Temporomandibular Disorders and Juvenile Idiopathic Arthritis: Scoping review with a case report

D. Viscuso, M. Storari, M. Aprile, G.Denotti

University of Cagliari, Department of Surgical Sciences, Dental School Medicine

e-mail: d.viscuso@libero.it

DOI 10.23804/ejpd.2020.21.04.9

Abstract

Background Juvenile Idiopathic Arthritis (JIA) encompasses a wide range of mostly idiopathic autoimmune arthritis which affect growing individuals. Temporomandibular disorders are a diffuse spectrum of diseases which involve temporomandibular joint (TMJ) and associated structures. However, much more need to be defined in order to detect and manage these conditions. Albeit satisfying evidences exist about their impact on the adult population, there is great lack of information in children. The current study has been developed in order to overview what it is known about these disorders and their mutual interactions. A case report as support to the scientific evidence has been further described.

Case report A 7-year-old patient affected by an undifferentiated form of JIA developed arthritis to TMJs, complaining pain and functional impairments. After 2 years, the follow-up with combined pharmacological therapies and a modified oral stabilisation appliance shows no objective worsening of the joints' structures. However, the more complex symptomatic management of inflammation highlights the need for further knowledge.

Conclusion The present study shows that both literature and clinical activity highlight a strong relationship between JIA and TMDs, that can affect the quality of life of children and adolescents. Diagnosis and management of these conditions are extremely complex, thus additional studies and evidence are needed. However, the need of an interdisciplinary approach between rheumatologists, paediatricians and dentists has been demonstrated.

KEYWORDS Temporomandibular disorders children; Juvenile Idiopathic Arthritis; Temporomandibular disorders treatment.

Introduction

Juvenile Idiopathic Arthritis (JIA) represents a main public health concern in children and adolescents. The term encompasses a wide range of mostly idiopathic autoimmune arthritis which affect growing individuals. However, much more needs to be defined in order to detect and manage these conditions.

Temporomandibular disorders are a diffuse spectrum of diseases which involve temporomandibular joint (TMJ) and associated structures. Albeit satisfying evidences exist about their impact on the adult population, there is great lack of information about children.

The aim of the present manuscript is to highlight the potential correlation between Temporomandibular Disorders (TMDs) and Juvenile Idiopathic Arthritis (JIA). Additionally, the authors report the case of a 7-year-old patient.

Methods

The aim of the current manuscript is to highlight the potential correlation between Temporomandibular Disorders (TMDs) and Juvenile Idiopathic Arthritis (JIA). A brief scoping review of the literature is reported about both the impact and the outcomes of TMDs in children and adolescents, and the involvement of Temporomandibular Joints (TMJ) in individuals affected by JIA. For this purpose, a search in Pubmed has been performed using as key terms "Temporomandibular Disorders children", "Juvenile Idiopathic Arthritis", "Temporomandibular Disorders treatment". Only full-length original publications dealing with human subjects have been taken into consideration.

Additionally, the authors describe a case report of a 7-year-old patient treated at the Dental Clinic of the University of Cagliari, Italy. The entire management and follow-up have been developed in accordance with the good clinical practice. The patient and his parents were informed about all the procedures and a written informed consent was signed. The patient and his parents gave also the consent for publication. Ethical approval for this study was not necessary as this is a retroactive single-case summary.

Scoping review

TMDs in children

TMDs refer to a wide range of TMJ disorders, masticatory muscles disorders, headaches and disorders affecting the

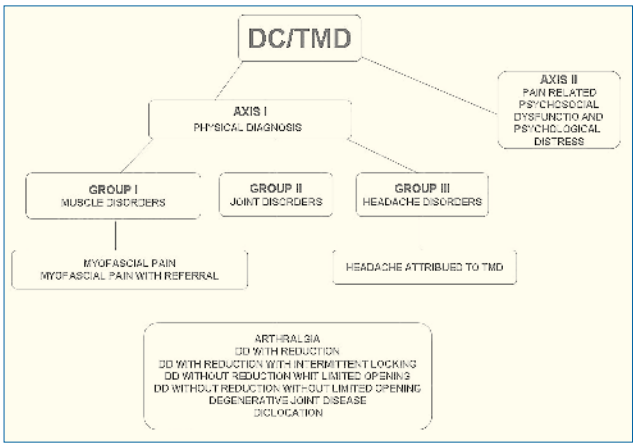

FIG. 1 Diagnostic Criteria for Temporomandibular Disorders.

