Cervical high-intensity intramedullary lesions without spinal cord compression in achondroplasia

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Object. In the authors’ experience, the appearance of a cervical high-intensity intramedullary (CHII) lesion on magnetic resonance (MR) images in the absence of local spinal cord compression is frequently observed in patients with achondroplasia, although it has been mentioned only sporadically in the literature. Hence, the authors conducted a retrospective study in a consecutive single-center series of patients with achondroplasia to determine the prevalence and imaging features of this entity. They also reviewed the literature.

Methods. Cervical MR imaging studies obtained to establish diagnoses in 25 adult patients with achondroplasia and assessed at the Leiden University Medical Center after neurogenic claudication developed were evaluated for the presence of a CHII lesion. Imaging features of the lesion were described, and a literature search was performed.

The CHII lesion was demonstrated in 16 of 25 adult patients with achondroplasia (64%) in the absence of local spinal cord compression. All lesions were located at the C-2 level and appeared to be confined to the gray matter. The CHII lesion was associated with local spinal cord thinning, most likely representing focal atrophy. In their literature search the authors found no description of the CHII lesion in adults, although its presence has been mentioned as a peculiarity in the pediatric achondroplastic population.

Conclusions. In this large series of adults with achondroplasia and symptomatic neurogenic claudication, a CHII lesion was frequently depicted on imaging studies, but it remains a fully explored imaging phenomenon. Its cause and clinical relevance require investigation, as does its prevalence in the general achondroplastic population.

KEY WORDS • achondroplasia • medullary high signal intensity • cervical myelomalacia • magnetic resonance imaging

Abbreviations used in this paper: CHII = cervical high-intensity intramedullary; MR = magnetic resonance; SSEP = somatosensory evoked potential.

Achondroplasia is the most common form of dwarfism; its incidence is approximately one in 26,000 live-born infants. Achondroplasia is well recognizable: its characteristic phenotype includes rhizomelic micromelia, frontal and parietal bossing of the head, saddle-nose deformity, and trident hand. The condition is inherited as an autosomal-dominant trait or is caused by a sporadic mutation. The frequency of this sporadic mutation is thought to be influenced by increased paternal age. A specific point mutation has been shown in the transmembrane region of fibroblast growth factor receptor 3, which exerts negative control on endochondral bone formation and results in disturbed bone development.

Neuroimaging features of the achondroplastic spine include pseudoscalloping of the vertebrae, extreme backward tilting of the sacrum, reduced pedicle length, and a reduced interpediculate distance in the lumbar spine that progressively narrows, going caudally (typical in achondroplasia). The skull features include a narrowed foramen magnum and shortening of the skull base and clivus. In the presence of a normal-sized nervous system, the deformities of the skull and spine may give rise to various neurological complications; for example, the narrowing of the foramen magnum may cause cervicomedullary compression with tetraparesis and central apnea as a result.

Magnetic resonance imaging is a very important diagnostic tool for investigating signs and symptoms of spinal cord compression. In assessing medullary lesion in patients with achondroplasia, we frequently observed a CHII lesion on T2-weighted images (Fig. 1). In cases of marked spinal cord compression, such a lesion is compatible with myelomalacia, but in the patients in the present study we found no local compression.

The prevalence and imaging features of this CHII lesion in a series of patients with achondroplasia were evaluated, and the literature on this topic was reviewed.
Cervical high-intensity lesion in achondroplasia

A literature search was conducted using Internet databases PubMed, Embase, Web of Science, Scopus, and Cochrane. We searched for the following key words: achondroplasia, myelopathy, myelomalacia, high-intensity signal, and MR imaging.

Clinical Material and Methods

Patient Population

Since 1980, 77 consecutive patients with achondroplasia have been assessed for a symptomatic lumbar spinal stenosis at the Department of Neurosurgery at Leiden University Medical Center. All patients were referred after clinically significant neurogenic claudication was diagnosed. The clinical charts were reviewed for signs and symptoms of cervical myelopathy attributable to the lesion.

A retrospective chart review of all 77 patients with achondroplasia revealed a subgroup of 25 patients in whom the diagnostic workup included additional MR imaging studies of the cervical spinal cord.

