ORIGINAL ARTICLE: CASE SERIES

Atlo-epistropheal involvement in oligoarthritis subset of Juvenile Idiopathic Arthritis (JIA): observation of five cases.

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Abstract

Cervical spine involvement is not unusual in rheumatoid arthritis in adults and in polyarticular and systemic juvenile idiopathic arthritis (JIA). Cervical spine involvement, particularly atlo-epistropheal (also known as atlo-oxoid or atlanto-axial) involvement, has not been reported commonly in either the persistent or extended form of oligoarticular JIA. We report five cases of children with oligoarticular JIA who developed atlo-epistropheal involvement and discuss the anatomy, clinical characteristics, and imaging findings in this syndrome. Though this problem is uncommon, clinicians should be aware of the possibility of atlo-epistropheal disease in oligoarticular JIA subtypes.

Introduction

Cervical spine disease is relatively common in rheumatoid arthritis in adults and systemic onset and polyarticular JIA. [1-2] It usually is a sign of significant polyarthritis. It can be quite painful and lead to cervical spine fusion with loss of range of motion of the neck and even cervical spine instability with neurologic compromise. [3-7] Oligoarticular JIA children have been thought to have little risk of this involvement, particularly atlo-epistropheal disease. *(Editor's note: atlo-epistropheal is identical to atlo-oxoid or atlanto-axial, i.e., denoting the joint between the atlas and axis vertebrae, C1-C2.)* We present 5 cases of children with oligoarticular disease who developed very severe atlo-epistropheal disease, one with neurological sequelae.

Patients and methods

We enrolled patients affected by oligoarticular JIA, either persistent or extended, that are or have been followed at our center (47.8% and 8.6% respectively, of 683 patients affected by JIA). A total of 60 patients affected by JIA extended oligoarthritis and 327 affected by JIA persistent oligoarthritis were evaluated with a standard X-ray of the cervical spine during full flexion and extension of the neck. The mean age at onset of JIA was 5 years (range 2 to 14 years). Lateral view cervical spine radiographs (in flexion and extension) were taken using a tube-to-plane distance of 150 cm.

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 greater than 3 mm. We used the 3 mm distance of Sharp and Pursner [3] rather than the 4 mm distance suggested by Locke [15] due to the older age of our patients at the time of our study. A CT or MRI confirmation scan was performed in patients whose standard X-ray suggested AAS. A rheumatoid factor, an anti-cyclic citullinate peptide antibodies titer, and an antinuclear antibody titer were assessed in each patient.

Results

We report 5 patients with the oligoarthritis form of JIA (2 extended oligoarthritis; 3 persistent oligoarthritis) who have atlo-epistropheal involvement. All patients were rheumatoid factor and anti-cyclic citullinate peptide antibodies negative; 3/5 patients were antinuclear antibody positive. One patient developed anterior chronic uveitis. No other causes were found for these neck problems other than JIA. Table 1 describes the 5 cases below.

Table I. 5 Oligoarticular JIA patients with atlo-epistropheal involvement

Patients # 1-5 in this case series	Subtype JIA	Age onset JIA	Age at time of study	Sex	Clinical symptoms and signs of arthritis	Radiographic changes	Narrowing spinal canal with or without neurological changes
1	OE	2 yrs	11 yrs	F	P and LOF	ST and anterior subluxation	NO
2	OE	8 yrs	11 yrs	F	P LOF	ST	YES papilledema spinal cord compression
3	OP	8 yrs	11 yrs	F	LOF only	erosions and dens dislocation	NO
4	OP	2 yrs	24 yrs	F	P LOF	erosions and dens	NO

						dislocation	
5	**OP**	**3 yrs**	**34 years**	**M**	**none**	**erosions and ST**	**NO**

OE = oligo extended
OP = oligo persistent
P = pain
LOF = loss of function
ST = synovial thickening

Patient 1 is a 11 year old girl (onset age: 2 years) with radiological evidence of anterior atlo-epistropheal subluxation caused by the presence of synovial thickening, leading to pain and loss of function (LOF) of cervical spine. The spinal canal diameter had no signs of narrowing. Patient 2 is a 11 year old girl (onset age: 8 years) with radiological evidence of synovial thickening between the dens and the atlas anterior arch. There was pain and limitation of motion (LOM) of the cervical spine. Spinal cord compression was present with concomitant bilateral papilledema. There was no other sign of increased intracranial pressure.

