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Original article

Radiological cervical spine involvement in young adults with polyarticular juvenile idiopathic arthritis

Muriel Elhai[1,*], Julien Wipff[1,*], Ramin Bazeli[2], Véronique Freire[2], Antoine Feydy[2], Jean-luc Drapé[2], Pierre Quartier[3], André Kahan[1] and Chantal Job-Deslandre[1]

Abstract

Objectives. Radiological cervical spine involvement in JIA has already been assessed with a large range of prevalence (5–80%), but most studies were performed a long time ago, in symptomatic JIA and without differentiating subsets of JIA. We set out to describe structural cervical spine involvement in young adults with polyarticular JIA (pJIA) regardless of the cervical symptoms and to compare lesions with those observed in adult RA.

Methods. All consecutive pJIAs followed in a transition programme were included. Standard radiographs of the cervical spine, hands, feet and hip were analysed by two independent radiologists blinded to the diagnosis. An RA control group (<55 years), matched for sex and disease duration, was recruited.

Results. Fifty-seven pJIA and 58 RA patients were included. Radiographs showed cervical lesions in 65% of pJIA and 67% of RA patients. In total, 51% of pJIA with radiographic abnormalities had no clinical symptoms. In pJIA, the most frequent structural lesions were anterior atlantoaxial subluxation (33%), erosion of the odontoid process (19%), C1–C2 arthritis (17%) and apophyseal joint arthritis (16%). Cervical lesions in pJIA were similar to those in RA except for ankylosis and hypotrophia ($P < 0.05$). The presence of cervical lesions correlated with a more severe disease.

Conclusion. Structural cervical spine involvement is common in pJIA persisting into adulthood, frequently asymptomatic and associated with a more severe disease. We suggest that radiographic assessment of the cervical spine should be done systematically at onset of the disease and regularly during its course regardless of clinical symptoms.

Key words: polyarticular juvenile idiopathic arthritis, radiograph, cervical spine, rheumatoid arthritis.

Introduction

JIA includes a heterogeneous group of diseases classified by the ILAR [1]. Among them, two subsets of polyarticular JIA (pJIA) were identified: RF positive and negative [1]. RF-positive polyarthritis is often considered as an early-onset form of adult RA, whereas RF-negative polyarthritis seems to represent a heterogeneous group of patients with a milder outcome [2, 3]. JIA persists into adulthood in ~60% of cases [4] and is often associated with significant functional impairment [3].

Cervical spine involvement was recently considered to be a feature of poor prognosis in cases of pJIA by the ACR [5]. Radiological involvement of the cervical spine in JIA has been assessed by several studies with a large range of prevalence (5–80%), but most of them were performed a long time ago and did not differentiate pJIA from the other subtypes of JIA [6–16]. Furthermore, little is known about cervical involvement in pJIA persisting into adulthood. Two studies assessed radiological cervical involvement in this particular subgroup of patients with a prevalence estimated at 79 and 62%, respectively [10, 16]. These studies had a trend in evaluating the most severe patients (symptomatic and pre-operative), with a possibility of misdiagnoses and were performed

[1]Department of Rheumatology A, [2]Department of Radiology B, Paris Descartes University, Sorbonne Paris cite, Cochin Hospital and [3]Department of Pediatric Immunohematology and Rheumatology, Paris Descartes University, Sorbonne Paris cite, Necker-Enfants Malades Hospital, APHP, Paris, France.

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Correspondence to: Julien Wipff, Service de Rhumatologie A, Hôpital Cochin 27 rue du Faubourg Saint-Jacques, 75014 Paris, France.
E-mail: julien.wipff@cch.aphp.fr

*Muriel Elhai and Julien Wipff contributed equally to this study.

40 and 10 years ago, respectively [10, 16]. It is noteworthy, however, that most advances in the treatment of JIA were performed during the past decade with the advent of biotherapies [4]. Consequently, the prevalence and characteristics of radiological cervical involvement in pJIA persisting into adulthood in the current era remain unknown.

In RA, structural cervical spine involvement occurs in more than half of patients and is usually asymptomatic. Several studies demonstrated that it is associated with a more severe disease [17–22]. It may lead to myelopathy, quadriplegia and even sudden death [23–25]. The most common abnormalities are anterior atlantoaxial subluxation (aAAS), erosion of the odontoid process and subaxial subluxation (SAS) [17, 18].

The aim of our study was 3-fold: (i) to assess the characteristics of structural inflammatory cervical spine involvement in pJIA persisting into adulthood regardless of the cervical symptoms; (ii) to compare cervical lesions in pJIA to those seen in the RA control group; and (iii) to detect an association between structural cervical involvement in pJIA and characteristics of the disease.