Magnetic Resonance Imaging

The MR imaging studies were performed in the period between 1990 and 2006. We used a T2-weighted turbospin echo 1.5-tesla system (Philips Gyroscan S15, Philips Gyroscan ACS-NT, or Philips Gyroscan NT Intera; Philips Medical Systems) at 3-mm intervals (TR ≥ 3300 msec, TE 150 msec). One study was obtained with 5-mm intervals, a TR of 2000 msec, and a TE of 100 msec. The available T2-weighted images were independently evaluated for the presence of a CHII lesion in the spinal cord by both an experienced neuroradiologist and a senior neurosurgeon.

The following characteristics of the lesion were recorded: location, length, shape, flow voids, mass effect, and multiplicity. To exclude known causes of a high-intensity lesion on T2-weighted MR imaging, signs of local spinal cord compression were assessed.

Results

Literature Findings

We found no reports in the literature in which the authors explicitly described a T2-weighted high signal intensity in the spinal cord in cases of adult achondroplasia in the absence of focal medullary compression. In two papers, one by Boor et al. and the other by Bruhl et al., the writers mentioned some cases of cervical myelomalacia without spinal cord compression in pediatric patients with achondroplasia, but the authors did not go into detail.

Magnetic Resonance Imaging Findings

The CHII lesion was observed in 16 (64%) of 25 patients without cervical cord compression (Table 1). In 13 cases we observed a focal CHII lesion and in three a more elongated lesion. The studies obtained in Case 5 are a good example of marked focal cord thinning resulting in an hourglass-shaped spinal cord at C-2 (Fig. 2). This thinning was seen more often in patients harboring the lesion.

Without exception the CHII lesion was observed at or centered around the upper C-2 level. In none of the 16 cases was spinal cord compression seen at this level. The CHII lesion varied in length (range 4–12 mm). No flow voids were seen in or around the lesion. One patient harbored two adjacent lesions at the C-2 level. The thinning of the spinal cord at the level of the lesion resulting in the medulla’s hourglass shape was documented in 10 patients, nine of whom harbored a CHII lesion. Axial MR images suggested that the CHII lesion was confined to the gray matter (Fig. 3).

Clinical Myelopathy

Some of the patients with achondroplasia who were assessed at the neurosurgical clinic for clinically significant neurogenic claudication were found to have additional signs and symptoms consistent with cervical myelopathy. In two patients (Cases 9 and 16) the initial neurological examination yielded insufficient findings. The Babinski sign, a common indicator of myelopathy, was documented in 10 patients, nine of whom harbored a CHII lesion. Consequently, the Babinski sign was absent in seven patients with the CHII lesion. Central hand-related deficits were found in seven patients, in five of whom the CHII lesion was also present. In 11 patients in whom the CHII lesion was identified, however, sensory and motor upper-extremity function disability was absent. The hourglass thinning of the cervical spinal cord was found not to have any significant relation to the Babinski sign or motor skills.

Discussion

Summary of the Literature

In this retrospective study, we documented a CHII lesion in 16 (64%) of 25 adult patients with achondroplasia in whom local spinal cord compression was absent, although it has to be emphasized that this prevalence was represented in a population of patients with a symptomatic neurogenic claudication. To date, this imaging phenomenon has not been described in adults with achondroplasia, although

Fig. 1. Sagittal T2-weighted MR image revealing a typical CHII lesion in a patient with achondroplasia.
Boor et al.\textsuperscript{1} and Bruhl et al.\textsuperscript{2} may have noticed the same phenomenon in a pediatric achondroplastic population. Boor et al.\textsuperscript{1} studied the correlation between SSEPs, MR imaging changes, and clinical status in 30 children with achondroplasia who were treated in their hospital. Magnetic resonance imaging changes included upper cervical cord compression and myelomalacia. In only one case (3\%) did the authors mention myelomalacia in the absence of local spinal cord compression. The exact location of this myelomalacia was not revealed. Notably, the patient in this case had normal SSEPs in contrast to the abnormal SSEPs detected in 12 other patients who had myelomalacia and spinal cord compression.

Bruhl et al.\textsuperscript{2} studied the correlation between MR imaging features and clinical findings in 25 children with achondroplasia who were referred because of neurological deficits. In five children (20\%) the authors documented a syrinx or myelomalacia in the upper spinal cord but no local spinal cord compression. Interestingly, in two patients with myelomalacia in the absence of spinal cord compression, they also observed the thinning of the cervical spinal cord.

