Intraarticular Corticosteroid Injections of the Temporomandibular Joint in Juvenile Idiopathic Arthritis

SARAH RINGOLD, TROY R. TORGERSON, MARK A. EGBERT, and CAROL A. WALLACE

ABSTRACT. ***Objective.*** To describe the clinical and radiographic outcomes in a series of patients with juvenile idiopathic arthritis (JIA) who underwent one or more intraarticular corticosteroid (IAS) injections of the temporomandibular joint (TMJ) performed without imaging guidance.

Methods. Retrospective chart review was performed for all patients with JIA diagnosed and treated at our institution between January 1, 2000, and January 1, 2006, who underwent one or more IAS injections of their TMJ. IAS injections were performed by the same oral and maxillofacial surgeon without imaging guidance, using either triamcinolone acetonide or triamcinolone hexacetonide. The primary outcomes assessed were maximal incisal opening (MIO) measurements, patient-reported symptoms, physical examination findings, and imaging results.

Results. Twenty-five patients were identified. Twenty-one (84%) had radiographic evidence of TMJ disease when TMJ disease was first suspected by their physician. The 25 patients underwent 74 IAS injections on 47 separate occasions. When baseline MIO measurements were compared to the last MIO measurements of the study period, there was a mean increase in MIO of 6.9 mm ($p = 0.002$; 95% CI 3, 10.7). There was a mean increase in MIO of 3.8 mm following each IAS injection ($p = 0.003$; 95% CI 1.4, 6.2). Patients who underwent multiple IAS injections had a mean increase in MIO after first injection of 6.6 mm ($p < 0.001$; 95% CI 4.1, 9.1); however, the mean increase in MIO after subsequent injections was 0.4 mm ($p = 0.8$; 95% CI –3.5, 4.4). One patient developed subcutaneous atrophy at the injection site. Two patients developed small, asymptomatic intraarticular calcifications. No additional adverse events were reported.

Conclusion. In this patient population, there was an overall increase in MIO measurements following initial IAS injection and during the study period. Patients tended to have minimal response to subsequent injections. IAS injections performed without imaging guidance by an experienced oral and maxillofacial surgeon were well tolerated with only rare adverse events. The presence of radiographic changes when the physician first suspected TMJ disease in 84% of patients emphasizes the need for better screening and early intervention for synovitis in this joint. (First Release April 1 2008; J Rheumatol 2008;35:1157–64)

Key Indexing Terms:
JUVENILE IDIOPATHIC ARTHRITIS TEMPOROMANDIBULAR JOINT ARTHRITIS
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Involvement of the temporomandibular joint (TMJ) in association with childhood inflammatory arthritis was initially described in Still's original case series, in which 3 of the 22 children were suspected to have TMJ involvement[1]. The first report to focus specifically on the effects of inflammation on mandibular growth and craniofacial development in children with inflammatory arthritis was published in 1949, and described the progressive deformity of the mandible associated with longstanding, untreated TMJ arthritis[2]. Arthritis of the TMJ is now a well described manifestation of juvenile idiopathic arthritis (JIA), with an estimated prevalence of 29%–62%, and it has been described in association with all of the JIA subtypes[3-5]. In some cases, undergrowth or asymmetry of the mandible may be the initial

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presentation of JIA, or the TMJ may be the only joint affected throughout the disease course[6,7]. Diagnosis is often delayed, as TMJ arthritis is frequently asymptomatic in children and evidence of TMJ damage on radiographic imaging in the absence of patient-reported symptoms has been reported in up to 25%–69.5% of patients with JIA[8-10].

The TMJ is particularly susceptible to damage from arthritis because of its unique anatomy. Because the primary site of mandibular growth lies directly beneath a thin layer of fibrocartilage, the mandibular growth plate is particularly vulnerable to damage resulting from inflammation and trauma occurring within the joint[11]. TMJ damage leads to significant morbidity, including poor oral intake secondary to decreased mouth opening, chronic pain and TMJ symptoms, tooth crowding, and poor cosmetic outcomes, which may require surgical repair and potentially cause psychological distress.