Materials and methods

All unselected consecutive pJIA followed in a transition programme in a single tertiary referral centre were included in this study. As these patients constituted a group of severe disease, it was necessary to have an ultrastructural evaluation at the beginning of this programme. All patients had already been registered in the CEMARA database, which was validated by the Commission nationale de l'informatique et des libertés. This cross-sectional observational study was performed from June 2009 to December 2010. All patients fulfilled the ILAR classification for pJIA [1]. Exclusion criteria consisted of a diagnosis of another subtype of JIA and a history of cervical surgery. An RA control group fulfilling the ACR criteria for RA [26] and matched for sex and disease duration was recruited. All RA control patients were $<$55 years old in order to avoid radiographic confounding lesions of cervical OA.

Clinical study

The clinical data collected, using medical records, were as follows: age, sex, disease duration, history of cervical symptoms (pain and/or limitation), and swollen and tender joints counts at the X-ray evaluation visit. Medical treatments (CSs, DMARDs and/or biological agents) were reported as well as surgeries. Neurological examination was performed on all patients.

Biological tests

ESR and CRP levels were recorded at the time of the radiography. ELISA methods were performed for RF (cut-off level 1 : 10) and anti-CCP (cut-off value 1 : 25) and immunofluorescence on Hep2 cells for ANAs (a titre of $\geqslant$1 : 160 was taken to be positive).

Radiological study

Standard radiographs of the cervical spine, hands, feet and hip are performed regularly for the usual follow-up of both pJIA and RA in our centre. For this study, the prescription of radiographs was standardized but was done as part of routine monitoring. Radiographs were analysed by two independent radiologists (R.B. and V.F.) blinded to the diagnosis. A third reader (A.F.) established a consensus when required. Cervical spine radiographs included antero-posterior, lateral with flexion and extension and open-mouth views. The following features were searched for: loss of cervical lordosis, erosions of the odontoid process, vertebral fracture (defined by a decrease in the vertebral body height), aAAS, C1–C2 arthritis, atlantoaxial impaction (AAI), inflammatory discitis, uncovertebral joint arthritis, apophyseal joint arthritis, anterior ankylosis, apophyseal joint ankylosis (AJA), anterior and posterior SAS and growth disturbances. Loss of cervical lordosis was considered in cases of rectitude of the cervical spine or cervical kyphosis on lateral view. Erosion of the odontoid process was defined by changes in the normal contour of the anterior, superior or posterior aspect of the odontoid process and was assessed on lateral- and open-mouth view. aAAS was considered to be present when the anterior atlantodental interval, measured from the posterior aspect of the anterior arch of atlas to the anterior aspect of the dens was $>$3 mm in neutral position or appearing during flexion or extension [18, 27]. C1–C2 arthritis was defined as lateral joint space narrowing between the lateral masses of C1 and C2 without osteophyte on open-mouth view. AAI was defined as migration of the odontoid tip by $>$4.5 mm above McGregor's line on lateral view [18]. Inflammatory discitis was diagnosed if there was disc space narrowing and endplate erosions without osteophytes. Anterior ankylosis and AJA were recorded when fusion was seen in the vertebral bodies or in the apophyseal joints, respectively, and the position of the vertebra was unchanged during both flexion and extension. SAS was diagnosed if a vertebra was displaced $>$1 mm in relation to the next lower vertebra when measured from the posterior line of the vertebral bodies. Growth disturbances included changes in vertebral size (i.e. hypotrophia or hypertrophia) as compared with adjacent vertebrae.

Structural lesions on the hands and feet were assessed by the modified version of Larsen's scoring method in posterior–anterior projection [28]. The hands and feet scores range from 0 to 110 and from 0 to 50, respectively. Hips were assessed for the presence of coxitis.

Statistical analysis

All data analyses were performed using MedCalc® version 9.2.1.0. Data were presented as mean (S.D.) for continuous variables and numbers (percentages) for categorical variables. Data were statistically analysed using chi-square tests for differences in frequency and the Student's *t*-test for comparison between two normally distributed continuous variables. $P < 0.05$ was considered statistically significant. A multivariate step-wise logistic regression

analysis was also performed for all variables identified with $P \leqslant 0.05$ univariately, with calculation of odds ratio (OR) estimates and 95% CI. Inter-observer reliability was determined by comparing the findings obtained by both investigators and by calculating the concordance correlation coefficient κ.

