Cervical spine in patients with juvenile chronic arthritis and amyloidosis

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ABSTRACT

Objective
To describe cervical spine abnormalities in a group of adult patients with refractory juvenile chronic arthritis (JCA) complicated by secondary amyloidosis (SA).

Methods
The series consists of 49 patients who fulfilled the diagnostic criteria of the European League Against Rheumatism for JCA, here complicated by secondary amyloidosis (SA). We evaluated their clinical records and most recent cervical spine radiographs taken in adult age (>18 years) at or after the diagnosis of SA.

Results
Forty-two (86%) patients evinced inflammatory changes in the cervical spine. Apophyseal joint ankylosis was seen in 31 (63%) and atlantoaxial impaction (AAI) in 28 (57%) patients; anterior atlantoaxial subluxation (aAAS) was noted in 17 (35%) patients, and 19 (39%) had the combination of AAI and apophyseal joint ankylosis. The size of the 4th vertebral body was small or narrow in 14 (29%) patients with JCA onset at a median of 3 years of age (range 1-12).

Conclusion
Inflammatory cervical spine disorders are common and may be detected along the entire length of the cervical spine in patients with severe refractory JCA. The disorders tend to ankylose the apophyseal joints and destroy the atlantoaxial joints, resulting in aAAS or impaction. These changes will restrict rotatory and bending movements in the cervical spine. A peculiarly small or narrow cervical vertebral body was seen mainly in patients with early onset disease. The present findings shed light on the characteristics and course of the inflammatory changes in the cervical spine in patients with refractory JCA.

Introduction
Juvenile chronic arthritis (JCA) often involves the cervical spine. This has been reported as occurring clinically in 49%, 52% and 66% of patients with JCA (1-3). Radiologic abnormalities in the cervical spine have been reported in 21%, 27% and 55% of patients in different series (2, 4, 5). Despite this common involvement, only a few detailed descriptions of cervical spine abnormalities in JCA are available (4, 6, 7).

Patients with JCA complicated by secondary amyloidosis (SA) have usually had continuously active and severe joint inflammation, possibly manifested in advanced cervical spine abnormalities. When the cervical spine in JCA patients is studied in the adult age a clearer conception of the cervical manifestations of the disease can obviously be formed than when studied in childhood. The aim of this study was to examine the radiographic features showing the outcome of cervical spine involvement in patients severely affected with JCA, who were adults at the time of the radiographs. SA was taken as a marker of severe disease.

Patients and methods
The patient records (from 1981 to May 2000) of the Rheumatism Foundation Hospital, Heinola, Finland were studied to identify patients with JCA (fulfilling the European League Against Rheumatism [EULAR] criteria for JCA) (8) complicated by SA. Seventy-one patients were found, 49 of whom (37 women, 12 men) had cervical spine radiographs available, taken at or after the diagnosis of SA in adult age (>18 years); these formed the study group. The median age at onset of JCA was 11 (range 1-16) years. As the onset diagnosis, 34 (69%) patients had polyarticular disease, 6 (12%) had pauciarticular disease, 7 (14%) had systemic disease, and 2 (4%) were affected by juvenile ankylosing spondylitis (AS). During the follow-up 3 patients developed psoriasis; their onset types were seronegative polyarthritis, pauciarticular disease, and AS, respectively. In all the patients the disease ran a polyarticular course. Fifteen (31%) patients were rheumatoid factor (RF)-positive. The median duration of JCA at the time of the latest radiographs was 23 years (range 11-64). Forty-eight (98%) patients showed erosions in hand radiographs. Thirty-eight patients had undergone major joint replacement [the
The diagnosis of SA was based on a subcutaneous fatty tissue aspirate or on a biopsy from the gum, kidney, stomach or rectum. The median age at diagnosis of SA was 26 years (range 11-64). The most recent cervical spine radiographs were used in the study. The median age of the patients at the time of radiography was 32 years (range 18-68), and the median period of time between the diagnosis of SA and the radiograph was 6 years (range 0-21). Lateral view cervical spine radiographs (in flexion and extension) and an anteroposterior open-mouth view were taken in every case using a 150 cm tube-to-plane distance.

