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Neurosurgical implications of achondroplasia

A review

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Object. Achondroplasia is the most common form of human short-limbed dwarfism. The pediatric neurosurgeon is frequently required to treat children with achondroplasia who have hydrocephalus, cervicomedullary compression (CMD), and spinal canal stenosis. Accordingly, the authors have reviewed the experience of neurosurgery in children with achondroplasia at The Hospital for Sick Children.

Methods. The medical records and neurosurgery database at The Hospital for Sick Children were searched to identify all children with achondroplasia who underwent at least 1 neurosurgical procedure between 1956 and the present.

Results. Twenty-nine children with achondroplasia underwent 85 surgical procedures: 52 for CSF diversion in 12 patients, 20 for CMD in 18 patients, 8 for spinal disorders in 4 patients, and 5 for miscellaneous purposes in 4 patients. The CSF shunts were placed almost exclusively before 1990 and were associated with a significant number of complications. Patients undergoing CMD did very well, with only 1 patient failing to improve clinically.

Conclusions. This review provides a historical perspective on the evolution of treatment of pediatric patients with achondroplasia. The use of CSF diversion procedures, formerly fraught with complications, is now rare following the realization of the natural history of CSF space enlargement in these patients. Cervicomedullary compression is more commonly recognized due to better imaging. Central apnea is now better detected by routine sleep studies. Spine surgery, although rare, requires evaluation of both spinal stenosis and instability. These patients are best evaluated by a multidisciplinary team. *(DOI: 10.3171/2009.3.PEDS08344)*

Key Words • **achondroplasia** • **hydrocephalus** • **cervicomedullary compression**

Achondroplasia is the most common form of human short-limbed dwarfism and is one of a spectrum of diseases caused by mutations in the *FGFR3* gene. Achondroplasia is estimated to occur in 1 in 10,000–30,000 live births.[22,25] The disease is autosomal dominant, but 80% of patients have new mutations.

The classic features of achondroplasia include a long, narrow trunk and short limbs. The head is generally large, with frontal prominence, and the face is hypoplastic. Hypotonia is a common feature in infancy and is a factor in motor developmental delay. The joints are often hyperextensible, and the hands are short and broad. Thoracolumbar kyphotic deformity is common. Children with achondroplasia are susceptible to compressive forces at a number of levels along the neuraxis, with hydrocephalus, cervicomedullary compression, spinal canal stenosis (both cervical and lumbar), syringomyelia, and spinal instability all being encountered. Thus, the general neurosurgeon, and the pediatric neurosurgeon in particular, will have exposure to patients with achondroplasia. For this reason, we reviewed our experience with these patients at The HSC over the past 5 decades and describe the current neurosurgical implications of the disease.

Abbreviations used in this paper: CCJ = craniocervical juction; CMD = cervicomedullary decompression; ETV = endoscopic third ventriculostomy; EVD = external ventricular drain; HSC = Hospital for Sick Children; ICP = intracranial pressure; JHU = Johns Hopkins University; LP = lumboperitoneal; OSV = Orbis Sigma valve; VA = ventriculoatrial; VP = ventriculoperitoneal.

Methods

A retrospective chart review of patients with confirmed achondroplasia who were treated by a neurosurgeon between 1956 and 2008 was undertaken at The HSC in Toronto, Ontario, Canada, after approval was obtained from the Research Ethics Board. The patients were identified by cross-referencing patients with a diagnosis of achondroplasia in the general hospital database with those listed in the neurosurgical database. The hospital chart was reviewed for information regarding admissions, consultations, images, and clinic visits. The patients' clinical presentation, age at diagnosis, imaging characteristics, sleep study reports, indications for surgery, date of surgery, age at surgery, type of surgery, duration of surgery, complications, and clinical follow-up were recorded and analyzed. We identified 29 patients undergoing a total of 85 procedures over the 52 years, representing the experience of the Neurosurgery Service at The HSC.

Descriptive statistics were used for most demographic and clinical variables. Differences in foramen magnum dimensions, controlling for age as a covariate, between decompressed and observed groups were compared using analysis of covariance tests. Statistical significance was set at $p = 0.05$. Analyses were performed using SAS version 9.1.3 for Windows (SAS Institute).

Results

Patient Characteristics

We identified 29 patients undergoing a total of 85 procedures over the entire study period of 52 years; there were 15 boys and 14 girls. Four of the 29 children had a parent with achondroplasia (13.8%). Fifty-two procedures were performed for CSF diversion (11 primary procedures with 40 revisions and 1 ETV), 20 for cervicomedullary compression, 8 for spinal stenosis or deformity, and 5 were classified as miscellaneous.

A dedicated clinical genetics database has been available since 1988. From January 1988 to the present, there are 162 children with achondroplasia in whom follow-up is ongoing at The HSC. During this time, 19 patients underwent neurosurgical procedures, representing 11.7% of the cohort. Seven of these 162 patients had shunts in situ (4.3%).

Patients With Hydrocephalus

In our series, only 11 patients underwent shunt insertion, and 1 ETV was performed. The total number of shunt procedures was 51 (39 ventricular and 12 lumbar). Of the primary procedures, 7 were ventricular and 4 were lumbar. Of the 40 revisions, 32 were ventricular and 8 lumbar. There was a paucity of new shunts inserted in the latter part of the series, with 1 shunt operation performed in the past 20 years (Table 1).

