschka and Magendie. The tonsils were separated easily. Post operative course was normal, pain was reduced significantly with no neurological deficit on 3 month, 6 month, and 1-year follow up. For thoracic kyphoscoliosis spinal extension brace was applied and further surgery was planned for kyphoscoliosis after 16 year of age.

DISCUSSION

AMD is an extremely rare,[1] inherited, progressive skeletal disorder that results in a particular form of short stature. The disorder is characterized by acromelia and mesomelia.[2] Over time, the apparent disproportion becomes even more obvious, especially during the first

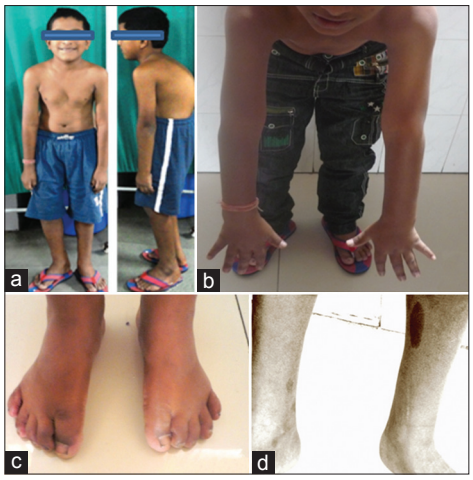

Figure 1: (a) Acromesomelic dwarfism with thoracic kyphoscoliosis: Bullet-shape thoracic and lumbar vertebrae with kyphosis. (b) Short and broad fingers (c) Short and broad toes (d) Café-au-lait spots over left leg

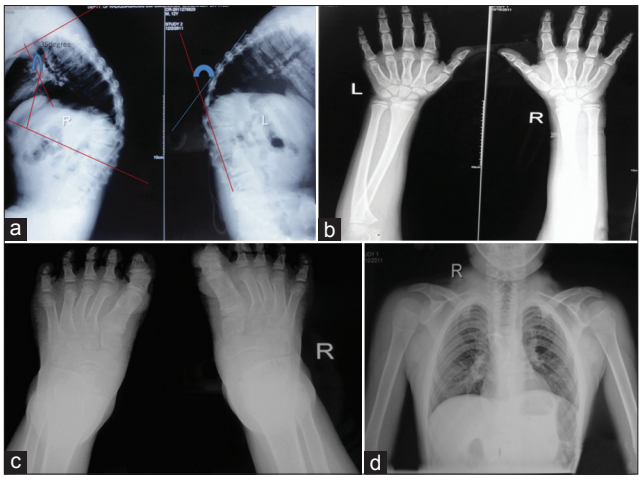

Figure 2: (a) Thoracic kyphosis with Cobbs angle -35 degree (b) Short and broad phalanges and metacarpal bone (c) Short and broad toes, metacarpal of great toes is larger than other toes. (d) Normal lung field with thoracic scoliosis