Results

Fifty-seven pJIA patients (47 females/10 males) were included in this study: mean (S.D.) age 23.1 (9.6) years (range 12–55 years); 37 patients were >18 years; mean disease duration was 12.8 (11) years. In 34/57 (60%) patients polyarthritis was RF positive, whereas in 23/57 (40%) it was RF negative; 23/41 (56%) patients were anti-CCP positive. Thirteen pJIA patients (13/55) had ANA; in 11/13 patients, ANA was associated with RF. None had suffered from uveitis. All but two patients were treated with DMARDs (52/55 received MTX), whereas 39/57 (68%) had received biological agents over the course of the disease (in 95% of the cases an anti-TNF agent). The mean (S.D.) disease duration was 8.2 (8.3) years before the introduction of the biological agents. Ten pJIA (17%) patients had undergone at least one previous surgery. Fifty-eight RA patients (51 females and 7 males) were recruited with the following demographic characteristics: mean (S.D.) age 43.4 (9.5) years; mean disease duration 12.2 (7.1) years; 79% were RF and 78% were anti-CCP positive. A history of neck pain was present in 23/56 (41%) pJIA and 24/58 (41%) RA patients. Clinical examination revealed limitation of neck motion in 11/56 (20%) pJIA and 11/58 (19%) RA cases ($P = 0.99$). No patient presented neurological manifestations. Further details are provided in Table 1.

Standard radiographs showed inflammatory lesions in 37/57 pJIA (65%) and 39/58 RA (67%) patients. The inter-observer concordance coefficient κ was 0.597 between the two investigators. The mean (S.D.) numbers of lesions per patient were 3.6 (2.7) in pJIA and 2.6 (2.2) in RA ($P = 0.08$). In pJIA, the most frequent structural lesions were aAAS (33%), erosion of the odontoid process (19%), C1–C2 arthritis (17%) and apophyseal joint arthritis (16%). In cases of aAAS, mean distances in flexion and in extension were 5.32 in pJIA and 2.07 mm in RA. Functional lesions, i.e. loss of cervical lordosis, were found in 16 (28%) patients, but this was not due to vertebral fracture ($n = 0$). No hypertrophia of vertebrae was detected, but hypotrophia was found in nine patients and was associated with AJA at the same level in three of those cases. C4 (44%) and C5 (67%) vertebral bodies were the most frequently involved in cases of hypotrophia. AJA affected 50% of cases at C4–C5 level. Apophyseal joint arthritis involved predominantly C2–C3 level and C5–C6 level (55% of cases). Examples of cervical structural lesions observed in pJIA are shown in Figs 1 and 2.

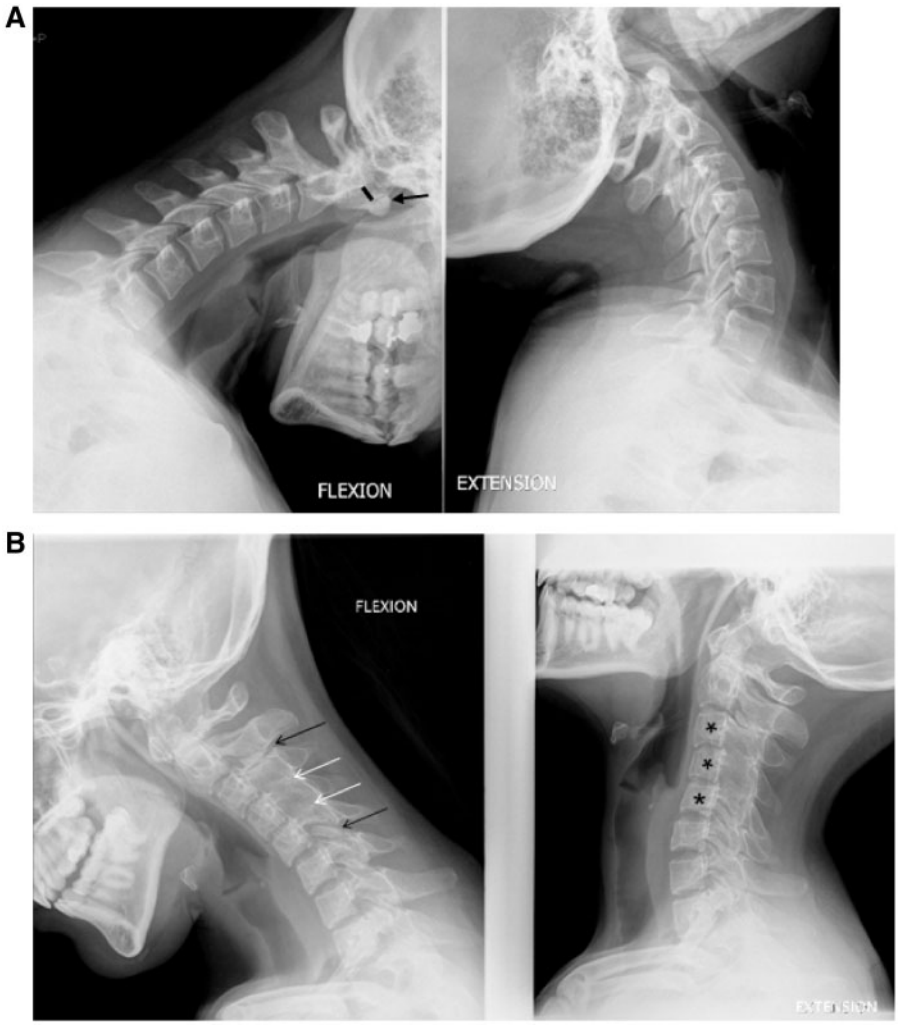
A comparison between pJIA and RA in radiographic findings showed differences for ankylosis (14 *vs* 0%, $P = 0.0002$), and especially for AJA (10 *vs* 0%, $P = 0.002$). Hypotrophia seemed to be more frequent in the pJIA subgroup compared with RA (16 *vs* 5%, $P = 0.04$). Other cervical lesions in pJIA and RA as well as comparison between these two groups are reported in Table 2. Demographic characteristics of RF-positive polyarthritis did not differ from RF-negative polyarthritis except for a longer disease duration in RF-negative pJIA (17.3 *vs* 9.8 years, $P = 0.01$) (Table 3). A comparison between RF-positive and RF-negative pJIA did not show any difference concerning prevalence or characteristics of cervical lesions (Table 3).