Despite the frequency with which the TMJ is known to be affected in JIA and the severity of the associated morbidities, data are not available regarding the optimal diagnosis and treatment of arthritis of this joint. Previous approaches have included the use of splinting and surgical repairs, which have demonstrated minimal efficacy. The effects of systemic medications on TMJ disease have not been studied, with the exception of one nonrandomized case series, which suggested that methotrexate (MTX) may decrease the severity of the condylar destruction and craniofacial changes associated with TMJ arthritis in children with oligoarticular and polyarticular disease[12].

Intraarticular corticosteroid (IAS) injections have been studied primarily for oligoarticular disease in children and have been found to treat joint inflammation effectively and to provide significant symptomatic relief[13,14]. Reports of IAS use in TMJ disease in adults have demonstrated mixed results, in part due to the heterogeneity of disease in the patients treated and the lack of control groups. In addition, reports of corticosteroid-associated TMJ damage have led to concerns about the safety of TMJ IAS injections in children[15,16]. However, recent data suggest that TMJ IAS injections may be an effective and safe treatment for TMJ involvement in JIA. A case report of a 15-year-old girl with isolated TMJ disease reported that a combination of arthroscopic synovectomy followed by IAS injections resulted in both clinical improvement and radiographic resolution of inflammation, which persisted 1 year after the procedure[7]. Two recent studies reported short-term improvements in patient-reported symptoms, maximal incisal opening (MIO) measurements, and magnetic resonance imaging (MRI) findings following TMJ IAS injections[17,18]. A prospective study of 23 patients who underwent computer tomography (CT)-guided TMJ IAS injections found an overall increase in MIO measurements and a decrease in patient-reported symptoms after injections[17]. A retrospective series of 15 patients who underwent CT-guided TMJ IAS injections reported the resolution of effusions on the majority of followup MRI, in addition to an increase in MIO measurements[18].

Data are not available on the outcomes of TMJ arthritis in patients with JIA after treatment with multiple IAS injections, and there are no published data reporting the safety of TMJ IAS injections performed without imaging guidance in children. We performed a retrospective chart review to evaluate these outcomes in a cohort of patients with JIA.

MATERIALS AND METHODS

Patients. Eligible patients were identified through a search of patients at Children's Hospital and Regional Medical Center (CHRMC) in Seattle, associated with the hospital's oral and maxillofacial surgeon and the Current Procedural Terminology (CPT) code for injection of the TMJ during or after the year 2000. Each chart was then reviewed to identify patients who also met the 2001 Edmonton International League of Associations for Rheumatism (ILAR) criteria for a diagnosis of JIA[19] and who were diagnosed and treated at the CHRMC rheumatology clinic between January 1, 2000, and January 1, 2006. We chose to limit our study population to those patients diagnosed during or after the year 2000 because this year marked the beginning of etanercept use in our patient population and the use of earlier, more aggressive systemic therapies. Because we hypothesized that use of these more aggressive treatments would change the patterns and severity of disease in our patient population and, by extension, the patterns and extent of TMJ disease, we felt that this cutoff would lead to a more comparable, homogeneous study cohort.

Patients were excluded if they had been diagnosed with JIA before the year 2000, if they had more than one visit with a rheumatologist outside of CHRMC, and if they had a history of facial trauma, or a preexisting jaw or craniofacial disorder unrelated to JIA. Institutional review board approval was obtained for this study.

Data collection. Retrospective chart review was performed to collect data on each patient's clinical and laboratory disease characteristics, age at onset of TMJ disease, timing and number of TMJ IAS injection procedures, MIO measurements, patient-reported TMJ symptoms, TMJ findings on physician examination, and results of TMJ imaging. Medication data were recorded for the first visit at which the patient was suspected to have TMJ arthritis and at the final visit of the study period. Laboratory data and imaging results from studies performed outside of CHRMC were reviewed when available.