The most common indication for surgery was progressive macrocephaly in infancy (in 9 patients). The imaging modality of choice prior to 1975 was an air ventriculogram, whereas afterward, axial imaging with a CT scanner and subsequently MR imaging was preferred. The average age at first surgery was 9 months, with 9 of the 11 patients ≤ 1 year of age. The early patients in the series had LP shunts inserted, and we then observed an expected progression through VA to predominantly VP shunt systems. There was no uniformity in the type of shunt system used, although medium-pressure valves or flow-regulated systems (for example the OSV) were preferred in the latter part of the series. No reoperation was performed for subdural hematoma formation. The average number of shunt revisions performed was 3.6 per child; however, the first 3 patients in the series account for 31 of the shunt procedures, thus elevating the average revision rate. In addition to a high rate of obstruction, significant complications were seen in these children. The shunt infection rate was (5.9%) per procedure (3 of 51), with 3 (27%) of 11 patients suffering infections. The responsible organism was *Staphylococcus aureus* in 2 patients and *S. epidermidis* in the remaining patient. All 3 were treated with shunt removal, external drainage, antibiotics, and reinsertion.

TABLE 1: Hydrocephalus in 12 patients with achondroplasia*

Case No.	Year	Age at 1st Insertion	Indication	Shunt/Valve Type	No. of Revs	Complications
1	1956	6 mos	macrocephaly	LP/LPV	9	thoracolumbar kyphosis, paraparesis, neurogenic bladder
2	1967	3 mos	macrocephaly	VA/LPV	9	infection w/ *S. aureus*
3	1968	9 mos	macrocephaly	LP/LPV	10	drowsiness, quadriparesis, CSF leak, wound infection; shunt ultimately removed
4	1974	2 yrs	respiratory arrest	VP/MPV	0	death
5	1977	6 mos	macrocephaly	LP/LPV	1	transfusion
6	1978	14 mos	macrocephaly	VA/MPV	3	retained VA catheter; endovascular retrieval
7	1981	1 yr	macrocephaly	VP/LPV	2	none
8	1983	2 mos	macrocephaly	VP/LPV	2	infection w/ *S. epidermidis*
9	1986	4 mos	macrocephaly	LP/MPV	0	none
10	1988	6 mos	apnea, ↓ GCS	VP/MPV	3	infection w/ *S. aureus*
11	1992	8 mos	macrocephaly	VP/OSV	1	CSF leak
12	2005	8 yrs	headache	ETV	0	bacteremia; *Klebsiella oxytoca*

* GCS = Glasgow Coma Scale; LPV = low-pressure valve; MPV = medium-pressure valve; Rev = revision; ↓ = decreasing.

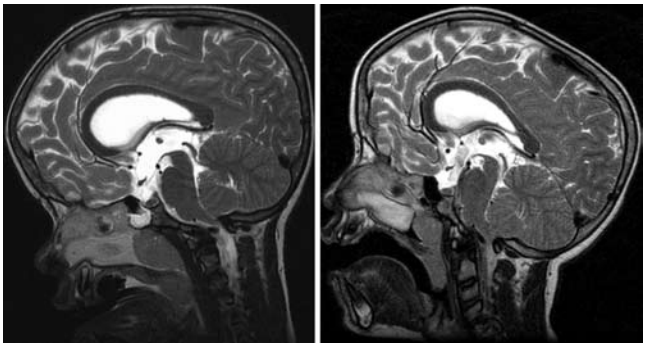

FIG. 1. Preoperative *(left)* and postoperative *(right)* sagittal T2-weighted MR images obtained in an 8-year-old patient with severe headache who underwent an ETV, showing a flow void in the third ventricle and a reduction in size of the third ventricle.

In this cohort of patients in particular there were problems associated with LP shunts. One patient experienced progressive thoracolumbar kyphosis thought to be exacerbated by laminectomy performed for LP shunting, and subsequently developed a neurogenic bladder with paraparesis after a further revision. There was an episode of cerebral herniation after insertion of an LP shunt that necessitated VP shunt insertion in addition to CMD. There was a retained atrial catheter in a patient who received a VA shunt that required endovascular retrieval. The single death in the series occurred in a 2-year-old child who presented to the hospital in a coma after respiratory arrest at home, who was treated with VP shunt insertion and a CMD, but did not regain consciousness.

In general, shunt placement in the child with achondroplasia is not straightforward, and the incidence of revisions and complications is higher than in the general patient population with shunts in our experience, although the infection rate of 3 (5.9%) of 51 procedures is comparable with large series of children without achondroplasia who were treated with shunts (8.1%).[10] The mean follow-up was 16 years and 3 months. In 1 child, the shunt was ultimately removed without requirement for reinsertion, highlighting the difficulty in identifying patients with achondroplasia who genuinely need shunt insertion. We have performed 1 ETV procedure that was technically feasible and resulted in symptom (headache) resolution (Fig. 1).

Patients With Cervicomedullary Compression

The HSC experience includes 18 patients and 20 CMDs (Table 2, Fig. 2). This procedure has been performed with a greater frequency in the latter part of the series, with 14 of the 20 that were documented having been performed in the past 11 years. The operation performed in all but 2 cases was suboccipital craniectomy, C-1 laminectomy, and division of the thick fibrous extradural bands, without formal dural opening. The C-2 lamina and spinous process were preserved in all cases, and no patient had a prophylactic EVD inserted. In 2 patients who presented with impairment of conscious state and quadriparesis, formal dural opening

