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Neurological Manifestations of Achondroplasia

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Abstract

Purpose of review This review is to delineate the neurological complications seen in patients with achondroplasia.

Recent findings As the understanding of the genetics of this disorder has advanced, the possibility of targets for intervention which might modify the development and management of the neurological complications of this disease may be identified.

Summary Achondroplasia is a hereditary short-limbed dwarfism which has been known for millennia. The genetic defect is a gain of function sequence variation in the fibroblast growth factor receptor 3 (FGFR3). This gene normally regulates (inhibits) bone growth thus the gain of function results in abnormal or excessive inhibition of growth. The resulting bone is subject to distortion and the result is that bone impinges on nervous tissue, most commonly at the foramen magnum, spinal canal, and nerve root outlet foramen. Awareness of the range of these complications will, hopefully, allow early and more effective intervention so as to ameliorate the nature and severity of the long-term effects of the neurological complications in patients with achondroplasia.

Keywords Achondroplasia · Spinal stenosis · Macrocephaly · Communicating hydrocephalus · Craniovertebral impingement · Claudication

Introduction

Achondroplasia is the most completely delineated of the short-limbed dwarfing conditions. It is also the most common of these conditions. Individuals affected with this condition demonstrate characteristic facial features with frontal bossing and midfacial hypoplasia. They have exaggerated lumbar lordosis and joint abnormalities including genu varum, limited extension of the elbow with hyperextensibility of other joints and short fingers and hands (called the trident hand) [1].

The disorder has been identified for many millennia and may be depicted in Egyptian art and these individuals are known to have been gladiators, court jesters, and circus performers in more recent times [2]. Recent recognition of the impact of the interplay between the skeletal abnormalities and the underlying nervous system on functions including respiration and sleep in addition to the more widely recognized complications has led to a more proactive approach to the management of these patients.

Achondroplasia is inherited as an autosomal dominant condition with a prevalence of 1–20–30,000 live-born infants though most cases are the result of spontaneous mutations and thus occur sporadically in a given family though there is an association with advanced paternal age [3–6]. The mechanism of the advanced paternal age effect is not understood and though unusual, gonadal mosaicism has also been documented [7]. The cause, in almost all cases, is G380R mutation in fibroblast growth factor receptor 3 (FGFR3) located on chromosome 4 at 4p16.3 resulting in an amino acid substitution in the transmembrane domain of the receptor. This change results in alteration of the activation of the receptor [1, 8]. FGFR3 is an important negative regulator of linear bone growth by decreasing chondrocyte proliferation and differentiation in the growth plate and mutations in achondroplasia, and related disorders activate the receptor resulting in the gain-of-function with inadequate growth of the affected tissues [9]. The identification of the molecular mechanism of the disease offers the promise of the identification of therapeutic targets for future interventions [10•].

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Though there is decreased reproductive efficiency in patients with achondroplasia, nevertheless, there is a roughly 50% chance of the product of a pregnancy occurring as a result of mating between two individuals with achondroplasia. The possibility of the fetus being homozygous for the mutation is about 25% but such an unfortunate circumstance leads to a severe lethal disease with demise shortly after or before birth; although recognition that some of the respiratory complications are the result of medullary compression has led to more aggressive approach, the outlook for long-term survival has not changed [11–14]. Prenatal detection/identification of the affected fetus is routine with in utero ultrasonography [11, 12]. Such an event should provide the opportunity to involve physicians, genetic councilors, and others experienced in the management of parturition to avoid injury to the fetus and the mother. There is a potential for difficulty on the mother's part due to likelihood of small pelvic outlet impeding vaginal delivery and on the infant's part due to the likelihood of macrocephaly.