The onset of TMJ disease was defined as the first clinic visit at which the patient reported TMJ symptoms or at which the rheumatologist first documented an abnormal TMJ examination or concerns regarding TMJ involvement. In cases where the patient was referred to our clinic specifically for suspected TMJ arthritis, the date of the patient's first rheumatology clinic visit was used as the TMJ arthritis-onset date. Each date that a patient underwent an IAS injection was documented as an IAS episode and each episode was documented as either unilateral or bilateral. MIO measurements were made in-clinic using a tape measure. When available, MIO measurements were collected for the clinic visit prior to each IAS injection episode, for the clinic visit following an injection episode, and at the patient's last clinic visit of the study period. Also, when available, patient-reported symptoms, physician findings on examination, and the results of imaging studies were recorded for these same visits.

IAS injections. All TMJ IAS injections were performed at CHRMC by the same experienced oral and maxillofacial surgeon. The injections were performed in the operating room with the patient under general anesthesia and without imaging guidance. Each TMJ was injected with 0.5–1 ml triamcinolone acetonide (40 mg/ml) or triamcinolone hexacetonide (20 mg/ml) using a 22-gauge, 1.5-inch spinal needle. The volume of corticosteroid injected was determined at the time of injection by the size of each joint

space and by the amount of resistance encountered with the injection, as judged by the operating physician. The type of corticosteroid used was determined by medication availability because triamcinolone hexacetonide was not available for roughly 1 year during the study period due to a suspension in manufacturing.

Statistical analysis. Paired t-tests were performed for comparisons of MIO measurements before and after IAS injections. The Wilcoxon signed-rank test was performed when nonparametric testing was required due to small sample sizes. All reported p values are 2-sided. Data analyses were performed using Stata statistical software, version 9.0 (2001; Stata Corp., College Station, TX, USA).

RESULTS

Patient characteristics. Twenty-five patients, 21 (84%) females and 4 (16%) males, met inclusion criteria for the study (Table 1). All the JIA categories were represented in the cohort, with the exception of systemic, undifferentiated, and rheumatoid factor (RF)-positive polyarticular JIA. Serologies were provided at the providers' discretion and were not uniformly obtained. Fourteen patients were antinuclear antibody (ANA)-positive and 5 were HLA-B27-positive. One patient with polyarticular disease did have both a positive RF and a positive anticyclic citrullinated peptide antibody result. However, because the patient's RF was not repeated, she did not meet criteria for RF-positive polyarticular JIA based on the ILAR criteria, and was categorized as RF-negative polyarticular JIA.

The mean age at diagnosis of JIA in this cohort was 8.9 years (range 1–16 yrs, median 8.4). The mean duration of time from initial diagnosis of JIA to the onset of TMJ symptoms or suspected TMJ arthritis was 11 months (range 0–55 mo, median 2). Ten patients (40%) had TMJ complaints or suspected TMJ arthritis at their first rheumatology clinic visit (3 polyarticular, 3 enthesitis-related, 3 oligoarticular, 1 extended oligoarticular). Three of these patients, 2 enthesitis-related and 1 oligoarticular, presented to the rheumatology clinic with their TMJ as their only active joint. Of note, none of these 3 patients developed additional joint involvement during the followup period. Thirteen patients (52%) had bilateral TMJ disease. Patients with oligoarticular, extended oligoarticular, and psoriatic arthritis had the highest proportion of bilateral disease in this sample. Patients were followed for an average of 33.6 months after TMJ arthritis was first suspected by their physician (median 35 mo, range 7–57).

IAS injections. The 25 patients underwent 74 IAS injections on 47 separate occasions during the study period (27 bilateral episodes; 20 unilateral episodes; Table 1). The range of TMJ injections per patient was 1–10 (range 1–5 injections per joint). Twelve patients underwent injections on more than one occasion (mean 2 episodes per patient, range 1–5 episodes per patient). Three patients had 5 injection episodes, 3 patients had 3 injection episodes, 4 patients had 2 injection episodes, and the remaining 15 patients had one injection episode each. Mean followup after initial TMJ injection was 26 months (median 25 mo, range 5–52).