A diagnosis of anterior atlantoaxial subluxation (aAAS) was made if the distance between the anterior aspect of the dens and the posterior aspect of the anterior arch of the atlas was >3 mm. Posterior atlantoaxial subluxation (pAAS) was diagnosed if the posterior aspect of the anterior atlas arch was situated posteriorly in relation to the anterior aspect of the dens in the lateral view radiographs of cervical spine in extension (9). Atlantoaxial impaction (AAI; i.e., vertical dislocation or vertical subluxation) was diagnosed using the Sakaguchi-Kauppi (S-K) method, which has been developed especially for screening purposes and evaluates the position of the atlas in relation to the axis (10). This method divides the condition into 4 grades (Grade I represents normal and Grades II-IV abnormal). Lateral-view radiographs taken in flexion were used for the evaluation of AAI. Subaxial subluxation (SAS) was diagnosed if a vertebra was displaced by >3 mm in relation to the next one below when measured from the posterior line of the vertebral bodies. The presence of apophyseal joint ankylosis was noted in the radiograph when fusion was seen in the joint and the position of the vertebra was unchanged in both flexion and extension. The size of the 4th vertebral body of the cervical spine and the diameter of the spinal canal of the same vertebra were measured. The 4th vertebral body was considered to be small or narrow when the height of the vertebral body was <11 mm or alternatively when the width of the vertebral body was <15 mm. Two patient groups were formed to study whether the patients with a small or narrow vertebral body were significantly younger than the remaining patients at the onset of JCA. The statistical significance of the difference between the median age of the two patient groups was calculated by the Mann-Whitney U-test.

### Table I. Radiographic features of cervical spine in 49 JCA patients with a polyarticular course and amyloidosis.

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Polyarticular* (seronegative) (n = 34)</th>
<th>Polyarticular (seropositive) (n = 15)</th>
<th>All (n = 49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior atlantoaxial subluxation (aAAS)</td>
<td>9</td>
<td>8</td>
<td>17 (35%)</td>
</tr>
<tr>
<td>Atlantoaxial impaction (AAI)**</td>
<td>19</td>
<td>9</td>
<td>28 (57%)</td>
</tr>
<tr>
<td>Apophyseal joint ankylosis</td>
<td>23</td>
<td>8</td>
<td>31 (63%)</td>
</tr>
<tr>
<td>Subaxial subluxation, &gt; 3 mm (SAS)</td>
<td>3</td>
<td>1</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>aAAS + AAI</td>
<td>6</td>
<td>4</td>
<td>10 (20%)</td>
</tr>
<tr>
<td>aAAS + apophyseal joint ankylosis</td>
<td>7</td>
<td>3</td>
<td>10 (20%)</td>
</tr>
<tr>
<td>AAI + apophyseal joint ankylosis</td>
<td>15</td>
<td>4</td>
<td>19 (39%)</td>
</tr>
<tr>
<td>Juvenile cervical vertebra</td>
<td>12</td>
<td>2</td>
<td>14 (29%)</td>
</tr>
<tr>
<td>Subluxation, impaction or apophyseal joint ankylosis</td>
<td>27</td>
<td>15</td>
<td>42 (86%)</td>
</tr>
</tbody>
</table>

*3 patients with psoriasis and 1 with sacroiliitis are included; **Sakaguchi-Kauppi method, grades II-IV.

### Results

The radiographic features of inflammatory involvement are shown in Table I. Apophyseal joint ankylosis was detected in 31 (63%) patients. Ankylosis solely at the C2-3 level was noted in 7 (14%) patients. In 24 (49%) apophyseal joint ankylosis was seen at C2-3 combined with ankylosis at another level of the cervical spine. A diagnosis of aAAS was made in 17 (35%) patients. Five had aAAS only in flexion, whereas in 12 patients the disorder (4-6 mm) was noted in both flexion and extension. The maximal atlantodental interval was 10 mm but most often aAAS was 4-5 mm (in 11 patients) in flexion. No radiograph revealed pAAS. AAI was diagnosed in 28 (57%) patients. The severity of AAI (S-K Grade II-IV) is shown in Table II and Figure 1. Eight of the 12 patients with aAAS in extension also had AAI. SAS was present in 4 (8%) patients; in 3 of them apophyseal joint ankylosis was seen at the next level immediately above the SAS. The displacement in SAS was 4-6 mm. One of the patients had two SAS displacements located at C3-4 and C4-5 and in two cases SAS was located at the C4-5 level. In 14 (29%) patients the 4th vertebra was small or narrow according to the study definition. In these 14 patients the median width of the 4th cervical body was 13 (range 10-16) mm and the median height of the vertebra was 12 (range 9-15) mm; in the remaining 35 patients these measurements were 17 (range 15-23) mm and 13 (range 11-18) mm, respectively. In the 14 patients the median spinal canal diameter at the level of the 4th vertebra was 17.5 (range 13-21) mm, and in the other 35 patients it was 18 (range 13-22) mm. The median age at onset of JCA of the 14 patients was 3 (range 1-14) years, and that of the 35 patients was 12 (range 1-16) years. Statistically the difference in age at onset of JCA between these two
Cervical spine involvement in adult rheumatoid arthritis (RA) has been described in several studies and constitutes one of the typical expressions of the disease, but in patients with JCA data on inflammatory cervical spine disorders are scarce.

