Psoriasis and Temporomandibular Joint Involvement: An Epidemiologic Survey

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Abstract

Background
Psoriatic arthritis (PsA) is a chronic, inflammatory, seronegative arthropathy associated with psoriasis, which is usually diagnosed years after the occurrence of psoriatic skin disease.

Although the CASPAR criteria has been adopted as standard, the temporo-mandibular joint (TMJ) has been neglected.

Up to date, the association between Psoriasis or PsA and Temporomandibular disorders (TMD) is poorly documented in the literature, although a possible linkage between these entities could be represented by the inflammatory pathway.

Objective
The goal of this work is to demonstrate how the TMJ could be involved in the pathological process of PsA and that it can be the first manifestation of the disease.

Results
The Maxillo-Facial consultation highlighted that in 61 patients with psoriasis (Group 1), forty patients (65.4%) showed signs and symptoms of TMJ involvement without signs or symptoms of PsA of the remaining joints; while all patients (100%) of Group 2 (33 patients with PsA) had TMJ involvement.

Conclusion
Concerning the similarity of pathogen ethic mechanisms for joint involvement in PsA and TMDs we can confirm the associations between the two pathologies in connection with the statistic comparison on the healthy group of controls.

Keywords: Psoriatic Arthritis; Psoriasis; Temporo-Mandibular Disorders; Temporo-Mandibular Joint.

Introduction
Psoriatic arthritis (PsA) is a chronic inflammatory arthropathy associated with psoriasis. PsA is classified among the seronegative spondyloarthropathies, characterized by joint destruction, extra-articular involvement (i.e. eye, gut, bowel, ureter), and a negative rheumatoid factor.

Psoriasis is immunologically mediated by aberrant skin-directed T-cells. Recent progress shows that Th1/Th17 type T-cell subsets play a distinct role in the pathogenesis of psoriasis. Th17 cells are activated by interleukin-23 (IL-23) released from dendritic cells (DC), tumour necrosis factor-α (TNF-α) and inducible nitric oxide synthase (iNOS)-producing DC. The Th17 subsets release IL-17A and IL-22, which promote neutrophil and keratinocyte hyper proliferation, respectively. Also, IL-17 proliferates downstream inflammatory molecules [1].

Similarly to the skin, the joints and inflamed entheses in PsA are invaded by a prominent lymphocytic infiltrate with activated T-cells and T-cell derived cytokines, including IL-1, IL-2, IL-10, IFN and TNFα [2].

The connection between arthritis and psoriasis was first observed by Alibert in 1818 and identified as a clinical entity by Bazin in 1860 [3,4] but the first set of criteria to define PsA was published by Moll and Wright in 1973 that proposed several variants of disease [5].

PsA exhibits, in fact, a wide range of clinical presentations. The recently published set of classification criteria for psoriatic arthritis known as CASPAR (Classification criteria for Psoriatic Arthritis) has been adopted as standard [6, 7]. Even though CASPAR has a specificity of 98.7% and a sensitivity of 91.4% for diagnosis, the temporo-mandibular joint (TMJ) has been neglected.

The clinical features of TMJ involvement are actually really complex.

Temporomandibular disorders (TMD) are a heterogeneous group of pathologies affecting the temporo-mandibular joint (TMJ) and/or the jaw muscles. They are characterized by a classically described triad of clinical signs: muscle and/or TMJ pain; TMJ sounds; and...
restriction, deviation, or deflection of the mouth opening path. Additional symptoms, often associated with TMD, are headache, cervical pain, brachialgia, ear fullness, tinnitus and vertigo. These symptoms may be present without TMJ local tenderness or swelling [8, 9].

In literature there are few data about the association between Psoriasis or PsA and TMD although we know that a possible trait d’union between these three entities could be represented by the inflammatory pathway. It’s widely accepted that inflammation together with biomechanical stress and trauma represents the first issue in determining TMDs [10, 11].

This triad has been theorized as responsible for the joint or enthesis up-regulation of proinflammatory cytokines in genetically susceptible subjects with PsA [12].

The triggering role of these factors in TMJ increases the levels of proinflammatory cytokines and free radicals on the synovial fluid such as IL-1, IL-2, i NOS, IL-6, IL-8 IL-10, IFN-γ AND TNF-alpha. Inflammation of the synovial membrane alters the synovial fluid (SF) viscosity and leads to impairment in the lubrication and nutrition of the articular cartilage and disk. This cascade of events leads to articular damage in the different features of TMDs.

Our aim was to perform an observational study, in order to demonstrate how the TMJ may be involved in the pathological process of PsA and how it can be the first manifestation of the disease.

**Materials and Methods**

A total number of 157 patients were screened at the outpatient service of the “Dermatological Clinic, Policlinico Umberto I, Sapienza University of Rome”. A Group of 80 healthy people (no diagnosis of PsO, PsA or TMDs) served as control.

All patients with an age ≤18 years old, and with active psoriatic skin lesions or a documented history of psoriasis, have been included in the study.