Maximal incisal opening. MIO measurements were available prior to first IAS injection and at the final documented clinic visit of the study period for 15 patients. The mean MIO measurement prior to first injection was 32.5 mm (median 34 mm, range 20–40) and the mean measurement at the last visit was 39.3 mm for these patients (median 39 mm, range 29–50). These patients had a mean increase in MIO of 6.9 mm over the study period (p = 0.002; 95% CI 3, 10.7). This group included 7 patients with oligoarticular JIA and the 4 patients with enthesitis-related arthritis. These patients accounted for 29 of the 47 IAS injection episodes.

MIO measurements were available for the clinic visits before and after 35 of the 47 injection events (74%). The followup visits occurred at a mean of 3.1 months after IAS injection (median 3 mo, range 1 day to 10 mo). The mean MIO was 31.5 mm (range 15–45 mm) before injection episodes and the mean MIO after these injections was 35.3 mm (range 20–48 mm). There was a mean increase in MIO of 3.8 mm (range –18 to 20 mm) (p = 0.003; 95% CI 1.4, 6.2) following each IAS injection episode.

Nineteen pairs of measurements were available before and after first IAS injection episodes. The mean MIO before

Table 1. Patient characteristics (n = 25).

JIA Category	N	Age at Disease Onset, yrs, median (range)*	Age at Onset of TMJ Arthritis, yrs, median (range)*	Duration of Disease to TMJ Onset, mo, median (range)**	No. of TMJ IAS Injections, total (bilateral)†
Oligoarticular	9	7 (1–15.5)	8 (3–15.5)	20 (0–55)	15 (8)
Extended oligoarticular	3	2.5 (2–8.5)	4 (3–8.5)	13 (0–17)	7 (6)
Polyarticular (RF–)	7	13 (4–15)	14.5 (4–16)	2 (0–28)	15 (8)
Enthesitis-related	4	12.5 (11–16)	14 (11–16)	0 (0–37)	4 (1)
Psoriatic arthritis	2	9 (3–15)	10 (4–15.5)	7 (2–12)	6 (4)

* Values rounded to the nearest half-year. ** Age at first clinic visit at which the patient was documented to have TMJ symptoms or abnormal findings on examination. Values rounded to the nearest month. † TMJ IAS injection: each separate date on which a patient underwent TMJ IAS injection. TMJ: temporomandibular joint; IAS: intraarticular steroid injection; RF: Rheumatoid factor.

first injection was 30.5 mm (range 20–40 mm, median 30). The mean MIO after first injection was 37.2 mm (range 24–48 mm, median 38). There was a mean increase of 6.6 mm after first injection (range –1 to 17 mm) ($p < 0.001$; 95% CI 4.1, 9.9). There was no significant difference in increase in MIO between patients who underwent unilateral versus bilateral injection for their first injection. These increases persisted when the group was divided into those patients who underwent one injection during the study period and those patients who underwent more than one injection during the study period.

For patients who underwent one IAS injection, the mean MIO before first injection was 33.3 mm and the mean MIO following first injection was 39.9 mm. There was an overall increase in MIO of 6.6 mm for this group after first injection ($p = 0.002$; 95% CI 3.2–9.9; $p = 0.008$ by Wilcoxon signed-rank test). For patients who underwent more than one injection during the study period, the mean MIO before first injection was 28 mm and the mean MIO following first injection was 34.7 mm. There was an overall increase in MIO of 6.7 mm for this group after first injection ($p = 0.01$; 95% CI 2.4–11; $p = 0.02$ Wilcoxon signed-rank test). Although the mean baseline MIO was somewhat lower in the group that underwent more than one injection, there was no statistically significant difference between the groups' mean baseline MIO measurements or mean MIO measurements after first injection ($p = 0.1$ for both comparisons). For patients who underwent more than one injection, the mean increase in MIO after subsequent injection was 0.4 mm. The mean MIO after subsequent injection episodes was 33.1 mm, which was not significantly different from the mean MIO prior to these episodes ($p = 0.8$; 95% CI –3.5, 4.4; Figure 1).