Infants born with achondroplasia are at risk for numerous bony and neurological complications and thus should optimally be managed by a multidisciplinary team of clinicians. The most severe neurological complications are the result of stenosis and compromise of the development of the posterior fossa and stenosis of the craniocervical junction and foramen magnum (Fig. 1). These alterations in the dimensions of the cranium and cervical junction can, over time or with neck injury, result in medullary and upper spinal cord compression leading to early demise or devastating disturbances of functions [13]. As the achondroplastic individual ages, spinal cord and nerve root compressions are significant risks. The malformation of the foramen magnum and the odontoid process, possibly problematic at any age, becomes more likely particularly associated with head and neck trauma (Fig. 2). In the adult with achondroplasia, age-related spondylosis, hypertrophy of the ligamentum flavum, foraminal stenosis, and vertebral canal/spinal stenosis may result in bladder, bowel, and sexual dysfunction from compression of the conus medullaris and or cauda equina, and claudication (spinal). Knowledge of the age-related clinical complications allows the physician to anticipate problems and enable early medical and/or surgical intervention.

Neurologic complications of achondroplasia have been attributed to the bony defects resulting in encroachment of the bone on the nervous system. This may be in the form of inadequate development of the spaces for the brain, spine, and brain stem or in the form of thickening of the bone and distortion of the outlet foramen over time. Both mechanisms result in the compression of the nervous tissue because of the configuration of the skull. However, thickening of the connective structures such as the ligamentum flavum may also contribute to the compression of the nervous system [14–19].

To further delineate these issues, it has been shown that defective endochondral ossification results in small or deformed foramina including the vertebral foramen; in addition to the foramen magnum abnormality, the cranial nerves and cranial vascular structures may undergo compromise as a result of narrow outlet foramen in the skull and vertebral column such as a narrow jugular foramen. Because of the abnormal growth of the vertebrae, these patients have a narrow spinal canal with stenosis [20]. The spinal narrowing becomes potentially more problematic at the cervical regions and at the cervical and lumbar cord enlargements. Nerve root and vascular compression may compromise the venous outflow from the skull which over time may have significant implications and the resulting "communicating hydrocephalus" is undoubtedly one of the important causes of macrocephaly in these patients (Fig. 3). Furthermore, because of the relative lack of rigidity of the bones, the structures such as the occipital condyle at the foramen magnum may distort over time making the

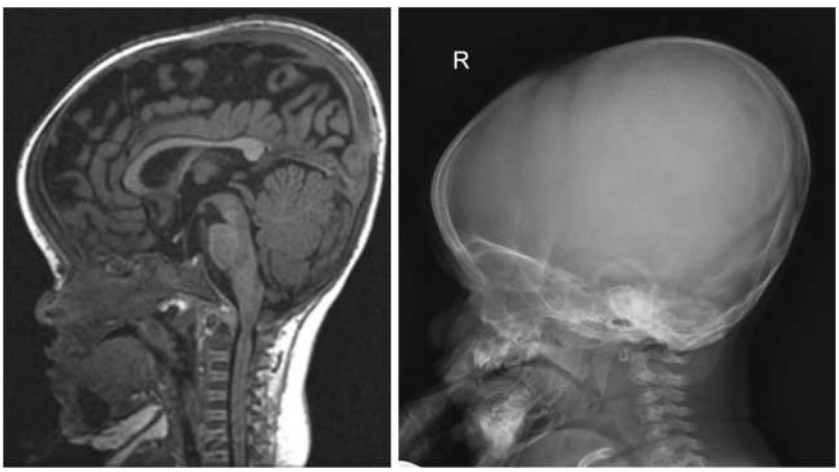

Fig. 1 (Left) The T-1 weighted MRI image of an infant with achondroplasia demonstrates a small posterior fossa and small short vertebral bodies. (Right) Lateral skull film of a patient with achondroplasia demonstrating macrocephaly, platybasia, and small short vertebrae. The radiographic and neuroimages are courtesy of Dr. Mai-Lan Ho MD, Associate Professor of Radiology/ Neuroradiology, Nationwide Children's Hospital, Ohio State University College of Medicine, Columbus Ohio