TABLE 2: Cervicomedullary decompression in 18 patients with achondroplasia*

Case No.	Year	Age	Indication	Op Time (mins)	Complication	Outcome
1	1970	2 yrs	deterioration post-LP shunt; drowsiness, quadriparesis	215	none	recovery, doing well
2	1974	2 yrs	respiratory arrest	190	none	death
3	1978	11 mos	hydrocephalus	90	none	doing well
4	1982	1 yr	hyperreflexia, clonus	110	none	doing well
5	1987	18 mos	rt hemiparesis, hyperreflexia	140	none	recovery, doing well
6	1988	7 mos	central apnea	115	none	doing well
	1997	9 yrs	central apnea (SS+), T2+	150	transfusion	doing well
7	1999	9 yrs	lt hemiparesis, T2+	210	none	doing well, OSA
8	1995	6 wks	apnea (SS–)	95	none	doing well
9	2006	9 yrs	apnea (SS–), thoracic syrinx, T2+	132	none	doing well
10	2001	2 yrs	central apnea (SS+), clonus, T2+	135	none	doing well
11	2002	4 mos	apnea (SS–), T2+	145	none	tracheostomy for OSA
12	2003	7 mos	cyanotic events (no SS), T2+	167	none	doing well (SS–)
13	2003	1 yr	central apnea (SS+), T2+	239	CSF leak, EVD	doing well (SS–)
14	2006	14 mos	T2 signal change, (SS–)	118	none	doing well
15	2006	9 mos	central apnea (SS+), T2+	120	tx failure	ongoing central apnea
	2007	2 yrs	central apnea (SS+), T2+	155	none	doing well (SS–)
16	2007	18 mos	central apnea (SS+), T2+	191	none	doing well
17	2007	8 mos	cyanotic episode (no SS)	90	none	FU out of province
18	2008	6 mos	central apnea (SS+)	160	none	doing well, awaiting SS

* FU = follow-up; OSA = obstructive sleep apnea; SS+ = sleep study positive for central apnea; SS– = sleep study negative for central apnea; T2+ = MRI with T2-weighted hyperintensity in cervical spinal cord.

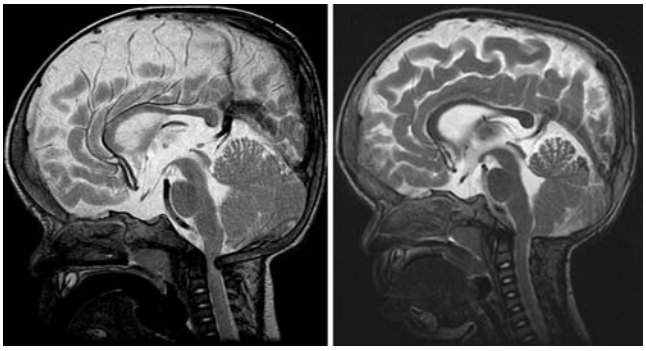

FIG. 2. Preoperative *(left)* and postoperative *(right)* sagittal T2-weighted MR images demonstrating the CCJ in a child with achondroplasia and central sleep apnea.

was performed to ensure adequate decompression. One patient required a reoperation for recurrent cervicomedullary compression and central apnea 8 years after the initial procedure, and another patient required early "redo" decompression when it was apparent that her symptoms had not resolved and residual bone compression was evident on imaging 1 year postoperatively.

The indication for surgery was T2-weighted signal change in the cervical spinal cord in 10 (56%), documented central apnea on sleep study in 7 (39%), cyanotic episodes and apnea not documented on sleep study in 5 (28%), focal neurological deficit or myelopathy in 3 (17%), and impairment of conscious state in 2 (11%). All but 1 patient was symptomatic in some way. Twelve of 18 patients underwent formal sleep studies prior to surgery.

The age distribution is bimodal, with the majority of procedures performed in the first 2 years of life (the average age at first surgery was 23 months), with a later peak at ~ 9 years of age. The average age at repeat surgery was 5.5 years, with a reoperation rate of 2 (11.1%) of 18. Of the 20 procedures in 18 patients, 14 procedures were preceded by preoperative MR imaging, and 2 each were preceded by CT myelograms, air ventriculograms, and CT brain scans only. The last 12 procedures in the series were performed with intraoperative ultrasonography and neurophysiological monitoring. The average operating time was 148.2 minutes (range 90–239 minutes).

Imaging to allow accurate measurement of the foramen magnum size was available in a subset of the symptomatic/surgical patients (7 children) and the asymptomatic/nonsurgical patients (8 children). We identified a significantly smaller transverse dimension of the foramen magnum in the surgical group, taking into consideration the age of the children (transverse 13.5 mm vs 18.8 mm, $p = 0.03$), whereas the differences in the sagittal dimensions were not significant (sagittal 15.2 mm vs 23.6 mm, $p = 0.10$).

In general, the complications of this procedure were low. Two patients experienced inadvertent durotomy intraoperatively, and 1 of them suffered a CSF leak postoperatively that required a temporary period of CSF diversion with an EVD, but did not require a shunt. One patient had significant blood loss from the dural venous sinuses intraoperatively, which required a transfusion. One patient had recurrent symptoms 8 years after decompression, and 1 child failed to improve and required early reoperation to relieve residual stenosis. One patient presenting in a comatose state after respiratory arrest at home did not improve following VP shunt insertion and CMD, and this individual died. The remaining 13 patients made uncomplicated recoveries and had improvements in their presenting symptoms. Of the 12 patients who underwent preoperative sleep studies, all but the one who required early reoperation showed improvement. There were no infections, no neurological deterioration postsurgery, and no delayed cervical instability. The mean follow-up duration was 8 years and 2 months.