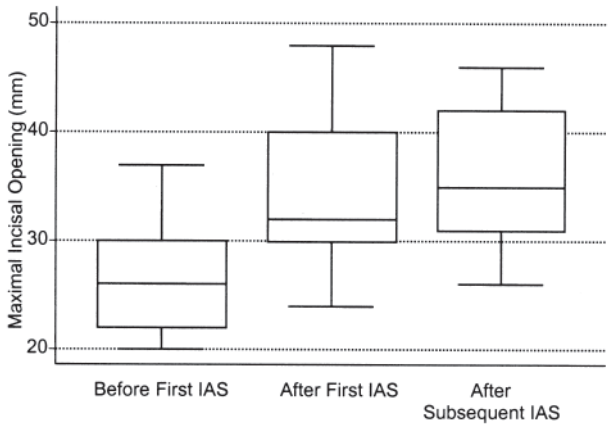

Figure 1. Comparison of maximal incisal opening (MIO) measurements of patients who underwent multiple intraarticular corticosteroid injections (IAS). Paired measurements are shown for 9 patients who had MIO documented before and after their first IAS injection, and before and after at least one subsequent injection. There was a statistically significant increase in MIO after first IAS injection. However, the increase following subsequent injections was not statistically significant, although the majority of the MIO measurements remained in the abnormal range for age prior to subsequent injections.

Twenty-four of the above 35 MIO measurements (68.5%) carried out prior to injection episodes were abnormal for the patient's age, based on published normal ranges for TMJ opening[20,21]. Of these 24 abnormal TMJ measurements, 10 (42%) improved to the normal range following injection. Fourteen joint measurements (58%) remained in the abnormal range following injection. Of these 14 measurements, 7 MIO measurements increased following injection, 4 decreased, and 3 were unchanged.

Of the 9 patients who underwent only one injection during the study period and who had documented baseline MIO as well as MIO after IAS injection, 8 (89%) patients had abnormal MIO based on age prior to injection. Following injection, 55% of these MIO increased into the normal range and 45% remained abnormal. Of the patients who underwent more than one IAS injection during the study period and who had documented baseline MIO as well as MIO after first injection, all had abnormal MIO based on age prior to first IAS injection. Following first injection, 55% of MIO remained abnormal, while 44% increased into the normal range. Data were available before and after 14 of the subsequent IAS injections. Prior to subsequent injections, 9 (64%) MIO were in the abnormal range prior to injection. After these subsequent injections, 57% of MIO were in the abnormal range based on age and 43% were in the normal range.

The small sample size in this case series limited further statistical analyses to assess for specific effects of single or multiple IAS injections on different disease and age categories.

Clinical outcomes. There was an overall decrease in documented patient-reported symptoms during the study period. The most frequently documented patient-reported complaints at the first TMJ visit were pain (48%), stiffness (24%), and difficulty eating (16%) (Table 2). Ten patients (40%) had no documented TMJ complaints at the first clinic visit when their physician suspected TMJ involvement. Following their initial IAS injection episode, 18 patients (72%) had no documented TMJ complaints. At the final clinic visit of the study period, 21 patients (84%) had no documented TMJ complaints.

The most commonly documented physical examination findings at the first TMJ visit were decreased MIO (68%), deviation on opening (40%), and asymmetry of the mandible (12%). Following their initial IAS injection episode, 15 patients (60%) had no abnormality on TMJ examination documented by their physician, and 5 patients were noted to have persistent deviation or asymmetry of their mandible. At the final clinic visit of the study period, 18 patients (72%) had no documented abnormalities on TMJ examination. Of the 12 patients who had deviation or asymmetry of the mandible noted at the first clinic visit when their physician suspected TMJ disease, 2 had persistent deviation on TMJ opening noted at their final clinic visit.

Table 2. Patient- and physician-reported outcomes*.