associated structures [Sciffman et al., 2014]. If diagnosed late, TMDs may cause irreversible destruction of the articular system and abnormal craniofacial growth during youth [Kang et al., 2017]. The prevalence of TMDs in young populations varies between 16.3% and 68%, probably because of differences in studies' methodologies [Fernandes de Sena et al., 2013]. Nevertheless, according to the Research and Diagnostic Criteria for Temporomandibular Disorders (RDC-TMD) [Dworkin and LeResche, 1992], considered as the gold standard for TMD diagnosis, or to the more recently modified Diagnostic Criteria for Temporomandibular Disorders (DC-TMD) (Fig. 1) [Sciffman et al., 2014], the frequency increases up to 34.9% [de Paiva Bertoli et al., 2018]. Myofascial Pain and Disc Displacement With Reduction appeared the most common diseases [de Paiva Bertoli et al., 2018]. Female gender is a potent predictor of TMDs [de Paiva Bertoli et al., 2018] due to sex-related differences in the somatic perception of pain and in self- reported symptoms, depression and anxiety, and hormones. Approximately 23% of post-pubertal girls show depressive symptoms, in contrast to 11% of boys [LeResche et al., 2005]. In addition, estrogens seem to represent a further risk factor. Estrogen Receptor Alpha (ESR1) gene is suggested to be associated with TMDs and β-estradiol has appeared to increase TMJ deterioration [Ribeiro-Da Silva et al., 2009]. Conversely, testosterones seem to play a protective role [Fischer et al., 2007] and to reduce joint mobility. However, other authors [Marpaung et al., 2018] reported contradictory results and no sex-correlation.

TMDs begin to increase with puberty since they affect 23.4% of children aged 7–12, and 36.9% of adolescents aged 13–18 [Marpaung et al., 2018]. Such age-dependent prevalence may be explained by the hormonal changes [Warren and Fried, 2001] and the mandibular growth spurt that leads to discrepancies between the condylar surface and the articular eminence [Marpaung et al., 2019]. Psychological factors should also not be neglected. Children are less susceptible to depressive symptoms than adolescents [LeResche et al., 2005]. Psychological problems are incontrovertibly recognised as important predictors of pain-related TMDs since the same neurotransmitters are involved in both mood regulation and pain perception. Moreover, stress and anxiety can lead to excessive muscles tension and parafunctional oral habits, which in turn may elicit tenderness and pain of masticatory muscles and onset of TMJ sounds [Alamoudi, 2001]. Bodily pain has been also hypothesised as another important risk indicator for TMDs in adolescents [LeResche et al., 2005; Marpaung et al., 2018]. With regards to the genetical susceptibility, evidences suggested the association of TMDs with several genes: COMT, HTR2A, NR3C1, CAMK4, CHRM2, IFRD1, and GRK5 seem to be the most significant [Smith et al., 2011]. The multifactorial aetiology of TMDs entails also biomechanical causes. Heavy, compressive and recurrent forces on TMJs due to oral parafunctions contribute to alter the normal function of the masticatory muscles and the proper interrelationship between the condyle and the disc [Alamoudi, 2001]. There are no sufficient evidences to support the impact of malocclusions [Stein et al., 2017] and socioeconomic status [Marpaung et al., 2018]. Lastly, the American Academy of Pediatric Dentistry [2015] assesses that TMJs can be further affected by trauma, rheumatoid arthritis, developmental alterations and tumours.