Table 1 Clinical characteristics of pJIA and RA patients

Clinical characteristic	pJIA ($n = 57$)	RA ($n = 58$)	P
Age, years, mean (S.D.)	23.1 (9.5)	43.4 (9.5)	<0.01
Gender, female/male	47/10	51/7	0.28
Disease duration, years, mean (S.D.)	12.8 (11.0)	12.1 (7.1)	0.70
RF positive	34 (60)	46 (79)	0.02
Anti-CCP positive	23/41 (56)	45/57(79)	0.03
ANA positive	13/55 (24)	10/58 (17)	0.49
Cervical symptoms	23/56 (41)	25/58 (43)	0.83
Previous use of steroids	30 (53)	55 (95)	<0.01
DMARDs	55 (96)	57 (98)	0.55
Number of DMARDs/patient, mean (S.D.)	1.7 (1.3)	2.9 (1.7)	<0.01
Use of biological agents	39 (68)	40 (67)	0.99
Number of biological agents/patient, mean (S.D.)	1.1 (1.17)	1.5 (1.48)	0.13
Surgery	10 (17)	16 (28)	0.20
Prosthetic surgery	5 (9)	5 (9)	0.99
Tenderness joints count, mean (S.D.)	3.4 (5.7)	6.4 (6.4)	<0.01
Swollen joints count, mean (S.D.)	3.1 (4.7)	5.2 (4.5)	0.02
ESR, mean (S.D.)	20.6 (21.4)	22.7 (23.2)	0.61
CRP, mean (S.D.) (/*n* available)	8.5 (17.5) (/52)	19.6 (31.9) (/45)	0.03

Values are *n* (%) unless stated otherwise.

FIG. 1 Representative cervical structural lesions in pJIA.