Symptom	Patient-Reported Symptoms, n (%) First TMJ Visit†	Clinic Visit After First IAS	Last Clinic Visit of Study Period
Pain	12 (48)	4 (16)	3 (12)
Stiffness/sticking	6 (24)	1 (4)	0
Difficulty eating	4 (16)	3 (12)	2 (8)
Clicking	3 (12)	1 (4)	0
None	10 (40)	18 (72)	21 (84)
Examination Finding	**Physician-Reported Examination Findings**, n (%) First TMJ Visit**	**Clinic Visit After First IAS**	**Last Clinic Visit of Study Period**
Deviation	10 (40)	4 (16)	5 (20)
Asymmetry	3 (12)	1 (4)	4 (16)
Crepitus/popping	1 (4)	1 (4)	1 (4)
Swelling	1 (4)	0	0
Other (pain, clunking)	1 (4)	2 (8)	2 (8)
No abnormalities documented	10 (40)	15 (60)	18 (72)

* Column totals may add to more than 100% if patients had more than one symptom or examination finding. ** Does not include maximal incisal opening measurements (reported in the text). † First visit at which physician suspected TMJ disease. TMJ: temporomandibular joint; IAS: intraarticular corticosteroid injection.

The other 3 patients had new deviation documented over the course of the study duration.

One patient also underwent TMJ synovectomy for worsening clinical and radiographic findings during the data collection period. This patient developed intraarticular rheumatoid nodules despite systemic treatment with MTX and 3 IAS injections.

Radiographic imaging. Radiographic imaging was not routinely obtained for each patient before and after each IAS injection. Following the clinic's current standard of care, the majority of imaging was done by CT scan and few MRI were obtained. Twenty-four of the 25 patients had abnormal CT scans of their TMJ prior to their first IAS injection. The remaining patient was considered to have TMJ arthritis based on the clinical findings of TMJ stiffness and pain, despite normal findings on baseline TMJ CT.

The median time from onset of suspected TMJ arthritis to abnormal findings on TMJ CT was 0 months (range 0–30 mo). Twenty-one patients (84%) were found to have abnormalities on the TMJ CT scan obtained at the first rheumatology clinic visit when they were suspected to have TMJ disease. Six of these patients had radiographic evidence of TMJ damage at their first visit to the rheumatology clinic.

The most common findings on baseline CT were joint space narrowing, erosions, and condylar flattening. Eighteen patients had erosions, condylar flattening, or both on their first TMJ CT.

Ten patients did not undergo repeat TMJ imaging secondary to stabilization of their symptoms. Of the 15 patients who did undergo followup imaging, 10 showed worsening changes despite IAS injection, 3 showed stable changes, and 2 showed improvement, including one that revealed healing of 2 small erosions (Figure 2).

MIO measurements for these 10 patients with worsening changes visible on followup CT were available before and after 19 of their IAS injections. Mean MIO prior to injection was 31.6 mm. Mean MIO after injection was 35.1 mm. Although there was a mean increase in MIO of 3.5 mm, this improvement was not statistically significant ($p = 0.08$; 95% CI –0.41, 7.4). The mean increase in MIO after each injection for patients with either stable imaging results, improved results, or no followup imaging was 3.8 mm ($p = 0.02$; 95% CI 0.6, 7).

Systemic medication use. At the time of their initial TMJ IAS injection, 22 patients were taking no daily medication or a nonsteroidal antiinflammatory drug (NSAID) only, 3 patients were receiving MTX, and one patient was receiving a tumor necrosis factor-α (TNF-α) inhibitor. At the end of the study period, 6 patients were receiving no daily medication or NSAID only, 15 were receiving MTX, and 9 were receiving a TNF-α inhibitor. A larger proportion of patients who underwent more than one injection were taking a TNF-α inhibitor than those who underwent only one injection (45.5% vs 28.6%), but a larger proportion of patients who underwent only one injection were taking MTX (64.5% vs 54.5%). The small sample sizes limited additional analyses of medication effects.

Adverse events. One patient developed subcutaneous atrophy at the IAS injection site. This patient had undergone 5 injections of her right TMJ and ultimately required surgery for facial asymmetry. Two patients had small, asymptomatic intraarticular calcifications noted on followup CT scans. No additional adverse events were reported.