The major complaint of the patients is usually pain of TMJs or masticatory muscles, perceived as steady and dull, and associated with function [Okeson et al., 1992]. Pain increases with age due to the higher adaptability of the masticatory system in younger patients and has a great negative impact on children and adolescents daily living [List et al., 2001]. In addition, patients affected by TMDs reported more psychological comorbidities if compared to normal individuals [List et al., 2001]. Joint sounds are common findings; noises can be provoked by the anterior displacement of the disc, changes in the articular surfaces, hypermobility of the disc-condyle complex, and degenerative phenomena [Wabeke et al., 1994]. However, they could even represent normal clinical outcomes [Wanman and Agerberg, 1990] because of the continuous remodeling of TMJs in children. Click is persistent only in 5% of children [Torii, 2011] and crepitations are rarely present [Wanman and Agerberg, 1990]. Jaw function is also affected with restricted and/or altered lateral and/or opening movements [Fernandes de Sena et al., 2013]. There is growing evidence that TMDs patients complain higher frequency of headaches, and neck pain and headaches tend to precede TMDs in adolescents [Nilsson et al., 2013]. By contrast, the relationship between head/neck posture and TMDs remains inconclusive [Olivo et al., 2006]. Furthermore, degenerative processes involving TMJs alter the craniofacial growth leading to a backward positioned mandible, hyperdivergent facial profile, increased overjet and delayed dental development [Kang et al., 2017].

There is the need of more univocal tools and methods to establish TMDs diagnosis in children and adolescents. However, the RDC-TMD (Research Diagnostic Criteria for Temporomandibular Disorders) showed accurate reliability [Christidis et al., 2019] and, furthermore, they comprise the most acceptable standard for TMD research. The revised version, i.e. the DC-TMD, has not yet been validated in children [Christidis et al., 2019]. Several questionnaires may be also used to assess the psychological impact. However, in order to correctly define TMDs, an appropriate instrumental diagnostic method is necessary. Magnetic Resonance Imaging (MRI) is considered the gold standard to examine the disc-condyle complex, the synovia layers and joint enhancements [Junhasavasdikul et al., 2018].

Dentists do not have enough experience and knowledge in the management of TMDs and orofacial pain in children and adolescents. Hence, it is crucial to provide information about the effectiveness of treatment modalities. A correct and early diagnosis is indeed essential to minimise and prevent subsequent disabling consequences [Kang et al., 2017].

Furthermore, practitioners must consider any potential negative effects on the oral health prior to any form of interventions since children and adolescents are growing individuals. Resilient occlusal appliances are indicated as standard therapy for adults, but few evidences exist for children. They are suggested to be used in combination with information in adolescents with late mixed or early permanent dentition [Wahlund et al., 2003]. Behavioural modifications with the aim to control oral parafunctions and diurnal bruxism are additional major goals to achieve [Alamoudi, 2001]. Lastly, with regards to the treatment of malocclusion, as the risk and impact on TMDs is not predictable, growing individuals should be followed longitudinally. Orthodontic therapy should be evaluated in order to solve potential occlusal problems after symptoms' stabilisation, possibly taking advantage of growth itself to simplify adaptation [Bilgic and Gelgor, 2017].

Juvenile idiopathic arthritis and TMDs

JIA usually affects TMJs. JIA is defined as "Arthritis of unknown aetiology that begins before the 16th birthday and persists for at least 6 weeks; other known conditions are excluded" [Petty et al., 2004]. Seven different subtypes have been described according to the most recently revised classification of the International League of Associations for Rheumatology (Table 1) [Petty et al., 2004]. The prevalence of TMJs involvement in JIA appears highly underestimated, as it is reported to peak up to 93% of affected patients, with a prevalence among females [Kuseler et al., 2005]. Inflammatory active states of the intra-articular structures are challenging to diagnose because patients are often asymptomatic. Pain should not be considered a reliable indicator because it is reported by only 25% of patients with radiographic signs of the disease. Joint sounds, such as click and crepitus, tenderness upon palpation and during mouth mobility, anterior rotation of the jaw, lateral and forward movements limitations, and reduced and deviated mouth opening can be present in different combinations. Furthermore, paediatric rheumatologists tend not to consider TMJ as the other joints. Therefore, usually a more qualitative assessment is performed to investigate TMJ and the diagnosis is prone to subjectivity and operator variability [Frid et al., 2017].