Patients With Syringomyelia

In 1 patient in our series a thoracic syrinx was diagnosed (Fig. 3); it was identified as an incidental finding on imaging. The patient had a reduced foramen magnum diameter without a Chiari malformation or local T2-weighted signal change in the spinal cord, and there was a large syrinx from T-5 to the conus medullaris in conjunction with moderate thoracolumbar kyphosis (segmental kyphosis between T-12 and L-3 measuring 42°). He was observed over the course of 4 years and developed hyperreflexia and sensory disturbance, with T2-weighted signal change on MR imaging in the high cervical region. As a consequence of these new findings, a CMD was performed without duraplasty, and the postoperative imaging revealed a decrease in the size of the syrinx at 18 months, without any clinical change.

Cervical Instability

No patient in our series, either before or after foramen magnum decompression and C-1 laminectomy, demonstrated CCJ instability. In the 1 patient undergoing a subaxial cervical procedure, laminoplasty followed by laminectomy after recurrent stenosis was identified, a posterior fusion was not performed. This patient did have a degree of kyphotic deformity of the cervical spine and may require further surgery if this were to progress.

Spinal Stenosis

The incidence of symptomatic spinal canal stenosis in children in our series was quite low, with only 3 patients undergoing surgery for this condition. One patient underwent a cervical procedure for cervical myelopathy, and 2 were treated for lumbar canal stenosis. The former was a 17-year-old girl with symptoms of cervical canal stenosis who was noted to have upper motor neuron signs on examination. Imaging of the spinal cord revealed cervical cord compression and T2 signal change in the cord at the C4–5 vertebral level (Fig. 4). The patient underwent a decompressive laminoplasty as an initial procedure; however, postoperative imaging showed ongoing compression, and ultimately a C4–5 laminectomy was performed, with improvement on postoperative imaging.

A lumbar decompression was performed in 1992 in a 15-year-old boy with back pain and symptoms of spinal claudication, which incorporated an L1–5 decompressive laminectomy after a myelogram revealed canal stenosis. This child had good symptom resolution, but went on to develop instability at the thoracolumbar junction 3 years later, requiring fusion. The second child was 8 years old

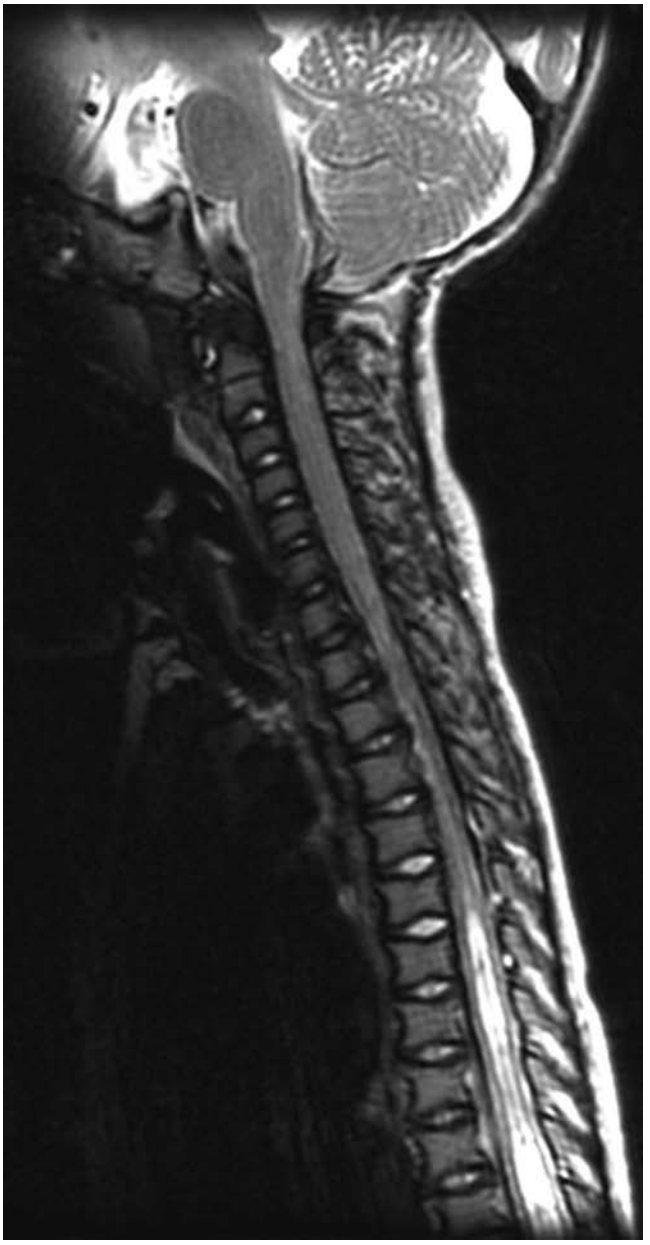

Fig. 3. Sagittal T2-weighted MR image obtained in a 9-year-old boy with cervicomedullary compression, cervical and thoracic canal stenosis, and a thoracic syrinx.

and underwent L2–4 laminectomy in 1985 for low-back pain, sciatica, bowel and bladder disturbance, and canal stenosis on myelography studies. This child returned home to a neighboring province and was lost to follow-up.