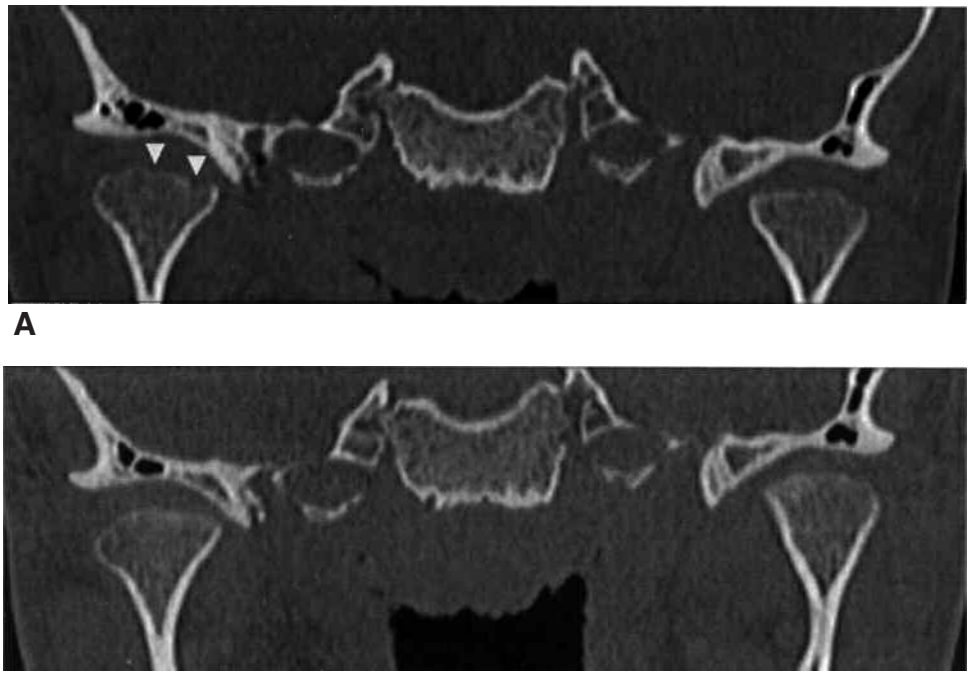

Figure 2. In a girl with ANA-positive polyarticular JIA diagnosed at age 14.75 years, comparison CT images show healing of condylar erosions after unilateral IAS injection of the TMJ. A. Image from the patient's first rheumatology clinic visit shows small erosions of the right condyle (arrowheads) with flattening of the condyles bilaterally. B. Followup image 9 months after she underwent IAS injection of the right TMJ shows healing of the small erosions on the right condyle. She also received weekly MTX during this period.

DISCUSSION

These results emphasize important aspects of patients with TMJ arthritis selected to undergo IAS injection. Consistent with prior reports, TMJ arthritis in this cohort tended to occur early in the JIA disease course (median 2 months from JIA diagnosis) and the majority of patients (84%) already had radiographic evidence of joint damage by the time TMJ arthritis was first suspected by their physician. About one-third of patients in this series were asymptomatic when TMJ disease was first suspected by their physician, despite radiographic evidence of joint damage.

This report also contributes additional information about the safety of TMJ IAS injection performed without imaging guidance. These injections, performed by an experienced oral and maxillofacial surgeon and without radiographic guidance, resulted in improvement in MIO and decrease in patient-reported symptoms that were similar to the results reported by Arabshahi and colleagues in their prospective cohort of patients with JIA treated with CT-guided IAS injections, which documented an increase in MIO by 5 mm in almost half their patients[17]. Further, in a group of patients from our cohort, these improvements in MIO measurements appear to have persisted over time, with an overall trend to increased MIO by the end of the study period. At our institution the cost of TMJ IAS injection performed with CT guidance is roughly twice that of TMJ IAS injection performed without imaging guidance. If future studies confirm these findings, TMJ IAS injection without imaging guidance may be a more cost-effective approach to TMJ treatment.