The diagnostic gold standard to evaluate the suspected TMJs involvement in JIA patients is MRI with Gadolinium, which shows degenerative signs in approximately 39%–75% of patients [Cannizzaro et al., 2011; Muller et al., 2009]. A common finding for early detection of arthritis is synovitis. However, even if considered a good indicator of the disease, there is no standardised quantitative method to distinguish the synovial thickening in healthy subjects than to that of inflammatory arthritis [Muller et al., 2009]. A recent retrospective study [Resnick et al., 2016] proposed the comparison of signal intensity between the synovial membrane and the longus capitis muscle, used as control. This technique showed a sensitivity of 91%. Thus, it appears reliable and tends to provide consistent results.

Since TMJs arthritis in patients with JIA is often asymptomatic, it is generally diagnosed when there are already noticeable morphological changes in hard structures. Condyle flattening, osteophytes, bone erosions and sclerosis, and subchondral cysts are the main radiographic findings [Cedstromer et al., 2013]. In the light of these evidences the therapeutic approach appears even more complicated.

TMJs' involvement in JIA is demonstrated to increase the worsening of patients' quality of life. Damages of TMJs may be responsible for orofacial pain, malocclusions and micrognathia. Such alterations can lead to difficulties in many daily activities, including eating, chewing, talking, smiling and keeping oral hygiene [Leskell et al., 2008]. Furthermore, JIA patients suffering from TMJs arthritis tend to have a worse prognosis because of the longer duration of the disease, defined as the time spent following the diagnosis. Moreover, higher inflammatory activity and more probabilities to develop polyarticular forms of the disease deteriorate the outcomes. The impact of such issues alters both physical and emotional well-being of children, lowering their quality of life. To assess the global influence of JIA several questionnaires have been developed over time with the purpose to evaluate more

Systemic Arthritis
One or more joints with or preceded by daily fever for at least 2 weeks 'duration and for at least 3 days; one or more must be present: evanescent erythematous rash; generalized lymph node enlargement; hepatomegaly and/or splenomegaly; serositis.
Exclusions: a, b, c, d.

Oligoarthritis
One to 4 joints during the first 6 months of disease. Two subcategories are recognized: Persistent oligoarthritis affecting not more than 4 joints throughout the disease course; Extended oligoarthritis affecting more than 4 joints after the first 6 months of disease.
Exclusions: a, b, c, d, e.

Polyarthritis (Rheumatoid Factor negative)
Five or more joints during the first 6 months of disease; a test for RF is negative.
Exclusions: a, b, c, d, e.

Undifferentiated Arthritis
Arthritis that fulfills criteria in no category or in 2 or more of the above categories.

Polyarthritis (Rheumatoid Factor positive)
Five or more joints during the first 6 months of disease; 2 or more positive RF tests at least 3 months apart during the first 6 months.
Exclusions: a, b, e, e.

Psoriatic Arthritis: arthritis and psoriasis, or arthritis and at least 2 of the following: dactylitis; nail pittingor/onycholysis; psoriasis in a first-degree relative.
Exclusions: b, e, d, e.

Enthesitis Related Arthritis: arthritis and enthesitis, orarthritis or enthesitis with at least 2 of the following: presence or history of sacroiliac joint tendemess and/or inflarnmatory lumbosacral pain; presence ofHLA-B27 antigen; onset of arthritis in a male over 6 years of age; acute (symptomatic) anterior uveitis; history of ankylosing spondylitis, enthesitis related arthritis, sacroiliitis with inflarnmatory bowel disease, Reiter's syndrome, or acute anterior uveitis in a first-degree relative.
Exclusions: a, d, e.

Exclusion criteria
a. Psoriasis or a history of psoriasis in the patient or first degree relative.
b. Arthritis in an HLA-B27 positive male beginning after the 6th birthday.
c. Ankylosing spondylitis, enthesitis related arthritis, sacroiliitis with inflammatory bowel disease, Reiter's syndrome, or acute anterior uveitis, or a history of one of these disorders in a first-degree relative.
d. Presence of IgM rheumatoid factor on at least 2 occasions at least 3 months apart.
e. Presence of systemic JIA in the patient.