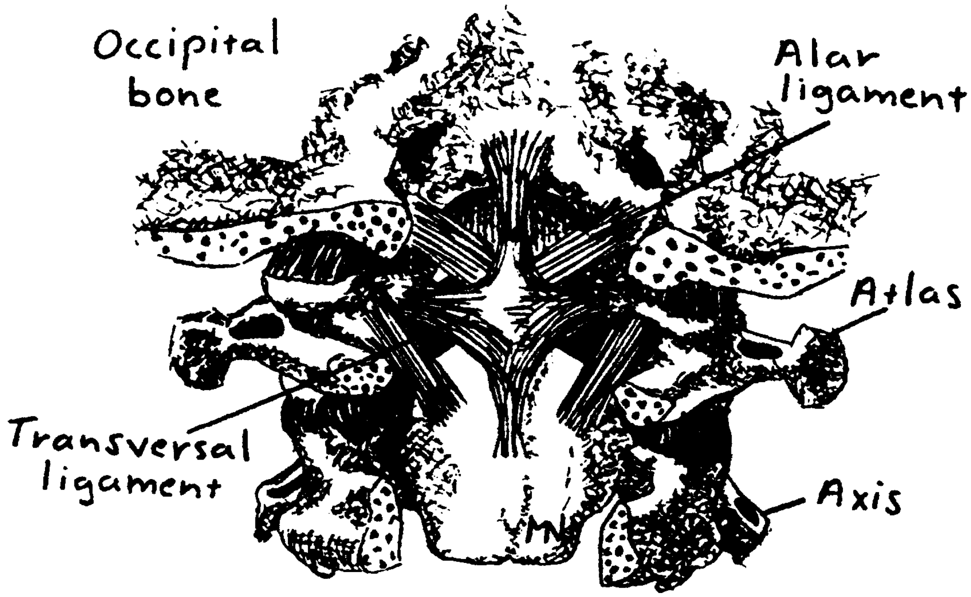
Patient 3 is a 11 year old girl (onset age: 8 years) with radiological evidence of erosions and vertical dislocation of the dens. Only loss of function of the cervical spine was present and there was no pain. No neurologic involvement was detected. Patient 4 is a 24 year old girl (onset age: 2 years) with radiological evidence of erosions and vertical dislocation of the dens. She also had neck pain and LOM of the cervical spine. No sign of neurological involvement was found. Patient 5 is a 34 year old man (onset age of JIA: 3 years) with radiological evidence of erosions of the dens and the presence of synovial thickening in the atlo-epistropheal junction. He had no neck pain or LOF. His spinal canal was without signs of compression.

Discussion

Anatomy

Human cervical spine consists of seven vertebrae C1 - C7. The two most cranial vertebrae have special architectural design and the other five share a similar structure. In this small area between the skull and first thoracic vertebra, there are 16 serially arranged apophyseal synovial joints, 12 uncovertebral joints and six intervertebral discs (Figure 1).

Figure 1 Atlo-epistropheal (atlanto-axial) anatomy by a anterior-posterior view

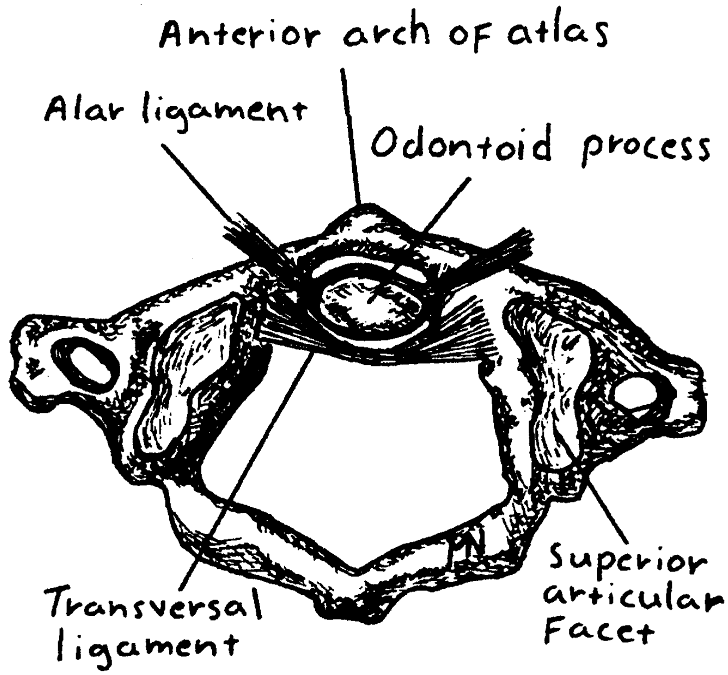


The most cranial vertebrae “atlas” is a solid bone ring with two lateral pillars for the apophyseal joints. It carries the skull by two ellipsoid shaped joints, which allows only flexion and extension movement. The second vertebrae “axis” has a special structure called “odontoid process” (or dens), which rises perpendicularly from midbody, acting as an eccentric pivot around which the atlas rotates. The odontoid process has articulation in the anterior surface with the anterior arch of atlas and in the posterior surface with the transversal ligament. In addition, the axis comprises two apophyseal joints with atlas and two with the third vertebra. Approximately 50% of head rotation occurs in the atlantoaxial joints and 85% of the whole head and neck movement in the skull-atlas-axis complex.