Grokoest and colleagues report that in a hospital-based series of 110 patients with juvenile rheumatoid arthritis (JRA), 27% had radiographic changes in the cervical spine. The changes are not described in detail, but they mention that 18% showed fusions of posterior segments, calcification of ligaments or obliteration of apophyseal joints. Two patients had a subluxation (5). Martel and associates found atlantoaxial subluxation in 9/28 and apophyseal joint ankylosis in 11/28 patients in a hospital-based study of JRA (4). Espada and colleagues in an institution-based study assessed 6 types of disorders of the cervical spine in detail in a series of 120 patients with JRA and found AAS in 20%, zygapophyseal joint fusion in 52% and growth disturbance in the vertebral bodies and decreased height of an adjacent intervertebral disc in 22% of the cohort. Forty patients were over 16 years of age (7). The median or mean age of the patients at the time of radiograph was not mentioned in these papers.

The aim of the present study was to describe the radiological outcome of cervical spine involvement in refractory JCA. Cervical spine involvement appears to be almost inevitable in patients with JCA complicated by SA, since it was evident in 86% (42/49) of our patients. The most frequent abnormality was apophyseal joint ankylosis, seen in 63% (31/49) of the cases, a higher frequency than that reported in previous studies (4,7). Most often apophyseal joint ankylosis was seen at the C2-3 level, which confirms the report by Ansell et al. (12).

AAS was seen in 35% (17/49) of the patients, again a higher value than that reported elsewhere (20%) (7). The finding that AAI was more common than AAS may be explained by the disease course of the cervical involvement described in adult RA. In chronic active inflammation the prevalence of AAS may be diminished, when the atlantoaxial facets are destroyed and AAI develops (11,13).

This is the first report of the existence of AAI in a series of JCA patients. AAI was detected in half of the patients, indicating that atlantoaxial facet joint involvement is typical, and their cartilage and bone surfaces are eroded in severe long-lasting JCA. The S-K method for diagnosis of AAI is based on the relationship between the atlas to the axis and is not disturbed even when the structures are small. Thus it is probably the most suitable method to be used in patients with JCA (11).

Another typical juvenile abnormality is the peculiar form of the vertebral bodies in the cervical spine. They are either small in size or narrow, but have a spinal canal of the same size as in other patients with JCA, i.e., “juvenile cervical vertebrae” (Fig. 1). Juvenile cervical vertebra is frequently combined with apophyseal joint ankylosis at the same level. The incidence of the juvenile cervical vertebra (29%) was based on measurements of the 4th cervical vertebra in this study, and might have been greater if the size of other vertebrae had been taken into account, or if the criteria had been less rigid. The patients with juvenile cervical vertebrae experienced the onset of their rheumatic disease at a younger age than the remaining patients. These findings are in accord with those reported by Espada and colleagues (7). If the
inflammation in the area begins early enough to disturb the growth of the vertebral arches, the apophyseal joints are also often affected. The juvenile cervical vertebral arches are not prone to complications since the spinal canal is normal, but narrow ankylosed vertebral bodies may be more dangerous in injuries and exert abnormal forces on adjacent mobile levels in the spine.

The prevalence of SAS was low, being detected only in 4 (8%) patients and almost always in association with apophyseal joint ankylosis. A similar result was also obtained by Espada et al. (7). The low prevalence of SAS was unexpected in the present study because the patients were affected with refractory disease; the explanation may be that the cervical spine in JCA is prone to joint ankylosis.

Several types of disorders were so frequent in the present study that their combinations were also typical for JCA. aAAS was combined with vertebral apophyseal joint ankylosis in 20% of the cases. This is in accordance with the conception of Ansell and Bywaters that a combination of AAS and joint ankylosis is not uncommon (3). RF-positivity was more frequently noted than in a population-based report of JCA (31% vs. 6%) (14). This again is in accord with the report by Walker and associates, who showed that RF may be considered to offer an important insight into the nature of inflammatory changes and the disease course in the cervical spine of JCA. The high prevalence of rheumatoid cervical spine changes in adult patients with long-lasting refractory JCA should be borne in mind when treating patients.

References