

A Case of Achondroplasia Associated with Cervicomedullary-Junction Compression

Toshiro Takezaki¹, Shinobu Nakai¹, Toshihiro Tajima¹, Koji Okuhara¹,
Kouhei Satoh¹, Yoshikazu Iwasaki² and Kenji Fujieda^{1,3}

¹Department of Pediatrics, ²Department of Neurosurgery, Hokkaido University School of Medicine,
Sapporo, Japan

³Present: Department of Pediatrics, Asahikawa Medical College, Asahikawa, Japan

Abstract. Achondroplasia is the most common skeletal dysplasia and is caused by defective fibroblast growth factor receptor (FGFR) 3 in endochondral chondrocytes. Children with achondroplasia may have high cervical myelopathy due to stenosis of the craniocervical junction and an increased risk of sudden death. We report a female patient with achondroplasia who required surgical decompression at the age of 13 mo. The female patient was diagnosed with achondroplasia clinically, radiologically and genetically shortly after birth. The newborn period was uneventful. She developed head control at the age of 6 mo, but she could not sit by the age of 12 mo. At the age of 8 mo, her parents noticed her eyes did not close and a diagnosis of left peripheral nerve palsy was made. Occasional hyperextension of the trunk was observed. There was also minimal asymmetry of voluntary leg movement and bilateral ankle clonus. By these findings craniocervical junction compression was strongly suspected. MRI examination revealed compression at the craniocervical junction by the occipital bone and myelomalacia. The patient underwent suboccipital decompressive surgery at the age of 13 mo. Recovery after surgery was uneventful, and although her left facial nerve palsy did not improve, gross motor function had improved by the age of 2 yr. The patient is now cognitive and neurologically normal at the age of 3 yr. Infants with achondroplasia are at risk of lethal sequelae of craniocervical junction abnormalities, so careful neurological assessment and early MRI examination is recommended.

Key words: achondroplasia, cervicomedullary-junction compression

Introduction

Achondroplasia is the most common skeletal dysplasia and is caused by defective fibroblast growth factor receptor (FGFR) 3 in endochondral

chondrocytes (1). A variety of skeletal malformations are observed and generally diagnosed at birth. Generalized spinal stenosis with spinal cord compression occurs, often requiring surgical decompression (2, 3). The anatomical stenosis at the craniocervical junction and upper cervical vertebral canal results in cervical cord or brainstem compression and may be accompanied by edema, gliosis, cystic myelomalacia and syringomyelic cavities (2-4).

Received: February 17, 2003

Accepted: May 16, 2003

Correspondence: Dr. Kenji Fujieda, Department of Pediatrics, Asahikawa Medical College, 2-1-1-1, Midorigaoka, Higashi, Asahikawa 078-8510, Japan

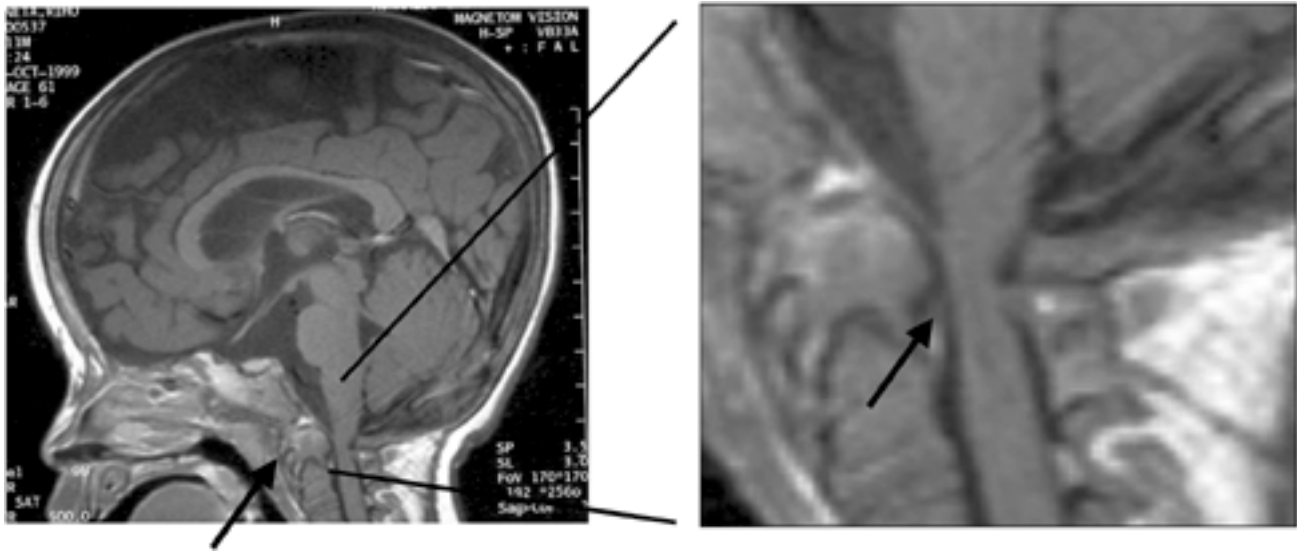


Fig. 1 Pre-operative sagittal MRI (T1-weighted) at 12 mo of age showing compression at the cranio cervical junction. Arrows indicate myelomalacia.