The odontoid process is fixed to the anterior arch of atlas by a strong transverse ligament. It allows rotational movement but prevents the atlas from slipping forward when the head is in flexion. In addition, the odontoid process is attached to the occipital bone by an apical and two alar ligaments, which increases the stability of both atlanto-occipital and atlantoaxial joints.. The junction of medulla oblongata and spinal cord is at the level of the odontoid process.

The third to the seventh cervical vvertebrae all consist of body, pedicles, laminae, vertebral arches, and spinous process. The most important ligaments connecting vertebral bodies together are the anterior and posterior longitudinal ligaments, which continue as membrane-like structures to the occipital bone [Figure 2]. The laminae of vertebrae are connected together by ligamenta flava.

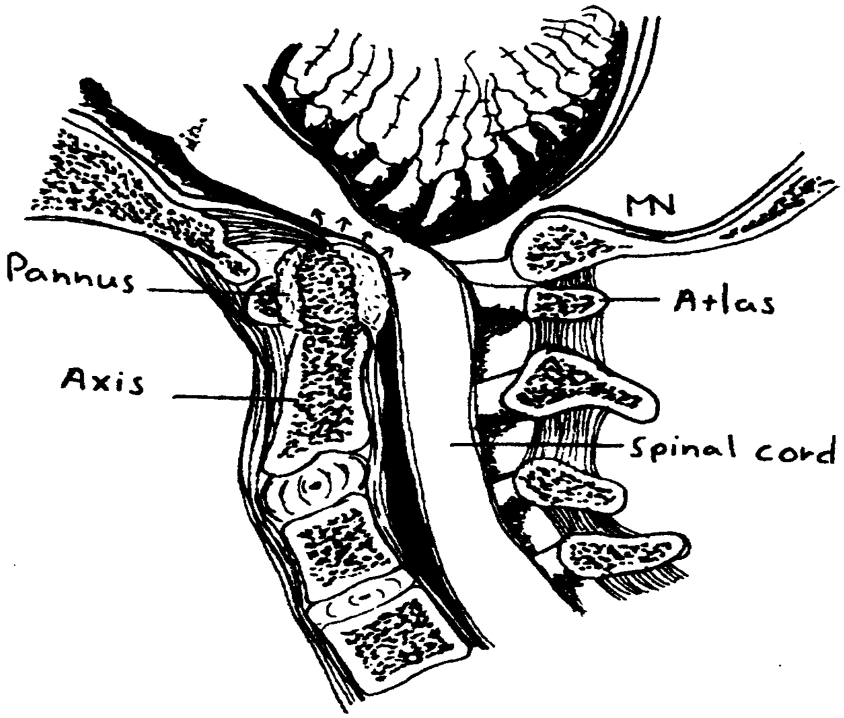
Figure 2. atlo-epistropheal anatomy in cross-section



Symptoms and signs

Neck pain is a common symptom in atlo-epistropheal arthritis in rheumatoid arthritis (RA) in adults, regardless of the findings in cervical spine radiographs (Figure 3). [1] However, neck pain is non-specific. It is also the most common and earliest manifestation of other cervical spine disorders involving any cervical vertebrae including chronic arthritis. [1-2] In addition to neck region, pain caused by cervical spine destruction may be experienced in occipital, retroorbital or temporal areas. [3] It is also important to bear in mind that subluxations of the cervical spine do not necessary cause pain or other symptoms. In a study by Mathews, two-thirds of patients with anterior atlantoaxial subluxation (aAAS) (atlanto-axial or atlo-epistropheal subluxation) did not have neck pain. [4] Moreover, Collins et al. reported that 50% of the patients with cervical spine instability were asymptomatic. [5]

Figure 3. An lateral view showing an atlantoepistropheal pannus due to chronic arthritis



Complications

Patients with severe cervical spine disorders may present symptoms and signs caused by compression of the spinal cord, cervical nerve roots or cranial nerves. [6] In addition, penetration of the odontoid process through the foramen magnum may cause the compression of brain stem and even sudden death. [7] Neurological symptoms and signs have been reported to correlate poorly with the degree of atlantoaxial instability. [8, 4, 9-10] An MRI in Figure 4 demonstrates the cord compression.