Thoracolumbar Kyphosis

At our institution, thoracolumbar spinal deformity has been typically managed by the Orthopedics Service, and therefore, the involvement of neurosurgeons has been limited. One patient is reported who had severe thoracolumbar kyphosis of 90°, and who underwent a combined anterior and posterior decompressive procedure in 1997 (Fig. 5). This patient developed flaccid paraplegia postoperatively and required removal of the hardware and

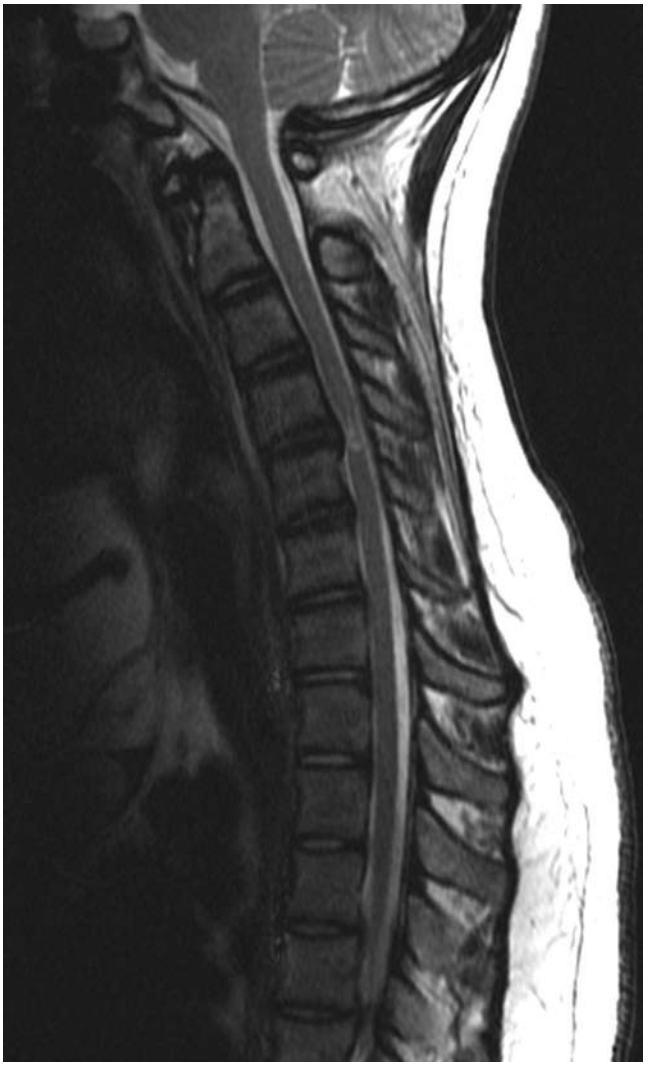

Fig. 4. Sagittal T2-weighted MR image of the cervical spine obtained in an asymptomatic 17-year-old girl with achondroplasia who had signs of cervical myelopathy.

a decompressive laminectomy, which was performed with the assistance of a neurosurgeon. The patient regained the ability to walk, with some residual distal weakness assessed at 4/5, and regained continence of bowel and bladder. No other fusion procedures were performed for thoracolumbar kyphosis during the study period.

Discussion

We have analyzed all patients with achondroplasia who underwent neurosurgery at The HSC in the past 52 years, and have identified 29 patients and 85 operations. The total number of children with achondroplasia under the care of The HSC during the entire study period has not been recorded. For the past 20 years of the series (January 1988 to the present), we have 162 children with achondroplasia in whom follow-up is ongoing at The HSC. During this time 19 patients underwent neurosurgical procedures, representing 11.7% of this group. Seven (4.3%) of these 162 patients had shunts in situ.

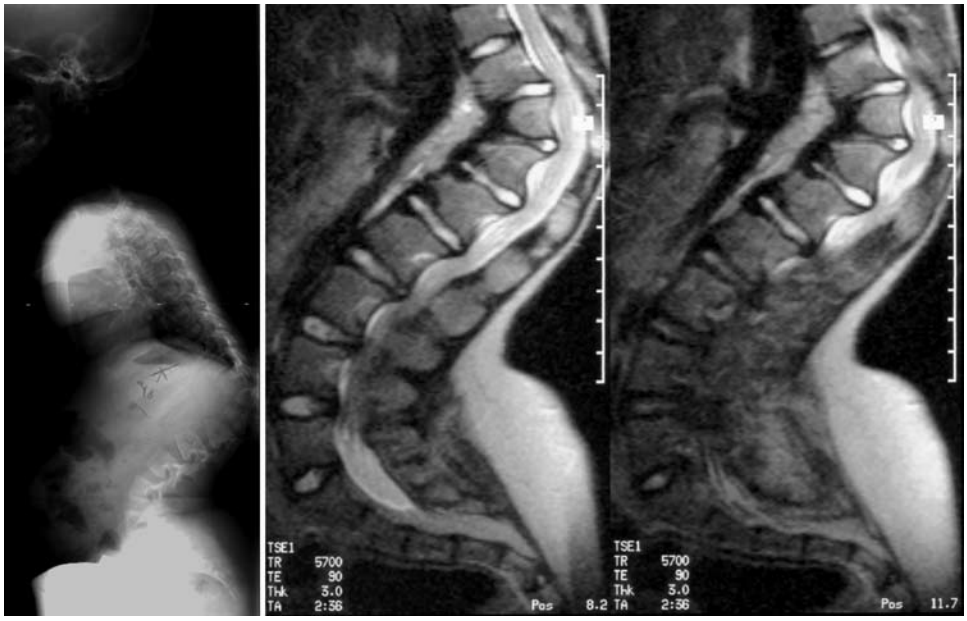

FIG. 5. Plain lateral spinal radiograph *(left)* and sagittal T2-weighted MR images *(right)* of the thoracolumbar junction obtained in a 7-year-old child with symptomatic progressive thoracolumbar kyphosis.

