# Assessment of foramen magnum in early infancy is efficient for patients with achondroplasia

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## Background

➢Achondroplasia (ACH) is the most common form of human short-limbed dwarfism. The most serious complication in children with ACH is narrowing of foramen magnum (FM) that results in cervicomedullary compression (CMC) and sudden infant death.

➢To avoid sudden infant death, early monitoring and implementation of the necessary medical intervention are important. However, the optimal method of screening for CMC continues to be debated.

## Objectives

➢Determination of time and frequency of the screening in the patients with ACH to avoid severe complications due to narrowness of FM.

## Materials and methods

➢Patients: Children with ACH who were born at or referred to our hospital between April 2002 and June 2014 were collected (18 cases in total).

➢Methods: We retrospectively examined for gestational age(GA), birth height, weight, head circumference, age at first screening MRI scan, age at presented radiological cervicomedullary compression, neurological or respiratory symptoms, and surgical history for FM decompression and ventriculo-peritoneal (VP) shunting in the patients.

## Results

➢Demographic characteristics

| Case No. | Age at analysis (y, m) | Gender | GA (w) | Birth height (cm, SD) | Birth weight (g, SD) | Birth head circumference (cm, SD) | Age at first MRI (m) | Age at presented CMC (m) | Age at surgery (y, m) | Neurological or respiratory symptoms | Other complications |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 12y5m | M | 37 | 42(-3.33) | 2,570(-1.02) | 35(+1.21) | 1m | 13m | 6y2m | 5y6m numbness in the hands, dyspnea | |
| 2 | 11y8m | F | 38 | 45(-1.62) | 2,848(-0.38) | 37.2(+3.07) | 3m | 3m | 11m | 11m severe hydrocephalus→ VP shunting | |
| 3 | 11y6m | M | 37 | 46(-1.43) | 2,358(-1.53) | 35.5(+1.57) | 3m | 7m | 9m | 8m hypotonia | |
| 4 | 10y10m | F | 38 | 42(-3.05) | 2,754(-0.62) | 34(+0.79) | 9m | 9m | | | |
| 5 | 8y1m | M | 37 | 41(-3.81) | 2,384(-1.47) | 34.5(+0.85) | 2m | 2m | 5m | 4m hypotonia on right side of the body | |
| 6 | 7y5m | F | 38 | 47(-0.67) | 2,922(-0.20) | 36(+2.21) | 1m | 1m | | 5m facial palsy, trigonocephaly | |
| 7 | 7y2m | M | 38 | 45(-1.62) | 3,168(+0.40) | 35(+1.21) | 4m | 7m | 8m | 1y intratracheal intubation when caught cold, SAS | |
| 8 | 6y6m | M | 38 | 46(-1.43) | 2,784(-0.51) | 33.4(+0.07) | 3m | 3m | | | |
| 9 | 6y2m | F | 35 | 46.4(-0.95) | 2,535(-1.16) | n.a. | 9m | 9m | | | |
| 10 | 4y9m | F | 38 | 45(-1.62) | 2,788(-0.53) | n.a. | 11m | 11m | | | |
| 11 | 4y2m | M | 39 | 48(-0.48) | 3,444(+1.06) | 37.4(+2.93) | 3m | 3m | | | |
| 12 | 3y2m | F | 39 | 47(-0.67) | 2,722(-0.70) | n.a. | 3m | 9m | | | |
| 13 | 2y4m | F | 38 | 44.6(-1.81) | 2,780(-0.55) | 34.5(+1.14) | 1m | 8m | 1y1m | 8m hypotonia of upper limbs | |
| 14 | 1y11m | M | 38 | 47(-0.67) | 2,718(-0.67) | 32(-0.93) | 4m | 4m | | | |
| 15 | 0y8m | M | 38 | 47.5(-0.71) | 2,802(-0.47) | 35(+1.21) | 4m | 4m | | 8m died of pneumonia | Down syndrome, VSD, PH |
| 16 | 1y2m | M | 37 | 44(-2.38) | 2,766(-0.56) | 35.3(+1.43) | 3m | 3m | | | |
| 17 | 0y11m | F | 38 | 51(+1.24) | 3,080(+0.20) | 36(+2.21) | 2m | 2m | 4m | 4m cardiopulmonary arrest | |
| 18 | 0y4m | F | 37 | 47(-0.67) | 2,672(-0.82) | 34.5(+1.14) | 4m | — | | | |

GA, gestational age; MRI, magnetic resonance imaging; CMC, cervicomedullary compression; VP, ventriculo-peritoneal; SAS, sleep apnea syndrome; VSD, ventricular septal defect; PH, pulmonary hypertension; n.a., not available

➢Age at diagnosis

Diagnosed at birth: 16/18 cases.

Diagnosed during infancy: 2/18 cases –8 mon (Case 9) and 10 mon (Case 10).

➢Age at performed first MRI

Performed between 1-11 mon of age in all the cases. Median age: 4 mon.

➢The frequency of CMC on MRI and the time presented CMC

17/18 cases (94.4%) presented CMC.

Age at presented CMC: 1 mon to 1 yr 1 mon. Average age: 5.8 mon.

15/18 cases had first MRI scan before 4 mon of age, 9/15 cases (60%) presented with CMC at the time of first MRI.

➢Symptoms and surgery

FM decompression: 6/18 cases (33.3%) had severe neurologic findings, all of which had surgery.

Age of surgery: 4 mon to 6 yr 2 mon.