TABLE 1 Classification of JIA according to the International League of Associations for Rheumatology.

appropriately children difficulties and abilities to perform daily actions. The C-HAQ and CPQ—both validated in several languages—have been approved for these purposes [Ruperto et al., 2001]. C-HAQ and CPQ questionnaires have shown a good reliability in defining the association between the disability due to the clinical outcomes of the involvement of TMJs and the subsequent lower quality of life in children [Frid et al., 2017].

In the present scenario the orthopantomogram, despite unable to highlight active inflammatory processes, is recommended during routine dental examinations. It can be a screening tool to diagnose early TMJs involvement in JIA patients via quantitative measures of the ratios between the length of the condyle, the branch and the body of the jaw [Klenke et al., 2017].

Case report

A 7-year and 10 months old patient came to our observation at the Dental Clinic of the University of Cagliari, Italy, in January 2018. The major complaints were the functional limitation in mouth opening associated with pain while chewing.

Anamnestic data collection revealed the presence of Thalassemic Trait and JIA, diagnosed in 2016. The first suspected episode occurred in March 2016, due to the onset of right gonalgia accompanied by ipsilateral swelling, lameness and fever, initially treated with Ibuprofen. In May 2016 at the pediatric department of the Antonio Cao Hospital, Cagliari, after further clinical investigations and haematochemical examinations, the patient was diagnosed with JIA in the form of undifferentiated arthritis. The positivity to Antinuclear Antibodies (ANA) was confirmed. As the disease worsened, the following month the patient was started on treatment with Methotrexate, 10 mg once per week. In December, Triamcinolone Hexacetonide was injected in the right knee in order to treat swelling, morning stiffness and pain. Meanwhile the patient started to complain pain and dysfunction to TMJs. Therefore, he was sent to our observation.

The physical evaluation was performed according to the RDC-TMD. It was demonstrated the presence of tenderness upon palpation of chewing muscles and TMJs, whereas no joints' sounds were detected. Likewise, no spontaneous pain was referred, albeit the mother reported nocturnal grinding and clenching. In April 2018, a Magnetic Resonance (MRI) of the TMJs was prescribed and behavioural indications were provided in order to avoid excessive activity of chewing muscles and excessive loads to the TMJs during wake. The MRI showed atrophy of both condyles, severe on the left side and milder to moderate on the right side. The opening of the mouth measured 34 mm. The patient reported also some improvement of painful symptoms related to chewing.

Therapy with an oral stabilization appliance was recommended, in order to prevent the negative potential consequences associated to nocturnal bruxism and TMJ loading. A maxillary, customised, full-arch covering hard acrylic appliance was delivered. The appliance was provided of a central expansion screw to allow normal growth (Fig. 1). The device was checked and adapted regularly and signs of wear typical of bruxism were always found. Pain and function in the facial district markedly improved.

As part of the periodic follow up, in November 2018 a new MRI scan of the TMJs was taken, which showed the presence of intra-articular effusion on the right side and still severe atrophy of the left condyle. Methotrexate was replaced by Etanercept. In January 2019 the patient reported a significative worsening of the overall systemic symptoms, associated with dull pain related to chewing muscles and TMJs. Headaches, dizziness, abdominal pain and constipation were also reported. The haematochemical tests revealed only a mild aeosinophilia which was attributed to the drug therapy. To avoid new more invasive exams, ultrasounds were performed to evaluate TMJs whose involvement was the main complaint of the patient; bilateral hyperaemia and effusion were found. Additionally, fibromyalgic syndrome was diagnosed.

FIG. 2 Upper, customised, hard and full arch covering acrylic appliance with a central screw of expansion to allow modifications in amplitude of the maxillary bone.