Achondroplasia may be a genetically inherited disorder for which neurosurgeons should have a heightened awareness. The genetic basis for achondroplasia was identified in 1994.[30,34] It has been shown that 95% of patients with achondroplasia have the same Gly380Arg amino acid substitution in the transmembrane domain of the FGFR3 receptor. The mutation has 100% penetrance. A Gly-375Cys mutation of *FGFR3* accounts for a small group of patients with achondroplasia. Different mutations in the *FGFR3* gene can lead to other disorders, which are considered part of a spectrum of disorders. Currently described are hypochondroplasia, severe achondroplasia with developmental delay and acanthosis nigricans, and thanatophoric dysplasia.

The FGFR3 receptor is one of a family of transmembrane tyrosine-kinase receptors for fibroblast growth factor. Of interest to the neurosurgeon, mutations in the *FGFR1* and *FGFR2* genes have been identified in human craniosynostosis syndromes.[18] Mutations in *FGFR3* associated with achondroplasia cause a gain of function.[7,9,23] Binding of fibroblast growth factor to the *FGFR3* receptor results in receptor dimerization, activation of tyrosine kinase activity of the receptor, and alters intracellular signaling.

The *FGFR3* gene is a regulator of bone growth, inhibiting proliferation and differentiation of growth plate chondrocytes.[7,9] Mutations resulting in achondroplasia exaggerate this inhibitory function. Diminished growth of the skull base in achondroplasia results in cranial foraminal stenosis, and it is postulated that jugular foramen stenosis, impairment of venous outflow, and subsequent intracranial venous hypertension is the basis for impaired CSF absorption, macrocephaly, and ventriculomegaly in this group of patients.[6,35] Enlargement of the subarachnoid spaces is commonly seen and is thought also to be a result of the venous hypertension.[41] Rarely is true obstructive hydrocephalus identified, although impairment of fourth ventricle outflow due to a small posterior fossa and a tight CCJ has been postulated to contribute to this phenomenon.[41]

A baby with achondroplasia very commonly will have an enlarged head. Monitoring of head growth should be performed at regular intervals and compared with control charts for children with achondroplasia, because comparison with the typical head growth curve of the general population will lead to unnecessary CSF shunting.[19] Observation for symptoms and signs of raised ICP should be undertaken and axial imaging performed if concerns are raised. A cranial ultrasonography study is an adequate screening test; however, MR imaging will allow both for an assessment of ventricle size and evidence of transependymal flow of CSF. An MR venography study can be performed in addition to an assessment of the CCJ. Classically, these patients have mildly to moderately dilated ventricles, but the majority of patients with macrocephaly stabilize spontaneously, and thus insertion of a VP shunt should be reserved for severely symptomatic cases.[11,27] There may be a role for ICP monitoring in the child with achondroplasia[11] and suspected progressive hydrocephalus, but an investigation to determine what level is pathological and harmful in these children has not been performed, except in small numbers.[35]

Neuropsychological outcomes for children with achondroplasia have been studied,[37] and these individuals are thought to have relatively preserved cognitive function. Accordingly, our current practice is to avoid shunt placement in these children unless there is overwhelming evidence of symptomatic raised ICP. Seven (4.3%) of the 162 patients in whom follow-up has been ongoing at The HSC since 1988 had shunts in situ, with the majority inserted prior to this date. The proportion of children with achondroplasia who undergo shunt placement varies considerably between centers, ranging from 4.3% in our series, to up to 50%.[2,21,28,29,35,41] In a recently reported pediatric spine surgery series from The JHU, 20% of the

44 patients had undergone shunt insertion.[33] We provide the example of a 6-year-old child with achondroplasia who had moderate ventriculomegaly and a head circumference on the 75th percentile for individuals with the disease, who was not treated with shunt placement, and who remains well and has had a normal developmental outcome to this point (Fig. 6).

If clinically significant intracranial hypertension exists and a decision is made to place a shunt, we would advocate the use of a flow-regulated system, such as the OSV II, in an attempt to minimize the risk of postshunting subdural collection and slit ventricle syndrome. In shunt-treated hydrocephalus associated with intracranial venous hypertension, the ventricles can become slitlike, leading to repetitive proximal malfunctions, as seen in the early cases in our series. Alternatively, a programmable valve system may afford flexibility in the situation of symptomatic overdrainage. Additionally, the unusual cranial morphological features may make traditional surgical landmarks less applicable for guidance of ventricular catheter placement, and in this situation, use of intraoperative ultrasonography and/or neuronavigation can be helpful.

There are reports of the successful use of ETV in patients with achondroplasia who have triventricular hydrocephalus;[12] however, altered anatomy in the region of the floor of the third ventricle is frequently encountered, making the procedure more demanding technically and possibly entailing increased risk. The role of ETV in children with achondroplasia has not been established.

A large head with weak cervical musculature and a small CCJ places significant stresses on this critical region. The clinical features of cervicomedullary compression can be quite varied, and include cervical pain; apnea and respiratory difficulties; and lower cranial nerve dysfunction, including bulbar dysfunction, bladder dysfunction, paresis, hyperreflexia, and hypertonia with clonus.[32] Indeed, children with achondroplasia are classically hyporeflexic, and normal (2+) reflexes in this population may be a sign of spasticity/myelopathy. There are reports of acute deterioration of neurological function after minor trauma,[4] and the increased incidence of sudden death at < 4 years of age in children with achondroplasia has been attributed to this pathological entity.[5,26]