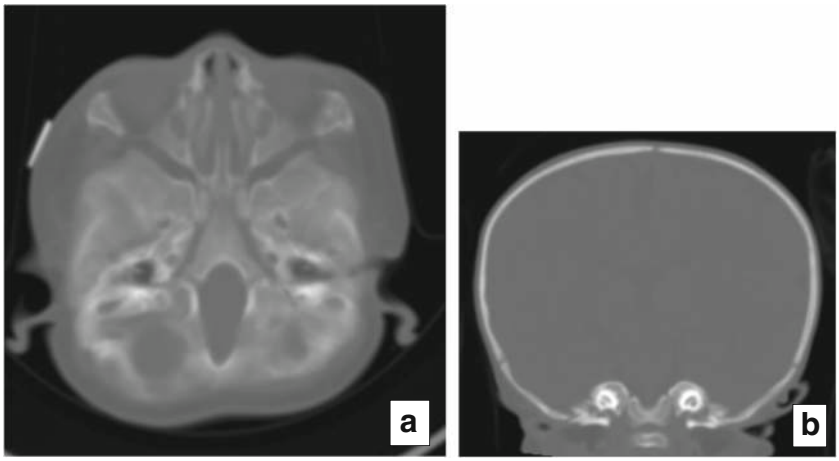

Fig. 2 Left is an axial MRI image at the level of the foramen magnum. Note the narrow and distorted shape of the foramen. In **b** which is a coronal image through the base of the skull showing elevation of the structures adjacent to the foramen due to distortion of the normal position of these structures as a result of pressures on the softened bone over time. The radiographic and neuroimages are courtesy of Dr. Mai-Lan Ho MD, Associate Professor of Radiology/Neuroradiology, Nationwide Children's Hospital, Ohio State University College of Medicine, Columbus Ohio

likelihood of compression of the cervical spinal cord greater (Fig. 2).

The vertebral column alignment may sometimes be or become faulty with scoliosis, kyphoscoliosis, gibbus deformity, and severe lumbar lordosis which can compress the spinal cord or cauda equina (Fig. 4). Ligamentous laxity may also result in increased movement of the bony structures and increase the possibility of compression of the cord [21, 22].

Macrocephaly and Hydrocephalus

Macrocephaly, head size more than two standard deviations above the mean for age, is a common feature of individuals with achondroplasia [2, 14] (Fig. 1). There are several potential causes for this feature some of which are of concern, particularly in children under 2 or so years of age. Although

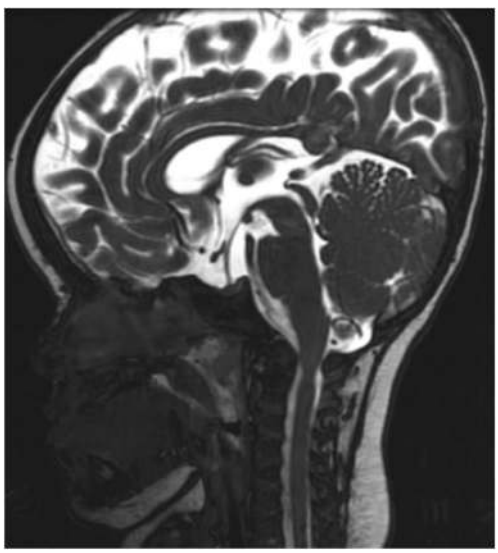

Fig. 3 T-2 weighted sagittal image of a patient with achondroplasia demonstrating abundant subarachnoid fluid, the macrocrania of communicating hydrocephalus, and the "shelf" at the foramen magnum resulting from premature closure of the posterior synchondroses and hypertrophied posterior margin of the foramen magnum at the craniovertebral junction. The radiographic and neuroimages are courtesy of Dr. Mai-Lan Ho MD, Associate Professor of Radiology/Neuroradiology, Nationwide Children's Hospital, Ohio State University College of Medicine, Columbus Ohio