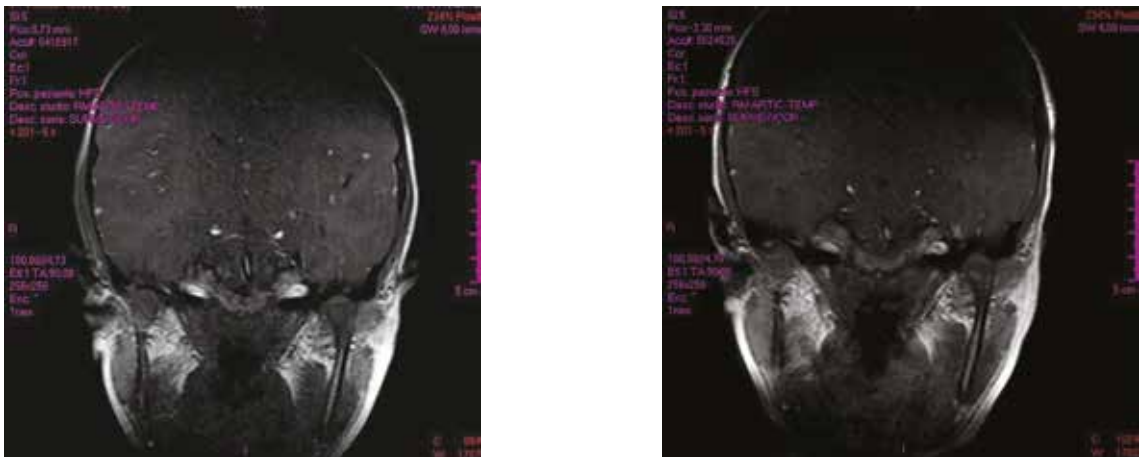

FIG 2 Coronal view of TMJs before treatment (left) and after 2 years of treatment (right).

The subsequent visit to our University Clinic highlighted the presence of normal mouth opening, 44 mm, and pricking pain elicited by palpation of both TMJs and chewing muscles. Allodynia and secondary hyperalgesia were also detected in the whole body, included the facial district. This was compatible with one of the centrally mediated chronic pain syndromes.

In July, Etanercept therapy was suspended because of the constant and progressive deterioration of the clinical picture. No other medications were prescribed. The overall symptomatology subsided after few weeks. Therefore, in November, Etanercept was reintroduced.

The visit made at our University Clinic in the following month revealed still adequate mouth opening (> 40 mm), and the lack of pain and tenderness upon palpation of chewing muscles and TMJs. In January 2020 a new MRI was prescribed and it was observed the presence of condyles' atrophy and mild bilateral effusion. However, the images collected did not show a significant difference compared to the previous exams about intracapsular structures and articular surfaces (Fig. 2–5). The patient is still under our supervision

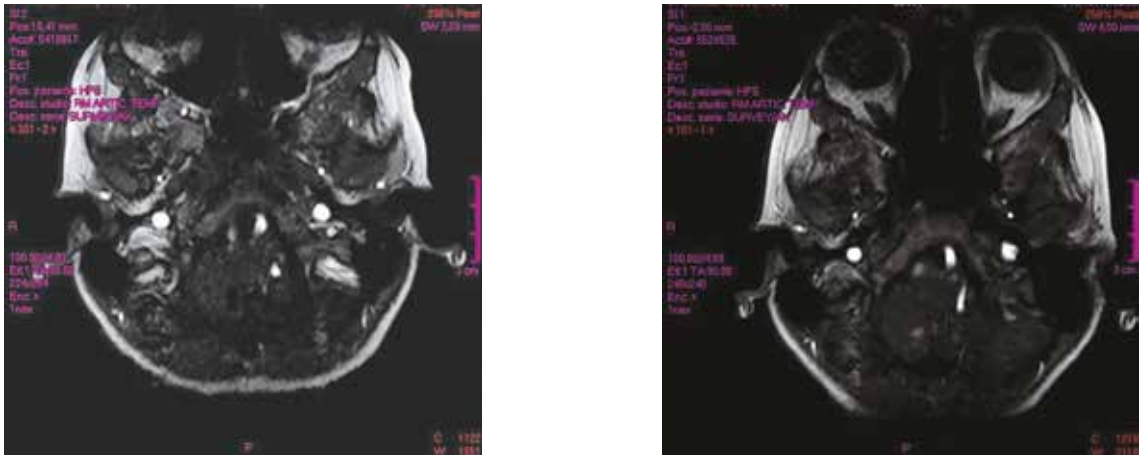

FIG. 3 transversal view of TMJs before treatment (left) and after 2 years of treatment (right).