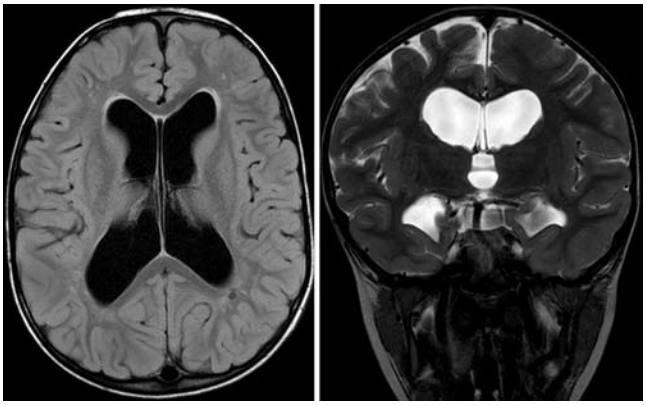

FIG. 6. Axial FLAIR-weighted *(left)* and coronal T2-weighted *(right)* MR images obtained in a 6-year-old child with achondroplasia who had moderate ventriculomegaly and a head circumference on the 75th percentile for achondroplasia, who did not undergo shunt placement and who has had a normal developmental outcome to this point.

Investigations in a child with suspected cervicomedullary compression include an MR imaging session and formal polysomnography. The use of polysomnography to assess patients for the presence of central and/or obstructive sleep apnea has been reported to identify central/mixed apnea in up to 60% of unselected children with achondroplasia.[39] Results of CT and MR imaging of the cervical region may demonstrate reduced tranverse and sagittal dimensions of the foramen magnum, and spinal cord compression with T2 signal change.[16,17] Recent reports have also stressed the importance of MR imaging performed with the neck in flexion and extension, highlighting transient compression of the cervicomedullary region, and/or impairment of CSF outflow in different positions of the head and neck.[8] The use of MR venography to identify a persistent occipital sinus seen in patients with achondroplasia may be a useful adjunct, especially if dural opening is contemplated at CMD.[24]

Indications for surgery include myelopathy with upper motor neuron signs such as clonus and hyperreflexia, and/or central apnea as documented on polysomnography, or the presence of a syrinx, with evidence of a narrow foramen magnum and/or T2 signal change in the spinal cord on MR imaging. The asymptomatic child with a narrow foramen magnum and T2 signal change in the cord may also be best served with a decompression, although this remains controversial;[4] 35% of patients with achondroplasia will have cervicomedullary compression on imaging, and almost all have an abnormally small foramen magnum.[29] The foramen magnum dimensions in children without achondroplasia and in symptomatic and asymptomatic children with achondroplasia have been studied.[16,17] Hecht et al.[16] found that, despite some overlap in the fitted mean curves of the sagittal and transverse dimensions in symptomatic and asymptomatic children with achondroplasia, > 70% of symptomatic children will have foramen magnum dimensions between the mean and 2 SDs below the mean for children with achondroplasia. Of the children undergoing CMD in our series, a subset underwent imaging to allow accurate measurement of the foramen magnum, and 78% were found to have dimensions below the mean for their age at the time of imaging. We found that the transverse diameter of the foramen magnum was significantly smaller in the surgical group than in the nonsurgical group, in concordance with Hecht et al.,[16] who stated that in achondroplasia "there is a dramatic reduction in the size of the foramen magnum, which is most marked in the transverse dimension." We believe that it remains difficult to determine the need for treatment on the basis of measurements alone, but they remain useful in the context of a complete evaluation of the child with achondroplasia. It is thought that ~ 5–25% of these children require CMD (17 [10.5%] of 162 at The HSC, 6 [3.2%] of 186 at the University of Iowa,[32] and 15 [25.8%] of 58 at The JHU[1]).

With regard to the demographics of this population, the gender distribution was relatively equivalent, and the percentage of patients with a family history of achondroplasia was as expected (14%). We did identify a mean age at primary surgery of 23 months, which is considerably younger

than the 70 months reported in the series from The JHU.[2] Furthermore, we identified a change in the presentation of these patients over time through this series, which we believe reflects the greater ability to diagnose CMD now at an early age with MR imaging and polysomnography (Table 2). Patients underwent surgery at a slightly older age in the early part of the series and were more likely to present with a neurological deficit than those identified in the latter part of the series, who presented with central apnea on polysomnography or T2 signal change in the cervical spinal cord on MR imaging.

A distinct entity described as cervical high-intensity intramedullary lesion, as characterized by T2 signal change in the cord in the absence of compression, has been recently described.[38] In this series of 25 adult patients, 64% had a cervical high-intensity intramedullary lesion in the absence of local spinal cord compression, raising the question of whether there is an intrinsic process affecting the cord at this level or whether there is intermittent compression related to instability or the abnormal morphometrics of the achondroplastic cranium. We have identified this phenomenon in at least 1 patient.

The surgery for symptomatic cervicomedullary compression is a subject of some controversy in terms of the procedure performed.[1,2] The procedure typically involves suboccipital craniectomy and C-1 laminectomy, usually without duraplasty. Preserving muscle attachment at C-2 may reduce the incidence of postoperative pain and/or instability. The anatomy of the occipital bone is often unfavorable, in that the orientation of the posterior occipital bone is horizontal or even curving cranially. The dura mater may be thin and fragile in these patients, but there are often dense fibrotic epidural bands to be released. Positioning and careful avoidance of venous hypertension are critical. Inadvertent durotomy in these patients may be a very difficult problem, and some surgeons would advocate the use of an EVD in this situation to reduce the high risk of CSF leakage from the wound.[1,2] The use of spontaneous ventilation and electrophysiological monitoring are techniques that can be helpful in detecting neurological compromise during the positioning and procedure. Intraoperative ultrasonography is recommended to assess the adequacy of the decompression by the presence of pulsatility of the brainstem and upper cervical spinal cord. This may be useful in determining which patients require formal dural opening.[32] Dural opening and duraplasty carries the additional morbidity of significant blood loss due to the venous hypertension and a potentially large circular sinus, but was performed in 2 patients in our series with life-threatening presentations. Both of these patients had preexisting VP shunts and did not experience CSF leakage postoperatively.