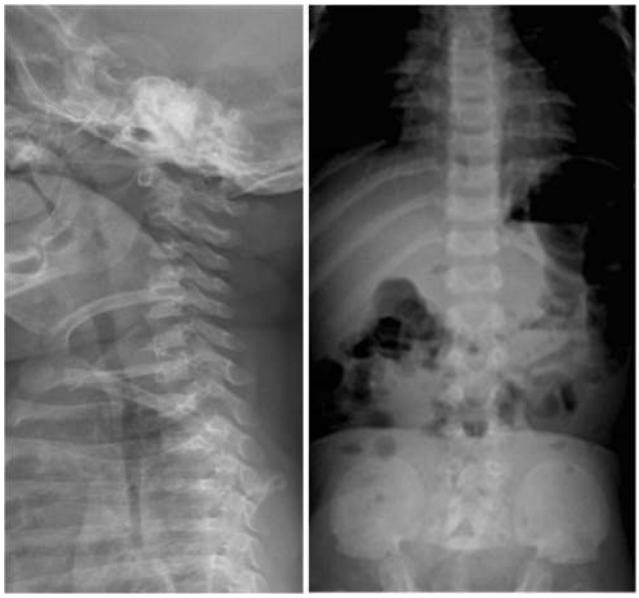

Fig. 4 (Left) Lateral spine film of a patient with achondroplasia showing the short vertebral bodies and somewhat narrow spinal canal in the cervical region. Right is an anterior-posterior spine film of an infant with achondroplasia demonstrating the small pedicles, narrow spinal canal diameter in the lumbar region suggesting Lumbosacral stenosis. The radiographic and neuroimages are courtesy of Dr. Mai-Lan Ho MD, Associate Professor of Radiology/Neuroradiology, Nationwide Children's Hospital, Ohio State University College of Medicine, Columbus Ohio

hydrocephalus can occur, it is not the most common issue. Megalencephaly, that is enlarged brain with normal size or slightly enlarged ventricles, is more common and presumably results from chronic low-grade impairment in flow of venous blood from the brain and thus a low-grade increase in the pressure in the cranial sinuses. Macrocephaly/megalencephaly is so common a feature in these patients that standard head growth curves as well as standard height and weight growth curves are now available for these children [23–25].

Hydrocephalus, that is enlarged head with enlarged ventricles, has been recognized in these children for years. There are several possible mechanisms which might be active in this setting [26]. Noncommunicating hydrocephalus due to aqueductal stenosis has been described but seems to be uncommon [26, 27]. It seems more reasonable that the obstruction of outflow of CSF thru the basal cisterns and posterior fossa because of the skeletal deformities of the skull is the more likely and more common cause of hydrocephalus and though this type would be considered "communicating hydrocephalus" in the standard terminology, in fact the flow is obstructed but not in the ventricular system. This communicating hydrocephalus results in prominence of the subarachnoid spaces throughout the skull with mild ventricular enlargement as seen in Fig. 3. While it is easy to visualize the tight posterior fossa inhibiting the free circulation of CSF, the chronic increased venous pressure is likely involved in most of these cases due to compression of the venous outflow from the brain and skull at sites such as the jugular foramen [28•]. Clinical features seen in patients with increased intracranial venous pressure include dilated venous structures in the scalp and face, bulging anterior fontanelle, cranial bruit, and headache. The persistence of the communicating hydrocephalus may not become apparent until or unless the situation results in gait impairment or the development of long tract signs. Serial imaging of the head in patients suspected of having hydrocephalus or who develop neurological signs is recommended. In general, and if possible, shunting of communicating hydrocephalus is not very helpful and is to be avoided if possible. The most useful approach is to decompress the posterior fossa and foramen magnum allowing better drainage of the CSF and venous blood from the head.

Craniocervical Junction Anomalies

The cranial base and the neural arches grow and enlarge by endochondral ossification. Furthermore, the base of the skull is constantly under pressure at least equal to the weight of the head and the tension of the cervical muscles. As a result of these forces and the "softness" of the bone, the foramen magnum invaginates upward into the skull and not surprisingly the integrity of the foramen is not retained (Fig. 2). Thus, abnormalities of the craniovertebral junction are essentially universal in patients with achondroplasia [19, 29, 30] and consist of foramen magnum stenosis, upper cervical vertebral canal stenosis, abnormal odontoid position and shape, ligamentous laxity in the cervical spine, and jugular foramen stenosis.