Case 1: Numbness in the hands at 5 yr 6 mon→Surgery performed at 6 yr 2 mon of age

Case 3: Hypotonia at 8 mon→ Surgery performed at 9 mon of age

Case 5: Hypotonia on right side of the body at 4 mon→ Surgery performed at 5 mon of age

Case 7: Sleep apnea at 7 mon→ Surgery performed at 8 mon of age

Case 13: Hypotonia of upper limb at 8mon→ Surgery performed at 1 yr 1 mon of age

Case 17: Hypotonia of left upper limb at 2.5 mon, cardiopulmonary arrest at 4 mon→Emergency surgery performed at 4 mon of age

Other than Case 7, symptoms seen in all other cases resolved after surgery. Because SAS of Case 7 did not improve after FM decompression, he had the adenoidectomy at 3 yr 7 mon of age.

VP shunting: 1/18 case (5.6%)

Case 2: Severe hydrocephalus without neurological symptoms→ Surgery performed at 11 mon of age

## Discussion

### The frequency of children with ACH who required operation

➢Comparison between rate of FM decompression with that of previous studies

| | Francomano[1)] | Ryken[2)] | Hunter[3)] | King[4)] | This study |
|---|---|---|---|---|---|
| Frequency(%) | 42 | 3.2 | 16.5 | 10.5 | 33.3 |

➢Comparison between use of shunt placement with that of previous studies

| | Yamada[5)] | Hunter[3)] | Sciubba[6)] | King[4)] | This study |
|---|---|---|---|---|---|
| Frequency(%) | 30 | 10.5 | 20 | 4.3～50 | 5.6 |

### Criteria for medical intervention and time for examination

➢Some[4)] advocated routine MRI and sleep study in the first 6 months of life, while others[5,7)] recommended undertaking investigation only if clear clinical evidence exits.

➢If no symptoms exist, clinical examination and neuroimaging are recommended at 3-6 monthly intervals until the age of 2 years[8)].

➢Surgery is indicated for ACH patients with progressive hypotonia, central hypopnea, complete lack of CSF flow on MRI, hyperreflexia, or clonus[9-11)].

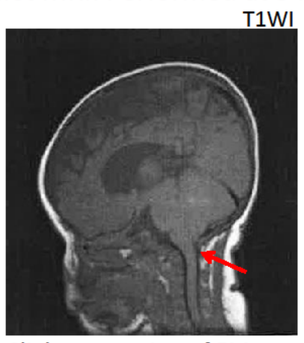
## Case 2: 11 years 8 months girl

Family history: Insignificant including short stature

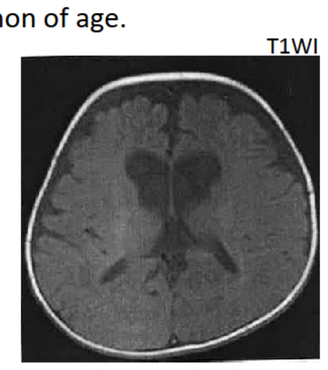
Disease history: Ultrasound at 35 weeks GA demonstrated shortened upper and lower limbs. Caesarean section was performed at 38 weeks due to CPD (Apgar score was 8/9).

The diagnosis of ACH was given based on bedside examination and X-ray finding.

First MRI: Performed at 3 mon of age.




Slight narrowing of FM
CMC(+)




Lateral ventricular distension

→ Because of no obvious neurological sign was seen, observation was recommended by the brain surgeon.

Progress: Although no obvious neurological symptoms developed, the expansion of the head circumference worsened -From 46.7cm(+2.12SD) at 6 mon of age to 49.0cm(+3.06SD) at 8 mon of age.


Hydrocephalus increased

→ Performed VP shunting


Post operative:
hydrocephalus resolved

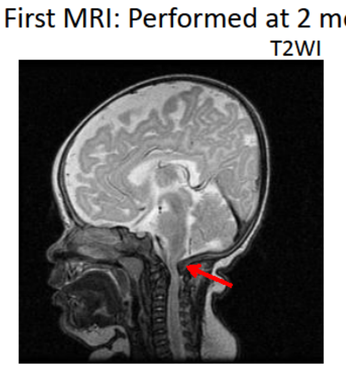
## Case 17: 11 months girl

Family history: Insignificant including short stature

Disease history: Ultrasound at 30 weeks GA detected short femurs. She was delivered at 38 weeks through normal vaginal delivery (Apgar score was 8/9).

The diagnosis of ACH was given based on bedside examination and X-ray finding.

First MRI: Performed at 2 mon of age.




Narrowing of FM
CMC(+)


Hydrocephalus (-)

→ Because no obvious neurological finding was seen, observation was recommended.

Progress: At the 4 mon visit, her mother explained that she had noticed hypotonia of the left upper limb since the patient was 2.5 mon old. She was then scheduled for a head MRI 2 weeks later. She cried at catheterization for venous access at admission, and ten minutes later, fell into sudden cardiac arrest. Cardiopulmonary resuscitation was successfully performed and she was then transferred to another hospital that specialized in pediatric brain surgery.


Narrowing of FM worsened
Severe CMC(+)

→ Performed FM decompression and C1 laminectomy


Post operative:
CMC resolved

## In this study

➢60% of patients presented with CMC before 4 months of age.

➢To avoid the risks of complications due to cervicomedullary compression, careful monitoring of any rapid changes in head circumference and observations of neurological and respiratory symptoms are important in patients with ACH.

## Conclusion

➢We advocate the first MRI scan to be performed before 4 months of age for all children with ACH.

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Conflict of Interest: The authors of this study have nothing to disclose.

ESPE 2015 235--P2

Bone, Growth Plate and Mineral Metabolism

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DOI: 10.3252/pso.eu.54espe.2015

Poster presented at: 54th Annual Meeting 1-3 October ESPE 2015 BARCELONA European Society for Paediatric Endocrinology

PosterSessionOnline.com