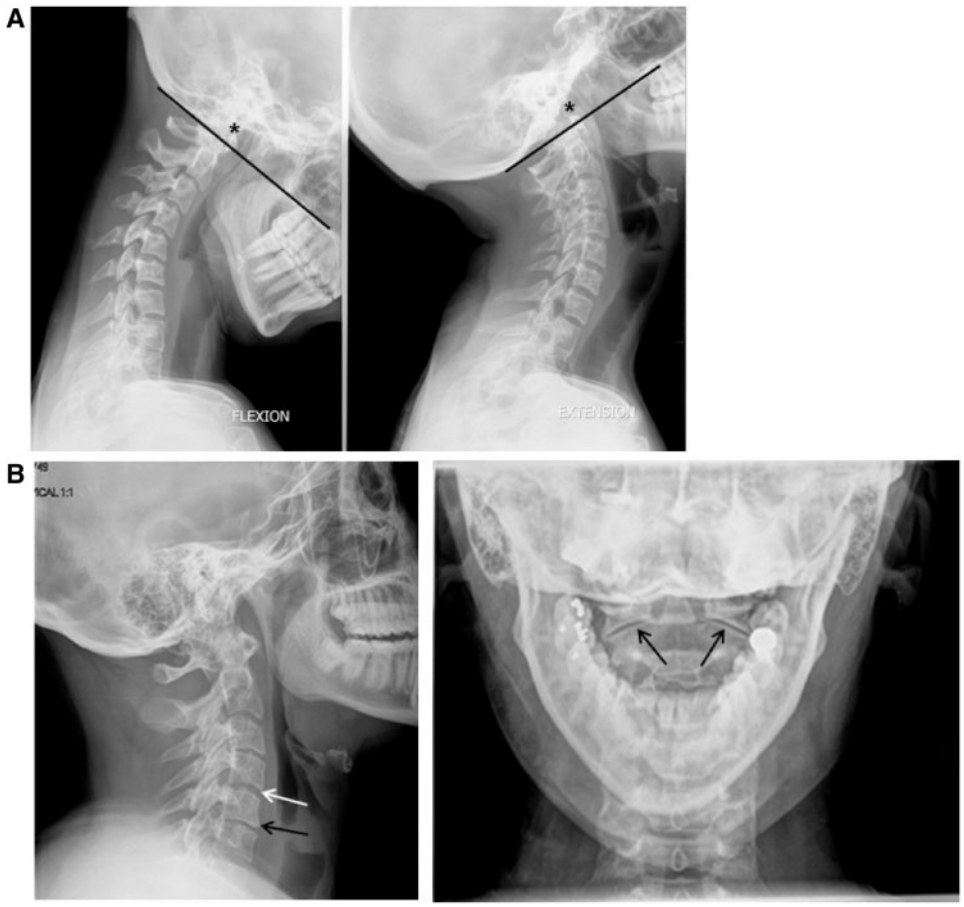
(**A**) Cervical spine radiographs (flexion/extension views) in a pJIA of 24 years with anterior erosion of the odontoid process (arrow) and aAAS (black line) with an atlantodental interval equal to 9.3 mm. (**B**) Cervical spine radiographs in a pJIA of 23 years with diffuse demineralization, loss of cervical lordosis, apophyseal joint arthritis at C2–C3 and C5–C6 levels (black arrows), AJA at C3–C4 and C4–C5 levels (white arrows) and hypotrophy of C3, C4 and C5 vertebral bodies (stars).

RA patients with radiographic cervical lesions did not differ from their pJIA counterparts, except for a higher number of DMARDs per patient in the RA subgroup ($P < 0.01$). However, concomitant peripheral erosive disease was a constant factor in RA patients with cervical lesions, whereas in five pJIA patients, cervical lesions were detected in the absence of both hand and foot abnormalities. These patients had a mean (S.D.) number of 4.4 (2.8) lesions per patient. The lesions detected were as follows: loss of cervical lordosis (in three of five), aAAS (in one of five), AAI (in one of five), C1–C2 arthritis (in one of five), inflammatory discitis (in three of five), ankylosis (in three of five), apophyseal joint arthritis (in one of five) and hypotrophia (in two of five).

In the pJIA subgroup, 19/37 (51%) patients with radiological cervical lesions had no clinical cervical involvement. The presence of radiographic cervical lesions correlated with a more severe disease phenotype (Table 4) with a higher number of biological agents per patient [$P = 0.003$), a more erosive disease (hands) ($P = 0.001$] and a higher frequency of prosthetic surgery ($P = 0.03$). The presence of cervical lesions was not associated with age at onset, disease duration, clinical cervical involvement or RF status. In multivariate analysis, only a higher number of biological agents per patient remained associated with radiographic cervical lesions [$P = 0.04$, OR (95% CI) 2.68 (1.05, 6.81)].

Eighteen (78%) pJIA patients with cervical symptoms and 19/33 (58%) without clinical sign (i.e. neck pain and/or limitation of the neck motion) had radiographic cervical lesions ($P = 0.11$). In the pJIA subgroup, patients with cervical symptoms seemed to be older, with a mean (S.D.) age

FIG. 2 Other examples of cervical structural lesions observed in pJIA.



(**A**) Cervical spine radiographs in a pJIA of 25 years with AAI (black star) >4.5 mm above McGregor's line (black line) in flexion and in extension. (**B**) Cervical spine radiographs in a pJIA of 23 years with erosion of the vertebral corner of C5 (white arrow) and discitis at C5–C6 level (black arrow) and C1–C2 bilateral arthritis (black arrows) on open-mouth view.

of 27.0 (11.9) *vs* 20.4 (6.7) years and a longer disease duration [17.2 (13.8) *vs* 9.6 (7.4), $P = 0.01$]. In this subgroup the disease was more severe with a higher number of DMARDs ($P = 0.02$) or biological agents ($P = 0.004$) per patient and a trend towards a higher frequency of prosthetic surgery ($P = 0.06$). The presence of clinical cervical involvement did not correlate with age at onset, antibodies status or other demographic characteristics. It seemed to be associated with AAI, which was present in 5/23 (22%) symptomatic and in 1/33 (3%) asymptomatic patients, respectively [$P = 0.02$; OR (95% CI) 8.89 (0.96, 82.11)].