The growth reduction of the occipital bones results in the small malformed foramen magnum with a critical feature being the decrease in the sagittal and transverse dimensions of the foramen [29–31]. Usually small at birth, the foramen magnum remains small, particularly in the transverse diameter. Growth of the skull is particularly robust and important in the first 18 months of life with achondroplastic patients growing significantly less rapidly. There is very little difference in the actual size of the foramen between symptomatic and asymptomatic patients; the average adult foramen in patients is the size of the average normal newborn in the transverse diameter and the size of the average 2-year-old in the sagittal diameter [29].

An additional factor in the failure of growth of the foramen is felt to be premature fusion and aberrant development of the posterior synchondroses at the base of the skull. This may contribute to the hypertrophied margin of the posterior aspect of the foramen magnum that appears as a bony shelf radiologically (and surgically) which projects into the posterior brain stem and the upper cervical spinal cord resulting in compression of the craniovertebral junction, anterior compression of the lower brain stem, and potential permanent injury to the nervous system at that level (Fig. 3). The situation is potentially worsened by the abnormal size and position of the upper two cervical vertebrae making up the atlantoaxial complex and contributing to the narrowing of the vertebral canal in this region. Among the clinical features that might occur due to this lesion are myelopathy, apnea, sudden death, and lower brainstem dysfunction (swallowing, speech, etc.)

Alteration of the size shape and position of the odontoid process of C-2 can also contribute to the neurologic morbidity in these patients. The odontoid may project back into the already small foramen and compress the already potentially compromised medulla. This phenomenon may result in damage to the anterior spinal artery, the medulla, and cervical spinal cord causing long tract signs including quadriparesis and milder gait abnormalities. Probably, laxity of the ligamentous structures in the craniovertebral region of the spine contributes to the potential for injury to the nervous system tissue [18].

The instability of the craniospinal junction due to ligamentous laxity along with bony stenosis and macrocephaly make injury to the cord which makes the infant particularly vulnerable to neurologic injury associated with head trauma. This might result in sudden infant death, sleep apnea syndrome, respiratory failure, myelopathy, syringobulbia/syringomyelia, and hydrocephalus.

Sudden unexpected death

Sudden unexpected death was identified in 13 cases in a retrospective case ascertainment study [32]. The risk of sudden

death was found to be 7.5% in children less than one year, 2.5% in patients 1 to 4 years of age, both significantly above the risks in the general population by a factor of 50-fold [22]. There is general agreement that the increased risk of sudden unexpected death in children with achondroplasia is due to the compression of the lower brainstem and medulla at the level of the foramen magnum [18, 32, 33]. There are also reports of recurrent diurnal apneic episodes, sometimes prolonged and often mistaken for seizure activity [34]. Postmortem examination in patients who have undergone sudden unexpected death had shown gliosis, edema, and cystic myelomalacia at the level of the craniovertebral junction and lower medulla resulting from acute and/or chronic compression of the cord and medulla at this level.

Sudden unexpected death is also a phenomenon with increased frequency in adults with achondroplasia. In one study of about 800 individuals with achondroplasia followed for 20 years, cardiovascular disease–related mortality between ages 25 and 35 was increased more than tenfold over the general population. Neurologic causes of death were also increased in this population although specific risk factors have not been clearly identified [21, 22].

Sleep Apnea and Disorders of Respiration

It is common for children with achondroplasia to present a history of excessive snoring at night with daytime sleepiness or other symptoms [18, 35]. Excessive snoring, particularly when associated with head retraction at rest, may be an important indication for further studies of respiration and its control as well as investigation of the anatomy of the craniocervical junction. Recurrent apneic episodes may lead to multiple arousals, poor sleep efficiency, somnambulism, daytime sleepiness, and enuresis. Another less widely known effect of these problems can be excessive weight gain which is a common issue with individuals with achondroplasia [18, 34, 35]. Lack of adequate sleep can present with, in addition to the weight gain and daytime somnolence, poor linear growth, fluid retention, headaches, behavior change, and dyspnea and chronic excessive snoring may lead to cor pulmonale with CO_2 retention and reactive constriction of the pulmonary vasculature.