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It has to be noted that both of the aforementioned articles lack any description of cervical medullary abnormalities in the absence of spinal cord compression. On the one hand, it is not certain that Bruhl et al.\textsuperscript{2} and Boor et al.\textsuperscript{1} have described the same lesion as we have detailed. On the other hand, even if they describe the same phenomenon, the prevalence in the present series is much higher, at 64\%. This huge difference may be explained by the selection of patients: the patients with achondroplasia in the Bruhl et al.\textsuperscript{2} and Boor et al.\textsuperscript{1} studies were all children (mean ages 6 and 5.5 years, respectively), whereas the mean age in the present series was 52 years. This could imply that the cervical lesion tends to appear during development.

In the present series of 77 patients with achondroplasia, assessed at the Neurosurgical Clinic for signs and symptoms indicating neurogenic claudication, MR imaging revealed a CHII lesion in 16 (64\%) of 25 patients with no cord compression. Without exception, the CHII lesion included the C-2 level in the absence of spinal cord compression. Some patients had a history of spinal cord compression at other levels, but these compression sites were too distant to explain the presence of the CHII lesion. Although achondroplasia causes primary stenosis of the entire spine including the foramen magnum, the described CHII lesions were only encountered at or around the C-2 level. None of the 25 patients had a history of trauma of the head or neck, which excluded this as a cause.

The CHII lesion exhibited several general characteristics. It was either oval shaped or elongated, and axial MR imaging showed that it was confined to the gray matter. In more than half of the patients with a CHII lesion (nine of 16) we observed an hourglass-shaped spinal cord at the level of the lesion, probably representing local atrophy. Because the origin is not clear, the possibility that all findings are within the same spectrum cannot be ruled out.\textsuperscript{4}

### Hypotheses of CHII

In the absence of an autopsy study or other histological

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<th>Case No.</th>
<th>Sex</th>
<th>Location of CHII Lesion</th>
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<th>Babinski Sign</th>
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* – = absent; + = present; ? = unknown.
† Compression present at the level of the CHII lesion.
proof providing more information about the CHII lesion and its possible causes, several theories can be posited. The first hypothesis involves the distorted morphometrics of the achondroplastic cranium and cervical spinal canal: normal movements of the head and neck could exacerbate the preexisting cervical canal narrowing, causing a transient but repetitive compression of the upper spinal cord. According to this line of thought, an abnormal craniovertebral angle during movement of the head might explain the documented CHII lesion, especially in the presence of the spinal cord or cauda equina tethering due to the well-known primary stenosis of the spinal canal in achondroplasia. The cause of the CHII lesion would then, be a (repetitive) stretch injury rather than a compression-related injury.

A second hypothesis focuses on atlantoaxial instability, a condition that is often seen in cases involving rheumatoid arthritis but is not particularly related to achondroplasia. Because we only had standard diagnostic MR images, taken in a resting position, for our patients, the aforementioned hypothesis on repetitive spinal cord trauma, either compressive or stretch related, could not be tested. Flexion and extension lateral cervical radiographs or, even better, flexion and extension MR images would definitely provide more information. If this hypothesis is correct, patients might benefit from undergoing upper cervical fusion surgery, depending on the clinical relevance and further development of the CHII lesion.

A third hypothesis emphasizes the impaired fetal development of the spine and spinal cord in achondroplasia with possible transitory impingement of the cervical spinal cord during its maturity.

Clinical Myelopathy

It is interesting that the CHII lesion can be or become clinically symptomatic. Based on findings in the present series, however, this issue cannot be resolved. All our patients with achondroplasia were evaluated at the neurosurgical clinic when neurogenic claudication was detected and not because they exhibited signs and symptoms compatible with cervical myelopathy. As such, a full neurological examination was performed solely at the initial clinical assessment. This aspect should be the subject of further prospective research.

Finally, it has to be emphasized once more that the present series consisted of patients with achondroplasia known at the neurosurgical clinic because of signs and symptoms indicating neurogenic claudication. The MR imaging studies were performed during a diagnostic workup; therefore, our series of patients represents a preselected group. As a consequence, it is not likely that the prevalence of the CHII lesion is representative of the general achondroplastic population. Further research on this subject is warranted to determine the true incidence of this particular phenomenon.

Conclusions

The CHII lesion was a common but still unexplored imaging phenomenon in this large series of adults with achondroplasia and symptomatic neurogenic claudication. Its origin and clinical relevance need to be investigated, as does the occurrence in the general achondroplastic population.

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References


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