Discussion

The main results of our study are as follows: (i) structural cervical spine involvement is a frequent manifestation in pJIA persisting into adulthood (65% of our cohort), asymptomatic in half of the cases; (ii) cervical lesions observed in young adults with pJIA are similar to those seen in RA except for ankylosis and growth disturbances; and (iii) cervical lesions in pJIA are associated with a severe disease.

Only two studies assessed the structural cervical involvement in JIA persisting into adulthood by X-ray with prevalence estimated at 79 and 62% of cases, respectively [10, 16]. Consistently we found a high prevalence of cervical lesions in our pJIA persisting into adulthood cohort (65%). Structural lesions were distributed as follows: aAAS, erosion of the odontoid process, C1–C2 arthritis and apophyseal joint arthritis. These results are slightly different from the two previous studies [10, 16]. However, certain limitations to these preceding studies are relevant for discussion: (i) in the first study, a high prevalence of sacroiliac disease existed (71%), which raises the question of possible misdiagnoses [10]; (ii) patients had longer disease duration; (iii) patients were assessed before the biotherapy era; and (iv) in the second study, radiographs were only performed in cases of clinical cervical involvement or before surgery [16]. By comparison, the patients in our study were assessed earlier in the course of the disease (13 years) and were

Table 2 Radiographic lesions observed in pJIA and RA patients

Radiographic lesions	pJIA ($n = 57$)	RA ($n = 58$)	P; OR (95% CI)
Radiographic cervical lesions	37 (65)	39 (67)	0.79
Number of lesions per patient, mean (S.D.)	3.6 (2.7)	2.6 (2.2)	0.08
Loss of cervical lordosis	16 (28)	18 (31)	0.80
Erosion of the odontoid process	11 (19)	11 (19)	0.88
aAAS	19 (33)	14 (24)	0.17
C1–C2 arthritis	10 (17)	12 (21)	0.72
AAI	6 (10)	8 (14)	0.63
Erosions	2 (3)	5 (9)	0.34
Discitis	7 (12)	4 (7)	0.28
Uncovertebral joint arthritis	3 (5)	1 (2)	0.71
Apophyseal joint arthritis	9 (16)	8 (14)	0.69
Ankylosis	8 (14)	0	0.0002; 2.34 (1.78, 3.09)
AJA	6 (10)	0	0.002; 2.26 (1.74, 2.94)
SAS	4 (7)	6 (10)	0.81
Hypotrophy of vertebrae	9 (16)	3 (5)	0.04; 3.86 (0.95, 15.59)
Hands	44 (77)	49 (84)	0.32
Hands score, mean (S.D.)	17.5 (21.1)	19.1 (16.9)	0.67
Feet	38 (67)	46 (79)	0.13
Score, mean (S.D.)	8.2 (10.9)	10.8 (12.3)	0.23
Hip, *n*/*n* available (%)	15/52 (29)	8/39 (20)	0.36

Values are *n* (%) unless stated otherwise. Hands and feet were assessed by the modified version of Larsen's scoring method [28]. The hand and feet scores range from 0 to 110 and from 0 to 50, respectively. Hips were assessed for the presence of coxitis.

Table 3 Clinical characteristics and cervical lesions observed in RF-positive and RF-negative pJIA

Parameter	RF-positive pJIA ($n = 34$)	RF-negative pJIA ($n = 23$)	P
Age, years, mean (S.D.)	21.5 (7.9)	25.5 (11.3)	0.1
Disease duration, years, mean (S.D.)	9.8 (8.7)	17.3 (12.6)	0.01
DMARDs	34 (100)	21 (91)	0.03
Number of DMARDs/patient, mean (S.D.)	1.8 (1.3)	1.6 (1.3)	0.6
Use of biological agents	24 (71)	15 (65)	0.7
Number of biological agents/patient, mean (S.D.)	1.1 (1.1)	1.1 (1.3)	0.9
Surgery	6 (18)	4 (17)	0.9
Radiographic cervical lesions	22 (65)	15 (65)	0.9
Number of lesions/patient, mean (S.D.)	3.4 (2.4)	4.0 (3.1)	0.5
Loss of cervical lordosis	7 (21)	9 (39)	0.1
Erosion of the odontoid process	7 (21)	4 (17)	0.8
aAAS	14 (41)	5 (22)	0.1
C1–C2 arthritis	4 (12)	6 (26)	0.2
AAI	2 (6)	4 (17)	0.2
Erosions	2 (6)	0 (0)	0.1
Discitis	3 (9)	4 (17)	0.3
Uncovertebral joint arthritis	1 (3)	2 (9)	0.4
Apophyseal joint arthritis	6 (18)	3 (13)	0.6
Ankylosis	4 (12)	4 (17)	0.5
AJA	3 (9)	3 (13)	0.6
SAS	1 (3)	3 (13)	0.1
Hypotrophy of vertebrae	6 (18)	3 (13)	0.6