The sleep apnea in patients with achondroplasia, thought to be due to upper airway obstruction due to tonsillar hypertrophy, glossoptosis, and pharyngeal wall laxity, has been shown to be more commonly due to central causes of the sleep apnea [35]. Regardless, polysomnographic studies have demonstrated obstructive, central, and mixed sleep apnea [36]. Improvement in both obstructive and central sleep apneas has been observed following surgical decompression of the medulla and upper cervical spine. Clearly, it is too simplistic to consider obstructive and central sleep apnea as distinct entities [37]. There is little doubt that foramen magnum stenosis with injury to the medulla and upper cervical spine can interfere with normal control of sleep. The motor nuclei of the brain stem and reflex pathways involving the larynx and pharynx may be affected resulting in discoordinated movements of the upper airway muscles during inspiration contributing to airway obstruction. In all probability, the documented presence of abnormal sleep patterns suggests the need for further evaluation and consideration of the value of surgical decompression of the medulla and or cervical spine in these patients [36].

Non-sleep-related respiratory dysfunction occurs in up to 85% of achondroplastic children [18, 33, 35]. There are, not surprisingly, a number of factors which have been identified as contributors to impaired inspiration and dyspnea in these children. Children with achondroplasia have a relatively small chest circumference which, although in theory could restrict air movement, in fact does not seem to contribute significantly to the sleep apnea syndromes [1, 18]. Usually by the end of the second year, the configuration of the chest has grown adequately that lung volume is not an issue. Compression of the cervical cord may impair the motor function aspect of respiration, and phrenic nerve damage as a complication of decompressive surgery is also not rare.

Myelopathy

Acute and chronic trauma to the lower medulla and upper cervical cord is a well-recognized complication of this disease and occurs at all ages though injury to the upper cord and medulla is more commonly recognized in children with achondroplasia. Spinal stenosis with cauda equina and conus compression and nerve root impingement at the outlet foramen is more common in the adult patients with achondroplasia. The infant with achondroplasia is hypotonic early on but injury to the cord results in a switch to hypertonicity, spasticity, and upgoing plantar responses. Older children may have demonstratable dorsal column dysfunction with a positive Romberg, spastic ataxic gait, and quadriparesis.

Syringobulbia/Syringomyelia

Syrinx formation whether in the brainstem (syringobulbia) or in the spinal cord (syringomyelia) is the probable end result of chronic compression associated with vascular compromise due to the tight constricted foramen magnum [38, 39]. Sometimes, these lesions are found incidentally while imaging the craniovertebral junction for other reasons. The patient may, however, have symptoms of medullary and cervical cord dysfunction before the injury to the structures becomes irreversible and develops cystic changes. These changes represent late stages in the evolution of compressive damage to the nervous system and as such are of less importance from the

interventional standpoint. Glial neoplasms have been described in the syrinx cavity in two patients. The neoplastic nature of the lesions, however, is difficult to ascertain with confidence.

Developmental Delay

Developmental psychomotor delay has been observed frequently in infants and children with achondroplasia [40, 41]. These delays are primarily in the motor milestones and in particular the gross motor functions. Generally attributed to the striking hypotonia, ligamentous laxity, skeletal deformities, and relatively large/heavy head and indeed hypotonia in and of itself can cause a slight delay in the acquisition of motor milestones. These hypotonic, motor-delayed infants usually have normal intellectual function. As a result, any achondroplastic infant with more than a pure motor delay should be evaluated further so as to be sure there is not an underlying neurologic cause of the delay. Similarly, any abnormality on neurologic examination that is not entirely due to the hypotonia should raise suspicion that something more serious is afoot. One study on achondroplastic children less than 40 months of age (using the Bayley scales of infant development) found a mean mental developmental index of 96 and a mean motor developmental index of 65 suggesting that this developmental delay is limited to the motor milestones alone [41].

There are many reasons why an infant with achondroplasia might fall behind on cognitive milestones and these reasons should be sought when the infant in question demonstrates cognitive as well as motor milestone acquisition delays. Among the most common reasons for both cognitive and motor delays are hearing problems, sleep disturbances, hydrocephalus, and foramen magnum stenosis with medullary compression. One common cause of difficulty with the development of proper articulation of speech sounds is tongue thrusting secondary to midfacial hypoplasia and requiring speech therapy for remediation.