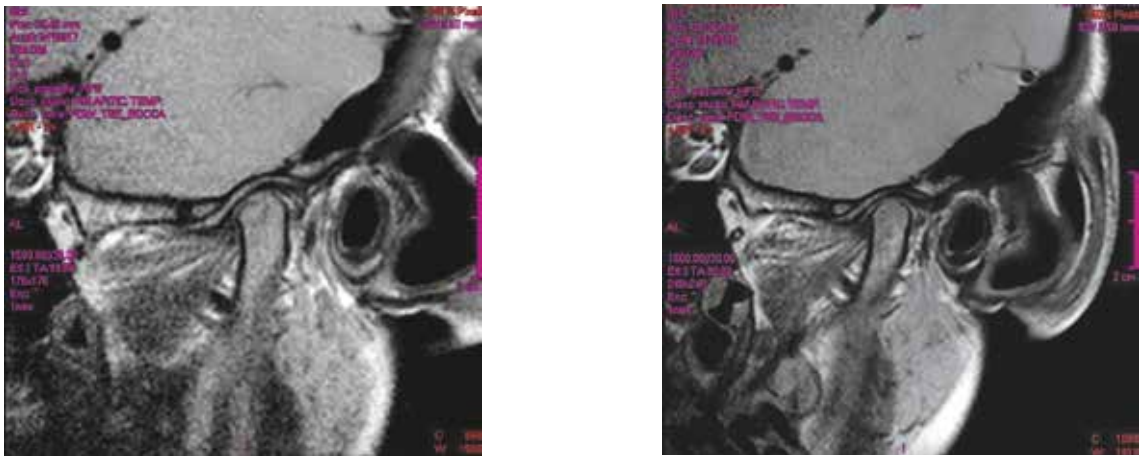

FIG. 4 Sagittal view of left TMJ in close mouth position before treatment (left) and after 2 years of treatment (right).

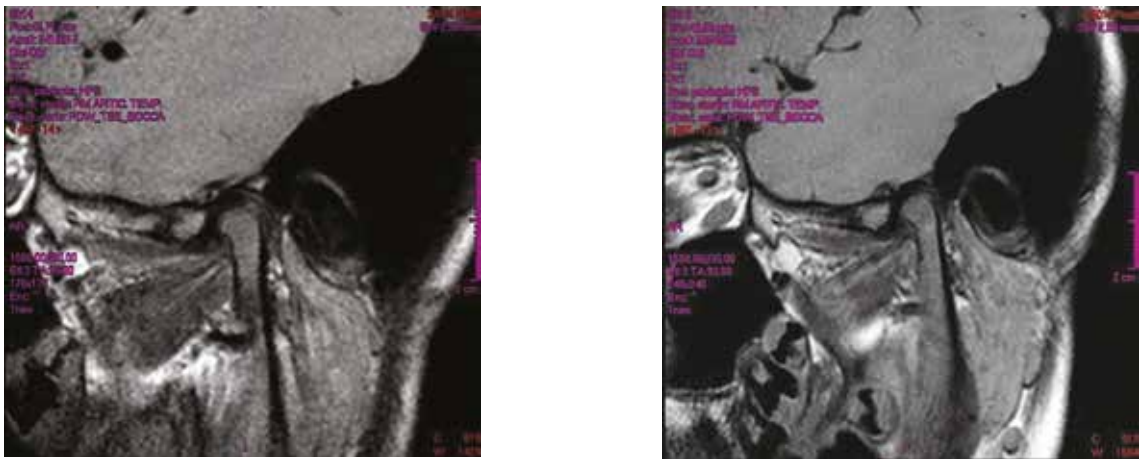

FIG. 5 Sagittal view of right TMJ in close mouth position before treatment (left) and after 2 years of treatment (right).

and, when possible, an orthodontic treatment should be considered.

Conclusion

The current study shows that both literature and clinical activity highlight a strong relationship between JIA and TMDs, and how this can affect the quality of life of children and adolescents. Furthermore the diagnosis and the management of such conditions are extremely complex, thus additional studies and evidence are required. However, the need of an interdisciplinary approach between rheumatologists, paediatricians and dentists has been demonstrated.

Conflict of interest statement

All authors disclose no financial and personal relationships with people or organizations that could inappropriately influence this manuscript.

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