Values are *n* (%) unless stated otherwise.

TABLE 4 Factors associated with structural lesions in pJIA in univariate analysis

Factor	Structural cervical lesions ($n = 37$)	Absence of structural cervical lesions ($n = 20$)	P
Age, years, mean (S.D.)	24.3 (11.1)	20.9 (5.2)	0.21
Age at onset, years, mean (S.D.)	10.2 (4.6)	10.7 (4.2)	0.69
Disease duration, years, mean (S.D.)	14.2 (12.5)	10.2 (7.0)	0.20
RF positive	22 (59)	12 (60)	0.99
Anti-CCP positive *n*/*n* available, (% of available)	16/28 (57)	7/13 (54)	0.84
Cervical symptoms	18 (49)	5 (25)	0.08
Previous use of steroids	22 (59)	8 (40)	0.16
DMARDs	36 (97)	19 (95)	0.65
Number of DMARDs/patient, mean (S.D.)	1.9 (1.4)	1.3 (0.7)	0.08
Use of biological agents	29 (78)	10 (50)	0.03
Number of biological agents/patient, mean (S.D.)	1.4 (1.3)	0.5 (0.5)	<0.01
Surgery	9 (24)	1 (5)	0.07
Prosthetic surgery	5 (14)	0	0.04
Painful joints count, mean (S.D.)	4.6 (6.6)	1.3 (2.8)	0.04
Swollen Joints count, mean (S.D.)	3.5 (4.7)	2.4 (4.8)	0.43
ESR, mean (S.D.)	21.9 (23.8)	18.2 (16.3)	0.53
CRP, mean (S.D.)(/*n* available)	11.6 (21.3) (/33)	3.2 (3.7)	0.10
Hands	32 (86)	12 (20)	0.02
Hand score, mean (S.D.)	23.1 (23.3)	7.3 (10.7)	<0.01
Feet	29 (78)	9 (45)	0.01
Feet score, mean (S.D.)	9.8 (11.9)	5.2 (8.1)	0.13
Hip	12/33 (36)	3/19 (16)	0.11

Values are *n* (%) unless stated otherwise. Hands and feet were assessed by the modified version of Larsen's scoring method [28]. The hand and feet scores range from 0 to 110 and from 0 to 50, respectively. Hips were assessed for the presence of coxitis.

more aggressively treated with DMARDs (96%) and biotherapies (68%). This may explain why our contemporary cohort most frequently presented aAAS, which is known to occur early in the course of the disease [13, 29].

Surprisingly, the radiological cervical pattern of our young adults with pJIA appeared similar to that of RA in adults, i.e. neither less frequent nor less severe. However, consistent with previous reports, two cervical features seem to have remained specific to pJIA: ankylosis, particularly AJA, and growth disturbances [8, 14, 30, 31]. Hypotrophy of vertebrae has long been considered as a hallmark of the disease in children [6]. However, previous reports were not controlled and as a result cannot accurately be used to assess the specificity of the lesions described. In the present study we found that growth disturbances affect predominantly pJIA, but can also occur in RA.

Clinical cervical involvement, which is an important part of the discomfort of JIA patients, is usually considered common in JIA, with prevalence ranging between 20 and 70% [6–8, 10–12, 31]. In our study, 41% of pJIA presented cervical symptoms. They were not associated with more frequent radiological cervical lesions, but correlated with a more severe disease. Furthermore, there was a trend of association between cervical symptoms and AAI. Therefore, clinical cervical involvement should be considered as a poor prognosis factor for the disease and perhaps as a warning sign for the presence of AAI.