Vertebral Canal Stenosis

Vertebrae are involved with achondroplasia and can be identified as abnormal at birth. Furthermore, since they are derived from endochondral bone ossification, they do not grow properly as the patient ages. Although there are short vertebrae with wedged vertebrae and posterior central bony spur formation, most of the neurologic problems are secondary to the short pedicles and narrowing of the interpedicular distances. Spinal canal stenosis occurs thus at all levels of the vertebral column and is particularly important at the cervical and lumbar cord enlargements, and in addition excessive lumbar lordosis may exacerbate the narrowing of the spinal canal. Lumbar stenosis usually becomes symptomatic in early adulthood and is exacerbated by the excessive lordosis and weight (both common in achondroplastic patients).

Clinical features depend largely on the location of compression of the nervous tissue and the severity of that compression. Thus, the symptoms may range from gradual impairment of gait, ataxia, and falling and/or spasticity, quadriparesis or quadriplegia, and pain are often the first symptoms [42]. As in other "compensated" neurologic states, sudden deterioration of function or increase in signs and symptoms may occur following what appears to be minor trauma. Presumably the minor disruption causes compensated compression of the cord to decompensate with sometimes disastrous results [43]. Other significant signs or symptoms in a patient with achondroplasia would be change in bladder function, claudication of the conus medullaris, or cauda equina which should prompt investigation of lower spinal cord compression [42]. Claudication in this context is described as pain, paresthesias, or dysesthesias apparent after minimal exercise such as walking a short distance. The mechanism is felt to be marginal blood supply to the compromised spinal cord which, with the increased demand associated with exercise, is unable to provide enough oxygen to the cord resulting in pain and weakness. When the patient with pain or weakness of the legs sits down to rest or squats with their back to a vertical wall or post, the physician should consider these maneuvers as signs of claudication of the cauda equina or conus medullaris. These maneuvers are felt to temporarily increase the blood supply to the spine. The identification of such symptoms or signs should prompt evaluation so as to avoid permanent injury to the spinal cord.

The level of spinal cord compression may be established by clinical exam in some cases. Dorsal column function may be easily demonstrated by testing vibration and proprioception but in younger individuals, somatosensory evoked responses may be more helpful [44]. Pain or Lhermitte's sign with neck flexion should suggest cervical cord compression/stenosis. In general, the evaluation of suspected compressive myelopathy in patients with achondroplasia is easier with magnetic resonance imaging but skill in dealing with children is a useful adjunct to the acquisition of quality images.

Vertebral Colum Malalignment

In infants with achondroplasia, as in any group of hypotonic infants, a gibbus deformity of the thoracolumbar spine is common. There is a possibility that such a deformity could lead to compression of the spine but this seems to be an uncommon event. In somewhat older children, wedging of the vertebrae is potentially more serious and once identified this deformity should be followed though once ambulatory the deformity usually disappears. Some advocate bracing but this is not effective in most children at this age. On rare occasion, particularly in the older patient, angulation is severe enough and

fixed in position so that it may impinge on the cord underneath resulting in paraparesis or intermittent claudication and requiring correction of the deformity surgically.

Scoliosis and kyphosis are uncommon in achondroplasia patients and are not a significant cause of neurological disability [15]. Likewise, lumbar lordosis and thoracolumbar gibbus deformity, though much more common, are only rarely a cause of neurologic morbidity. Structural abnormalities of the sacrum is a relatively common spinal malformation in this disease and if accompanied by vertebral subluxation this deformity could be more problematic. Occasionally nerve rood compression is associated with this deformity as well. The list of symptoms described in association with these spinal deformities includes claudication, pain, exercise intolerance, and the tendency to squat and rest the back against a wall or post.