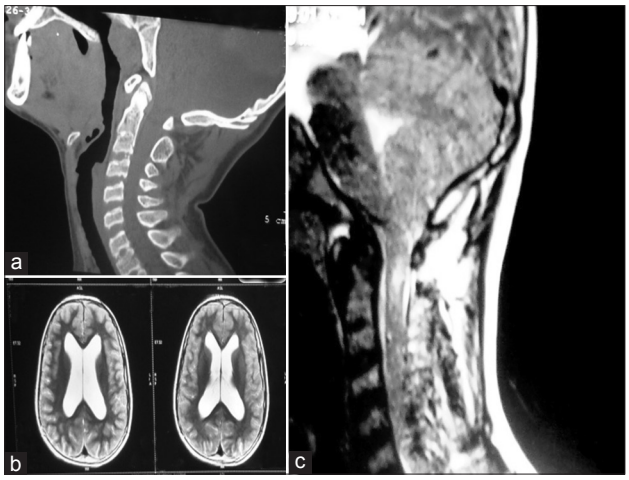

Figure 3: (a) Klippel Feil anomaly with congenital OS odontoideum: Figure depicted the vertebral bodies of 2nd and 3rd vertebral body are fused along with fusion of posterior element. Separate bony ossicle adjacent to odontoideum process [OS odontoideum]. (b) Hydrocephalous: Ventriculomegaly includes lateral, 3rd and 4th ventricle with per ventricular infiltration of CSF suggestive of chronicity. (c) Thoracic kyphoscoliosis with bullet-shaped vertebral body with syringomyelia at thoracic vertebrae includes T6-T8 level. (d) Cervical syringomyelia with Arnold-Chiari malformation type-1

few years of life. Affected individuals may have additional abnormalities resulting from abnormal cartilage and bone development, including limited extension of the elbows and arms and/or progressive abnormal curvature of the spine. Other characteristic abnormalities include a relatively enlarged head (macrocephaly), slightly flattened midface, and/or small, pug nose. AMD is inherited as an autosomal recessive genetic trait.[3-6] Genetic counseling is of benefit for affected individuals and their families. As genetic evaluation was not possible in these patients, AMDM was diagnosed on clinical ground.

Treatment may require the coordinated efforts of a team of specialists. Pediatricians, specialists who assess and treat skeletal abnormalities (orthopedists), physical therapists, and/or other health care professionals may need to systematically and comprehensively plan an affected child's treatment.[7-12] Abnormal curvature of the spine (i.e. low thoracic kyphosis and/or lumbar hyperlordosis) may be treated with a combination of exercises and physical therapy, other supportive techniques, braces, casts, and/or, in severe cases, corrective surgery.

ACM is a heterogenous develomental disorder of imparied CSF circulation at foramen magnum due to tonsillar herniation which leads to blockage of pathway. Treatment, if indicated, is surgical decompression of posterior fossa. Although there are various treatment for the disease, removal of foramen magnum through a posterior approach with partial or complete cervical

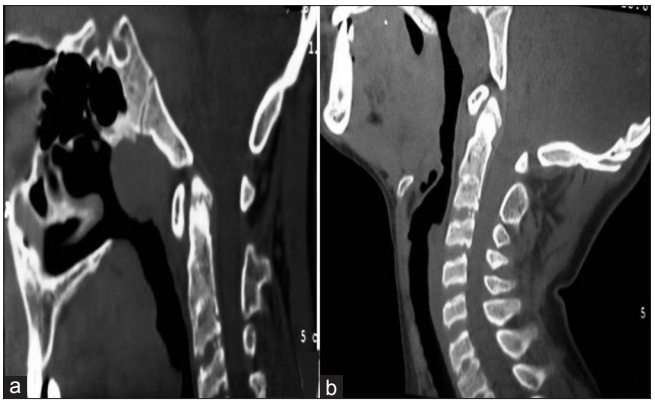

Figure 4: (a and b) Cervical spine lateral flexion (4A) and extension (4B) view suggestive of os odontoideum with normal atlanto dental interval

posterior arch excision {lamincetomy} is considered standard in majority of pateints. It is usually associated with syringomyelia (30-70%).

Incidence of KFS in this disease remains unknown due to its rarity and the fact that it is frequently asymptomatic.[13] Due to rarity of disease and paucity of literature available for such CV junction anomaly associated with AMDM, management strategy has not yet been established. ACM type-1 was probably correlated with congenital low-lying tentorium and crowding of posterior fossa structure or may be due to hydrocephalus. As pain in this patient may be related due to ACM, further CSF flow obstruction may progress the syringomyelia caudally and hydrocephalus proximally. Foramen magnum decompression was the best possible treatment option to arrest further neurological deficit. As odontoid process anomaly and Klippel-Feil anomaly was incidental finding and atlanto dental interval (ADI) was normal, it was treated conservatively.[13] Kyphoscoliosis treatment remains conservative in this patient as it was planned that it will be corrected surgically if the patient remains symptomatic for long. On follow-up after 2 months, the patient was having complete relief from back pain. Till date 40 to 50 cases have been reported; those all were about AMDM type. To the best of author knowledge till now there has been no case report available in which AMDM is associated with ACM type-1 and Klippel-Feil syndrome.