Clinically, upper cervical myelopathy may manifest with recurrent apnea, extreme muscular hypotonia, developmental delay, and spastic diplegia with increased reflexes (2-4). Especially, interference with the respiratory control centers creates a risk of sudden death in early life (4-9).

Here we report the case of one female patient with achondroplasia who had cervicomedullary junction compression and required craniocervical decompression surgery.

Case Report

The female patient was born by vaginal delivery following an uncomplicated pregnancy. Achondroplasia was diagnosed clinically and radiologically shortly after birth. Gene analysis of FGFR 3 identified a hot spot mutation (G380R). The newborn period was uneventful. She developed head control at the age of 6 mo, corresponding to motor development expected for a child with achondroplasia (10). At the age of 8 mo, her parents noticed that her left eye did not close and the left labial angle did not depress. She was diagnosed as having left peripheral facial

nerve palsy at this time. By the age of 12 mo she had gross motor delays beyond those expected for a child with achondroplasia (10), and had not developed independent sitting. Occasional arching and hyperextension of the trunk was observed. There was also minimal asymmetry of voluntary leg movement and bilateral ankle clonus at this time. By these findings craniocervical junction compression was strongly suspected. Sagittal T1-weighted MRI showed compression at the cranio-cervical junction (Fig. 1) and there was an increased signal intensity of the spinal cord, indicating myelomalacia (T2-weighted). There had been no history of apnea and cyanosis since birth. Given these findings, the patient underwent suboccipital decompressive surgery at the age of 13 mo. Postoperative MRI (T2-weighted) showed no further constriction, but myelomalacia remained (Fig. 2). The patient's recovery was uneventful, and she had rapid resolution of hyperextension. While her facial nerve palsy did not improve, gross motor development accelerated with completely normal milestones by the age of 3 yr. She now shows normal motor and mental development. No hearing abnormality is present.

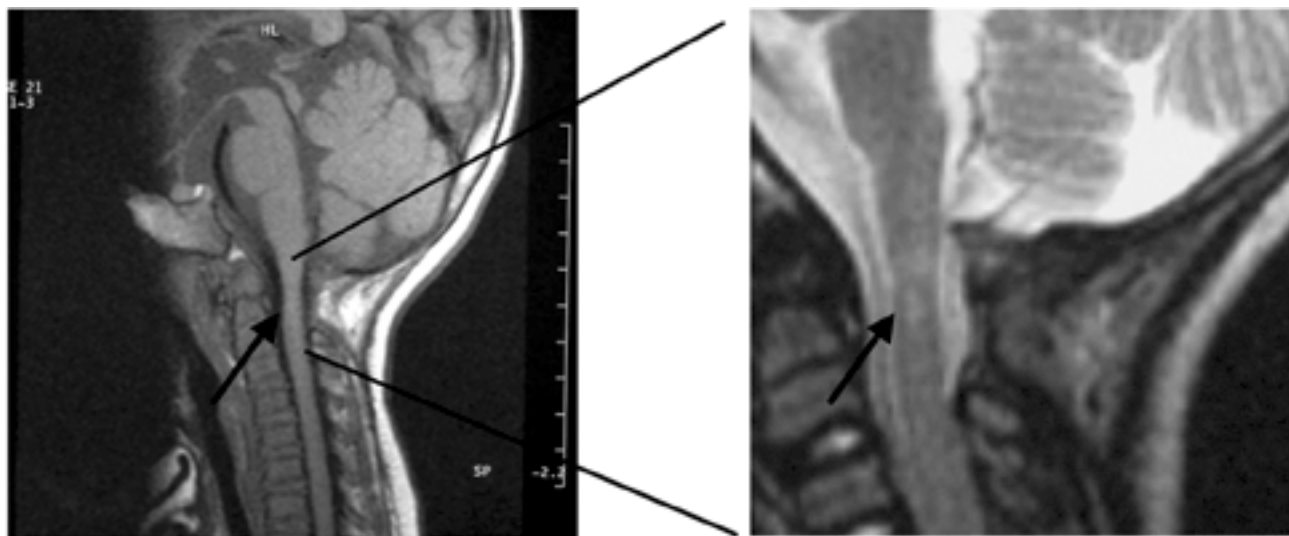


Fig. 2 Postoperative sagittal MRI (T2-weighted) showing no further compression. An area of high signal intensity indicating myelomalacia remained (arrows).