Nerve Root Compression

Nerve root compression is relatively common in patients with achondroplasia. The abnormal shortening of the pedicles and the small intravertebral foramina both contribute to this problem. The foramina narrowing occurs at several if not many levels and is most likely to be symptomatic in the cervical and lumbar roots. Pain is the most common complaint but dysesthesias and paresthesias in the distribution of the nerve are more localizing and loss of reflex activity and muscle weakness and/or wasting is more convincing of the need for intervention.

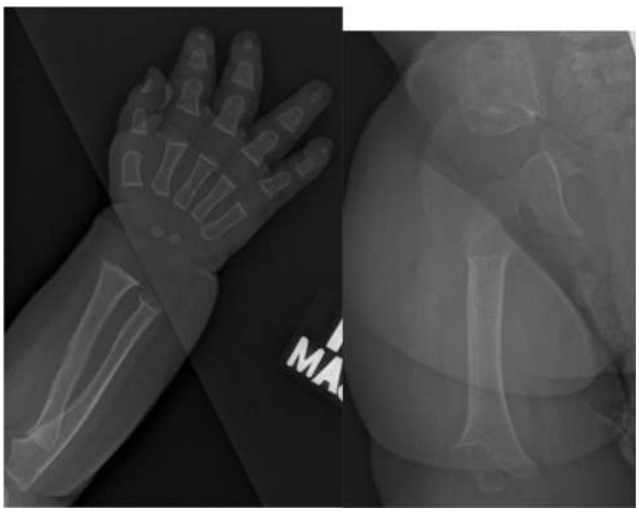

Fig. 5 Plain films of the hand and forearm (left) and the hip (right) from a child with achondroplasia demonstrating the abnormalities of bone growth in the extremities. These abnormalities are evident even at birth and allow for diagnosis with high confidence at that time. The radiographic and neuroimages are courtesy of Dr. Mai-Lan Ho MD, Associate Professor of Radiology/Neuroradiology, Nationwide Children's Hospital, Ohio State University College of Medicine, Columbus Ohio

One of the nerve root compression syndromes not due to vertebral anomalies in the usual sense is the possibility of occipital nerve compression or occipital neuralgia. This syndrome is due to the entrapment of the nerve as it exits the spinal canal through the posterior atlanto-occipital membrane and is more likely to happen with achondroplasia due to the anomalies of the foramen magnum and C1 and C2. Careful history of the resulting headaches can usually suggest the location of the entrapment but it may be difficult to distinguish occipital neuralgia from more serious compression of the nervous system at the craniovertebral junction. The ability to reproduce the pain with manual compression of the occipital nerve may be useful to distinguish the two possibilities. The entrapment of the occipital nerve may also be the result of scar formation after procedures to enlarge the foramen magnum [45]. There is a large headache literature regarding management options in occipital neuralgia [46].

Conclusion

The comprehensive management of patients with achondroplasia is a multidisciplinary approach and the priority of the issues is somewhat age dependent. Diagnosis is usually made at birth and is not difficult with characteristic radiographic features present at that age (Fig. 5). Following diagnosis, it is appropriate to do a complete neurological assessment to establish a baseline if nothing else. Serial assessments are required evaluating several aspects including tone, motor and cognitive milestones, head growth, and evidence of increased pressure. Needless to say, deviation from the expected norms for these children should prompt further evaluation. The recognition of the impact of sleep and respiratory abnormalities on the well-being of the patient with achondroplasia has resulted in a more proactive approach to the assessment and intervention related to these potential complications of the disease [47••].

The development of MRI and more recently the use of a variety of spin echo protocols has made the serial evaluation of the structures at the base of the skull and within the spine considerably easier than it was in the past. Nevertheless, awareness of and assessment for the development of any of the myriad potential neurological complications can keep the possibilities of permanent injury and disability to a minimum.

The participation of neurology, neurosurgery, pulmonary, genetic, orthopedic, and other specialists in the longitudinal management and care of the individual with achondroplasia is necessary to ensure the prevention identification and amelioration of emerging problems, and the anticipation of impending problems is optimal for the long-term survival of these patients with minimum neurological disability.

Compliance with Ethical Guidelines

Conflict of Interest John B. Bodensteiner has received paid travel accommodations from the ABPN.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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