The detection of cervical lesions appears fundamental for several reasons. First, cervical lesions are found in asymptomatic patients (51%) and in patients without peripheral erosive disease (14%), which is not the case for RA. Secondly, the need for surgery is more common in pJIA with cervical lesions (24%) than without (5%). Diagnosis of cervical spine instability before surgery is necessary as recommended in RA [32] to prevent brain stem or spinal cord compression during the intubation [24, 25]. Finally, in RA, some data suggest that cervical surgery may be the most beneficial at an earlier age [30, 33]. For all these reasons, as suggested in RA [21, 29], radiological assessment of the cervical spine (including flexion and extension views) in pJIA might be performed systematically at onset and regularly during the course of the disease. Frequency of radiological assessment of the cervical spine remains to be determined but should depend on the severity of the disease.

These proposals to follow-up with pJIA must be considered in the context of using X-irradiation on this particular subgroup of young patients. Without international recommendations, limitation on the use of radiation is the rule. Nevertheless, this rule does not negate our proposals, due to the advent of a new 2D and 3D imaging called EOS, which features low radiation doses.

Despite a high prevalence of cervical lesions, neurological manifestations were uncommon in our cohort, as in previous studies [6, 10, 12, 14, 18, 31]. However, two of our patients had severe aAAS, as reflected by an anterior

atlantodental interval equal to 9.3 and 10 mm [23]. Neurological symptoms were absent in both patients but one underwent preventive cervical surgery after the end of this cross-sectional study.

Our study is the first to specifically assess structural cervical spine involvement in pJIA persistent in adulthood regardless of the clinical symptoms and with a control RA group matched for sex and disease duration. Compared with previous studies performed before the recent ILAR criteria of classification [1], the strength of our study primarily lies in the following criteria: (i) the homogeneity of our JIA group, which consisted only of the polyarticular form of JIA, excluding other subtypes of JIA; (ii) the RA control group results, which were similar to those expected when taking into account the literature [17, 21], support the specificity of the lesions described herein; and (iii) good inter-examiner reproducibility for radiograph assessment.

Our study should be interpreted within its limitations. First, it was a cross-sectional study, thereby preventing assessment of the natural history of cervical spine involvement in pJIA. As it was a retrospective study, the cervical symptoms were assessed by medical records and questions during the consultation; mild and transient symptoms could have been omitted. Secondly, MRI was not included in this study. MRI allows assessing synovial involvement, particularly C1–C2 pannus and neural structure compressions in the cervical spine [21, 34]. However, the measure of subluxation might be more reliable on dynamic radiography with flexion and extension views [35]. Furthermore, MRI is not widely available and is expensive and time consuming. Therefore, standard X-ray could remain the first-line investigation for cervical spine, whereas MRI might be used in the presence of neurological symptoms or as a pre-operative examination [34]. Moreover, our patients were recruited from a tertiary referral centre and 16/57 (28%) patients were referred from other parts of France or other countries. Therefore, our cohort might have a more severe disease, as reflected by high-frequency use of biological agents and surgery. The higher prevalence of RF-positive polyarthritis could also be explained by the severity of our patients; it is well known that RF-positive pJIA is the most severe form of the disease, persisting almost always into adulthood and associating with poor outcome [2, 3]. However, RF-negative pJIA could also be associated with structural osteoarticular damage, and it is these severe destructive RF-negative forms that persist more frequently into adulthood. This may explain why RF-positive and -negative pJIA did not differ in prevalence and characteristics of cervical lesions when we focus on the young adults subgroup with a long disease duration.

The majority of our patients had disease onset before the introduction of biological agents, with a previous mean disease duration of 8 years. Therefore, we can hypothesize that our patients were less early and less aggressively treated than would be the case now; that may explain a part of the severity of cervical involvement of our patients. Particularly, it is noteworthy that RF-negative polyarthritis had much longer disease duration than RF-positive polyarthritis. This difference may suggest that RF-negative patients with cervical involvement were in the majority in the group of late treatment with biological agents, and that early aggressive treatment may reduce cervical involvement in this subgroup. In conclusion, our results suggest that, in pJIA persisting into adulthood, structural cervical spine involvement is frequent and is associated with more severe disease whatever the RF status. Altogether our results suggest monitoring cervical spine by performing systematic radiological assessment at onset and regularly during the course of the disease regardless of clinical symptoms but according to the severity of the disease. Further larger prospective studies are warranted to confirm our results and to evaluate the potential benefit of biological agents in order to prevent the development of cervical lesions.

Rheumatology key messages

- Structural cervical spine involvement is frequent in pJIA persisting into adulthood.
- Cervical lesions are frequently asymptomatic and associated with more severe disease in pJIA.
- Posterior ankylosis and growth disturbances seem to be specific to pJIA as compared with RA.

Disclosure statement. The authors have declared no conflicts of interest.

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