Discussion

In our patient with achondroplasia MRI examination revealed cervicomedullary compression and myelomalacia. It is known that infants with achondroplasia are at risk of cervical cord compression (2-4). Reported neurological symptoms in these conditions include quadriplegia, paraparesis, feeding problem, dysphasia, poor head control, hypotonia, and delayed motor developmental milestones (2-4). Especially, apneic spells may cause sudden death (4-9). Hecht *et al.* (7) calculated a 7.5% risk of dying suddenly during the 1st year and a 2.5% risk between the ages of 1 to 4 yr in patients with achondroplasia. Boor *et al.* (9) reported that 13 out of 30 patients with achondroplasia showed signs of myelomalacia on MRI examination. Pauli *et al.* (4) also reported that by MRI examination 5 out of 53 patients with severe craniocervical junction compression required surgical decompression and all children operated on showed marked improvement of neurological function and respiratory problems. Furthermore, Aryanpur *et al.* (3) reported that early neurological suboccipital

surgical decompression brought about a dramatic and sustained improvement in neurological and respiratory function in 15 patients with achondroplasia. Our patient did not show respiratory problems, however she showed delayed motor development and neurological problems. After decompression surgery, her neurological symptoms disappeared and her motor development accelerated. Therefore the surgery is considered to have been effective. Accordingly, MRI examination of cervicomedullary junction should be performed if infants with achondroplasia reveal developmental delay, neurological and/or respiratory symptoms.

The patient also showed left peripheral nerve palsy. Since this did not improve after surgery, nerve palsy was not due to stenosis of the foramen magnum. Instead, craniofacial bone deformity may be the cause of the peripheral nerve palsy. The exact incidence of nerve palsy in achondroplasia is not known. Pauli *et al.* (4) reported one patient with left vocal cord paralysis in 10 achondroplasia patients. Ryken *et al.* (11) also described one patient with abducens nerve palsy in 6 achondroplasia patients. Therefore, cranial nerve

abnormality should be carefully evaluated.

In conclusion surgical intervention in achondroplasia can be life and health saving. Careful neurological assessments are required if craniocervical junction compression is suspected, and early MRI examination is recommended.

References

1. Shiang R, Thompson LM, Zhu YZ, Church DM, Fielder TJ, Bocian M, *et al.* Mutations in the transmembrane domain of FGFR3 cause the most common genetic form of dwarfism, achondroplasia. *Cell* 1994;78:335-42.
2. Morgan DF, Young RF. Spinal neurological complications of achondroplasia. *J Neurosurg* 1980;52:463-72.
3. Aryanpur J, Hurko O, Francomano C, Wang H, Carson B. Craniocervical decompression for cervicomedullary compression in pediatric patients with achondroplasia. *J Neurosurg* 1994;73:375-82.
4. Pauli R, Horton VK, Glinski LP, Reiser CA. Prospective assessment of risks for cervicomedullary-junction compression in infants with achondroplasia. *Am J Hum Genet* 1995;56:732-44.
5. Fremion AS, Garg BP, Kalsbeck J. Apnea as the sole manifestation of cord compression in achondroplasia. *J Pediatr* 1984;104:398-401.
6. Pauli RM, Scott CI, Wassman ER, Gilbert EF, Leavitt LA, Ver Hoeve J, *et al.* Apnea and sudden unexpected death in infants with achondroplasia. *J Pediatr* 1984;104:342-48.
7. Hecht JT, Francomano CA, Horton WA, Annegers JF. Mortality in achondroplasia. *Am J Hum Genet* 1987;41:454-64.
8. Hecht JT, Butler IJ. Neurologic morbidity associated with achondroplasia. *J Child Neurol* 1990;5:84-97.
9. Boor R, Fricke G, Bruhl K, Spranger J. Abnormal subcortical somatosensory evoked potentials indicate high cervical myelopathy in achondroplasia. *Eur J Pediatr* 1999;158:662-7.
10. Todorov AB, Scott CI, Warren AE, Leeper JD. Developmental screening tests in achondroplastic children. *Am J Hum Genet* 1981;9:19-23.
11. Ryken TC, Menzes AH. Cervicomedullary compression in achondroplasia. *J Neurosurg* 1994;81:43-8.