REFERENCES

1. Faivre L. Cormier-daire V. Acromesimyelic dysplasis, maroteaux type, Orphanet Encyclopedia, April-2005. Available from: http://www.orphadata.org/data/xml/en_product1.xml.
2. Nakamura M. Acromesomelic dysplasia. Ryoikibetsu Shokogun Shirizu 2001;33:138-40.
3. Ianakiev P, Kilpatrick MW, Daly MJ, Zolindaki A, Bagley D, Beighton G, *et al*. Localization of an acromesomelic dysplasia on chromosome 9 by homozygosity mapping. Clin Genet 2000;57:278-83.
4. Geister KA, Brinkmeier ML, Hsieh M, Faust SM, Karolyi IJ, Perosky JE, *et al*. A novel loss-of-function mutation in Npr2 clarifies primary role in

female reproduction and reveals a potential therapy for acromesomelic dysplasia, Maroteaux type. Hum Mol Genet 2013;22:345-57.
5. Khan S, Ali RH, Abbasi S, Nawaz M, Muhammad N, Ahmad W. Novel mutations in natriuretic peptide receptor-2 gene underlie acromesomelic dysplasia, type maroteaux. BMC Med Genet 2012;13:44.
6. Hume AN, Buttgereit J, Al-Awadhi AM, Al-Suwaidi SS, John A, Bader M, *et al*. Defective cellular trafficking of missense NPR-B mutants is the major mechanism underlying acromesomelic dysplasia-type Maroteaux. Hum Mol Genet 2009;18:267-77.
7. Faiyaz-Ul-Haque M, Ahmad W, Wahab A, Haque S, Azim AC, Zaidi SH, *et al*. Frameshift mutation in the cartilage-derived morphogenetic protein 1 (CDMP1) gene and severe acromesomelic chondrodysplasia resembling Grebe-type chondrodysplasia. Am J Med Genet 2002;111:31-7.
8. Huang PC, Chang JH, Shen ML, Chen KB. Management of general anesthesia for a patient with Maroteaux type acromesomelic dysplasia complicated with obstructive sleep apnea syndrome and hereditary myopathy. J Anesth 2012;26:640-1.
9. Al Kaissi A, Chehida FB, Ben Ghachem M, Klaushofer K, Grill F. Distinctive tomographic features of atlantoaxial dislocation in a boy with acromesomelic dysplasia du Pan syndrome. Clin Dysmorphol 2009;18:122-6.
10. Güven A, Dagcinar A, Ceyhan M. Coexistence of craniovertebral junction stenosis with pancake kidney in an adolescent with acromesomelic dysplasia. J Pediatr Endocrinol Metab 2008;21:941-2.
11. Farnaz S, Gothi D, Joshi JM. Acromesomelic dysplasia with bronchiectasis. Indian J Chest Dis Allied Sci 2005;47:131-4.
12. Al-Yahyaee SA, Al-Kindi MN, Habbal O, Kumar DS. Clinical and molecular analysis of Grebe acromesomelic dysplasia in an Omani family. Am J Med Genet A 2003;121A: 9-14.
13. Kumar R, Nayak SR. Management of Pediatric congenital atlantoaxial dislocation. A Report of 23 Cases from Northern India. Pediatr Neurosurg 2002;36:197-208.

How to cite this article: Sardhara JC, Ashish K, Mehotra A, Srivastava AK, Das KK. Acromesomelic dysplasia (Marotaeux type) associated with craniovertebral junction anomaly: A report of a rare case and review of literature. Indian J Neurosurg 2014;3:106-9.
Source of Support: Nil, **Conflict of Interest:** None declared.