Our reoperation rate of 2 (11.1%) of 18 for residual or recurrent stenosis is in keeping with reported rates in the literature (9.3%).[2] The low infection rate in our series may reflect the fact that only 2 of the 20 operations involved duraplasty, with 1 additional inadvertent durotomy, and that external drains were not used in the perioperative period.[2]

In terms of formal screening of all children with achondroplasia, we would advocate an MR imaging and sleep study in the first 6 months of life. Symptomatic patients with notable cervicomedullary compression should be treated. Those with a radiographic abnormality alone should undergo repeat imaging in 1 year. Based on the fact that almost 90% of those patients in our series who underwent CMD became symptomatic and had their procedure performed prior to the age of 2 years, we would advocate clinical review over repeat imaging after this age. In summary, suboccipital craniectomy with C-1 laminectomy is an effective operation for symptomatic patients, with relatively low morbidity and mortality rates.

Syringomyelia in conjunction with achondroplasia is uncommon, but is seen in severe cervicomedullary compression, with what is thought to be a similar etiology to syringomyelia in Chiari malformation Type I.[3,31] It is also reported to have occurred in an adult with achondroplasia who had a posterior fossa arachnoid cyst and tonsillar herniation.[3] We believe that symptomatic patients should undergo foramen magnum decompression as the primary procedure for the treatment of the syrinx, with a bone-only decompression providing a lower risk of postoperative complications in this group.

Patients with achondroplasia have short pedicles, small neural foramina, and reduced interpedicular distance, and with age these individuals are prone to the development of thickening of the ligamentum flavum and subsequent cervical, thoracic, and lumbar canal stenosis.[2,20] This is evident in older children, and by the 6th decade 80% of patients will have symptomatic stenosis.[20] Laminectomy will be performed in 10–25% of these patients.[14]

Symptomatic canal stenosis requiring surgery in the pediatric population is thought to be relatively rare. The Dutch experience (Leiden group) involved just 2 patients < 18 years of age who had undergone surgery for lumbar canal stenosis since 1975;[36] however, a recent publication from The JHU reported 44 pediatric patients who underwent 60 spinal decompressive procedures in the past 9 years, of which 65% were thoracolumbar and 20% lumbar. The cohort of children with achondroplasia seen in this quaternary referral center is a superselected group, and is unlikely to represent the general pediatric population of patients with achondroplasia.[33]

Symptomatic spinal canal stenosis in our pediatric series was only identified in 3 patients. One patient underwent surgery prior to 1988 and was not followed in our clinic, so for the period in which we have an accurate total number of children with achondroplasia in whom follow-up was ongoing, 2 (1.2%) of 162 underwent decompressive surgery.

The presence of scoliosis and thoracolumbar kyphosis can complicate decompressive surgery in this skeletally immature group of patients, necessitating interapophyseolaminar decompression without laminectomy,[36] or the use of instrumentation postlaminectomy to prevent postoperative instability.[33] Immediate postoperative morbidity is reported to relate primarily to durotomy and subsequent CSF leakage. Delayed instability is also a major consideration, with some authors advocating fusion in pediatric patients following decompression[33] if there is evidence of a thoracolumbar kyphosis at the surgical level(s). Delayed instability was evident in 1 of our 3 patients who underwent decompression.

Atlantoaxial subluxation has been reported in children with achondroplasia, both de novo[13,15] and following foramen magnum decompression and C-1 laminectomy. Preservation of the musculature at C-2 may limit the incidence of this phenomenon.

The incidence of instability following laminectomy is difficult to assess, with a number of authors preferring to instrument the spine in patients with achondroplasia following decompressions. Our experience is too small to comment on this. In general, these patients often undergo multilevel laminectomies at a young age, thus putting them at increased risk of delayed instability.

Thoracolumbar kyphosis is often present at birth in children with achondroplasia and usually is evident at 4 months of age, reportedly in up to 90% of children. Its cause is thought to be truncal hypotonia, and this improves by 12–18 months of age. The use of thoracolumbosacral orthoses is often sufficient to prevent progressive deformity and the need for surgical intervention. A small group of children will develop progressive deformity and require intervention. The single child who underwent such a procedure in our series sustained a spinal cord injury, highlighting the potential complications of such a major operation.

Conclusions

Our series reports the neurosurgical experience of a large center in treating children with achondroplasia. There have been few referrals from outside the province or the country in this series, and thus, we believe that our estimates of the frequency of the need to perform neurosurgical procedures in these children are broadly applicable. The indications for neurosurgery in children with achondroplasia are being further defined as greater experience of the natural history of the condition accumulates. An understanding of the macrocephaly and mild-to-moderate ventriculomegaly that is very common in achondroplasia, and tends not to be progressive in most cases, has led to a practical cessation of CSF diversion for these children. Only 1 shunt has been inserted in a child with achondroplasia in the past 20 years at The HSC. The practice of decompressive surgery for cervicomedullary compression, however, appears to be increasing with the recognition of the incidence of sudden death in children with achondroplasia,[33,40] a greater ability to document central apnea on sleep studies, and good-quality MR imaging of this region on which stenosis and spinal cord signal change can be identified. There are many unique features to consider when contemplating surgery in the child with achondroplasia, and these need to be assessed to minimize unnecessary procedures and operative morbidity.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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