One patient in this cohort developed steroid atrophy after 5 injections. It is unclear if patients undergoing injection of their TMJ without imaging guidance are at higher risk for steroid atrophy, or if the risk of atrophy is associated with multiple injections of the TMJ or injection of severely abnormal TMJ, regardless of technique. We found no increased incidence of additional adverse events in the short term or over the significant followup period.

In the report by Arabshahi, *et al*[17], 77% of participants reported resolution of their TMJ symptoms after IAS injection. Our patients had a similar decrease in symptoms and 84% had no documented symptoms at the last visit of the study period. However, a larger proportion of patients in our series were asymptomatic at baseline (40%). In the same report[17], no patient had resolution of jaw deviation noted on baseline examination. In our series, 3 of 5 patients had resolution of deviation during the study period. Whether this is a result of the longer followup period, or decreased inflammation and pain, or due to differential TMJ examination documentation by healthcare providers requires further exploration.

A subset of patients in our cohort had disease progression over time documented by CT, despite one or more IAS

injections and an escalation in systemic medications. On average, this group of patients did not have a statistically significant increase in their MIO following injections. In contrast to results reported by Wenneberg and colleagues[22] from a series of 16 adults followed for 8 years after IAS injections who were reported to have evidence of remodeling and remineralization of the mandibular condyle on plain radiographs, radiographic improvement was seen in only 2 patients in our series. However, followup imaging in our cohort was likely to be obtained for patients with more severe disease, biasing the sample towards more severe disease.

Importantly, the effects of multiple TMJ IAS injections in children with JIA have not been reported previously. While children who underwent more than one injection in this series had a mean baseline MIO and improvement in MIO following first injection similar to those children who had only one injection, the children who underwent more than one injection did not have a statistically significant increase in their MIO following additional injections. This finding may be a result of selection bias, because patients with more severe disease are more likely to be referred for additional injections; or it may reflect that the patients in this series tended to have advanced disease with abnormalities already present at first imaging; or it may indicate that there is no additional benefit to multiple injections of the same TMJ. The reason for this decreased response requires further investigation.

Our report is limited by the small sample size, observational design, and lack of a control group. We are unable to account for missing data, incomplete documentation, lack of standardized injection protocol, lack of routine clinical and radiographic followup, and the limited use of gadolinium-enhanced MRI for tracking disease. The results of this series may also be confounded by the effects of systemic medications, as there was an increase in systemic medication use over the study period, reflecting the tendency for TMJ damage to occur early in the disease course prior to the initiation of systemic medications, and also reflecting that patients with evidence of joint damage tend to receive more medications. The sample is likely biased by physician behavior regarding the decision to order baseline and followup TMJ imaging and to refer the patient to oral and maxillofacial surgery. However, the majority of patients in our clinic with TMJ arthritis documented on CT, an abnormal examination result, or significant symptoms are referred to oral and maxillofacial surgery and undergo IAS injection. Therefore, we were unable to identify a sufficient control group of patients with radiographic evidence of TMJ disease who did not undergo IAS injection. As a result, we are unable to draw conclusions regarding a causal association between increased MIO and reduction in TMJ signs and symptoms with TMJ IAS injection.

MIO measurements are likely subject to variability and were performed by physicians who were aware of the patients' injection status. Measurements were not documented before and after every injection for each patient. However, we anticipated that the documented data would represent the patients with the worst TMJ disease, as their TMJ examination would be more likely to be followed closely and more frequently than those patients whose TMJ complaints or physical examination findings improved. This series therefore most likely represents the patients with the most severe disease and would be expected to identify adverse events and treatment failures. Because all but one patient in this series had TMJ damage documented prior to injection, it is not possible to make conclusions about the efficacy of IAS injection in early disease.

Our results reinforce prior data indicating that destructive TMJ arthritis in JIA occurs early in the disease course and is frequently asymptomatic. Systematic and prospective evaluation is required on the role of IAS injection in early TMJ disease and in the context of more systemic medications, to determine the optimal balance and timing of therapies to prevent and treat joint damage.

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