Figure 4: An MRI of a cord compression (upper panels) due to JIA alto-epistropheal involvement.

The primary radiological examinations of the cervical spine in patients with RA are plain radiographs. The standard cervical spine radiographs include anteroposterior, odontoid, lateral and oblique projections. In the majority of rheumatological units, lateral view radiographs are taken during full flexion and extension of the neck.

Sharp and Purser [3] measured the distance between the anterior arch of atlas and the anterior surface of the odontoid process in two lateral view cervical spine radiographs (flexion and extension views) taken from a general population and from patients with RA. They demonstrated that in an adult population more than 3 mm separation is abnormal and in RA patients a greater than 3 mm finding is likely due to the arthritis. Hereafter, more than 3 mm anterior atlantoaxial distances have been considered to indicate aAAS in RA by the majority of the investigators. [11-14] Locke and colleagues found this distance to be more than 4 mm in normal children. [15]

Boden et al. [16] defined a new radiographic parameter, i.e., the posterior atlanto-odontoid interval (PADI), which is the distance between the posterior aspect of the odontoid process and the anterior edge of the posterior arch of atlas in lateral view cervical spine radiographs. In their study, the sagittal diameter of the bony spinal canal was the most important predictor of paralysis and postoperative neurological recovery in patients with aAAS. [16] Values of 14 mm or less were determined to be critical for the development of irreversible myelopathic changes.

CT scan has been particularly valuable in the evaluation of the severity of aAAS. However, after the development and increase in availability of MRI, the need for these examinations in clinical work has decreased. MRI provides detailed information on soft tissue lesions, pannus formation, vertebral subluxations and compression of the spinal cord, and is therefore the most important imaging method in patients with suspected spinal cord compression. [17-18]

Cervical spine disease in JIA

Cervical spine involvement in adult rheumatoid arthritis has been described in several studies [7-10] and constitutes one of the typical expressions of the disease. Juvenile idiopathic arthritis (JIA) is a systemic disease of childhood affecting primarily the joints (Durban’s 1997 Criteria). [19] Detailed information on cervical spine changes in patients with JIA is available in only a few studies. In patients with JIA, the cervical spine is often affected usually at level of the interapophyseal joints (often+ starting at C2-C3), leading to pain and functional limitations (Figure 5).

Figure 5. A lateral radiograph of the cervical spine demonstrating C2-C3 interapophyseal disease in a child with JIA.

Other typical changes in the cervical spine of systemic and polyarticular JIA children include fusion of adjacent spinous processes, narrowing of the intervertebral disk, and atlantoaxial subluxation. [20]

The atlantoaxial involvement has been considered uncommon in JIA, with the exception of the RF+ forms (analogue to adult RA). [20-24] It is important to note that in adult RA and in JIA, sustained rheumatoid inflammation of the atlantoaxial apophyseal joints causes cartilage destructions and finally bone erosions leading to atlantoaxial impaction, which has also been referred to as vertical atlantoaxial subluxation, basilar invagination, or cranial settling. [6]

In the oligoarthritis JIA, common findings include large joint arthritis of 4 joints or less in the first six months (e.g., knee, ankle, wrist, hip) and anterior chronic uveitis that is associated with a positive antinuclear antibody titer. Only rare cases have been reported previously of atlantoepistropheal involvement in JIA oligoarticular children. [20-24] For example, Hensinger et al. reviewed 121 JRA patients in 1986, among whom were 57 children with pauciarticular subtype. None had signs or symptoms of cervical spine disease including neck pain or neurological changes and only one child had roentgenographic involvement. [22] Our experience suggests that atlo-epistropheal disease including neurological compromise due to subluxation may occur in children with oligoarticular disease and though unusual in our population (5/387 or 1.3%), does not appear to be rare and should be watched for. It suggests that oligoarticular JIA is not always a benign disease.

Conclusions

Atlo-epistropheal arthritis with possibe subluxation has previously been described in the rheumatoid factor positive JIA group. [19-23] This report emphasizes that atlo-epistropheal involvement may occur in oligoarthritis JIA, including in both the extended and the persistent oligoarticular forms. More studies are necessary to assess the true prevalence of atlo-epistropheal involvement in different populations of children affected by JIA. In the meantime, it is important to be vigilant for cervical spine disease in children with oligoarticular JIA, including regular range of motion exams of the neck, particularly as the children may not complain of neck pain.

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