We have excluded from the analysis patients that have performed a systemic treatment (cyclosporine, tacrolimus, DMARDs or oral retinoids) in a period ≤ 4 weeks from the baseline and patients that have performed an anti TNF-alpha therapy ≤ 12 weeks. Regarding the maxillo-facial consultation, we have excluded from the analysis patients with a dento-skeletal malocclusion, vertical height loss, history of traumas, and parafunctional habits such as clenching or grinding.

Enrolment screening procedures included both Dermatologic and Rheumatologic visits, a routine laboratory test, rheumatoid factor (RF) status, Antibodies to cyclic citrullinated peptide (anti-CCP), evaluation of CASPAR criteria, Dermatology Life Quality Index (DLQI) and Psoriasis Area Severity Index (PASI) [13].

Joint disease parameters assessed included swollen and tender/ painful joint counts (66 swollen/68 tender joint counts (JC66/68)), presence of spondylitis and/or enthesities and joints ultrasound scans (hands, feet, elbows, knees).

Data were recorded on standardized forms and included demographics (sex, age), psoriasis history (whether currently evident or previously observed, nail involvement), time of onset of skin disease and associated co morbidity.

At baseline, mean age of patients was 54 years old, with mean psoriasis duration of 14 years; mean PASI score of 15, 5 and a mean DLQI was 26.

According to the enrolment screening procedures described, patients were divided, upon opinions by dermatologist and rheumatologists with long standing expertise, into two groups: patients affected by psoriasis (PsO) and patients affected by arthropatic psoriasis (PsA).
Clinical evaluation was performed to measure mandibular kinetics, disc displacement with reduction (DDWR), disc displacement without reduction (DDWOR), osteoarthritis. Correlated symptoms such as headache, neck pain, brachialgia, tinnitus or vertigo were evaluated with a Visual Analogue Scale (VAS) [14, 15, 16, 17].

All positive patients to TMJ assessment underwent orthopantomography and dynamic TMJ Magnetic Resonance.

Analysis of variance (ANOVA) was performed to test for the existence of differences in all the variable means, with significance level set at P less than 0.05.

**Results**

Among the 94 stratified patients, 61 patients (group 1) were affected by psoriasis and the remaining 33 patients by PsA (group 2).

The Maxillo-Facial consultation highlighted the following results. In Group 1 forty patients (65.4%) showed signs and symptoms of TMJ involvement without signs or symptoms of PsA of the remaining joints. Thirty-three patients (100%) of Group 2 had TMJ involvement.

TMJ local pain showed higher levels in Group 1. Accordingly headache and neck pain resulted to be higher in this group. Dealing with brachialgia the highest levels were recorded in Group 1. Tinnitus and vertigo were significantly higher in the PsA sample as well as the prevalence of clinical DDWR and DDWOR or crepitus indicating internal derangement.

Mandibular kinetics showed mean values close to the normal population for Group 1, while in Group 2 the range of motion was considerably reduced. In particular the opening pattern was characterised by deviation in 16 patients for Group 1 and 10 patients for Group 2.

Orthopantomography and MRI were examined together for each patient to highlight condylar profile remodelling, disk displacement and osteoarthritis signs. Disk displacement was observed in 5 (17%) patients in Group 1 and 19 cases in Group 2 (57.15%). These results are significantly higher than what is reported in international literature [18].

Osteoarthritis was observed in 3 (11.54%) cases in Group 1 and 12 (35.71%) in Group 2.

Osteophytes and condylar flattening were seen in 27% of all cases, erosions in 13%, and sclerosis in 9%. Our results confirmed that the prevalence of osteophytes and flattening was significantly higher in patients with TMJ dysfunction such as DDWR and DDWOR.

**Discussion**

The estimated frequency of PsA in psoriatic patients is quite spread and varies from 1% to 39%. This wide range may be explained by the different case definitions, the different settings (rheumatology or dermatology clinics) and to the length of follow up [19].

These achievements markedly improved the management of PsA in the daily clinical practice and led to suggestions in assessing the disease-related activity [20].

Pathology of the TMJ affects an important part of the population, though it is not viewed as a public health problem. Between 3-7% of the population seeks treatment for pain and dysfunction of the TMJ. The literature reports a great variability in the prevalence of the clinical symptoms (6-93%) and signs (0-93%), probably as a result of the different clinical criteria used [21].

The pathogenic mechanisms underlying PsA and TMD have been widely investigated and a common trait is represented by the inflammation cascade. Pro-inflammatory cytokines and especially TNF-alpha are more likely to play a determining role in cartilage degradation by its enhancement on the production of matrix metalloproteinases (MMPs) which in turn mediate cartilage erosion and the increased expression of angiogenic factors (1,10,11).

The path from inflammation to articular damage is well known for PsA. Dealing with TMJ the author’s hypothesis is that inflammation of the synovial membrane alters the synovial fluid (SF) viscosity and leads to impairment in the lubrication and nutrition of the articular cartilage and disk. This cascade of events leads to articular damage in the different features of TMDs.

The similarity of the two pathological entities has never been deeply studied in international literature and the few existing reports present a very small number of cases.

Some authors showed a significant increase of TMD symptoms (TMDs) in patients with psoriasis and, even more, with PsA, as...
Table 4: TMJ involvement in PsA, Pso, healthy group patients

<table>
<thead>
<tr>
<th></th>
<th>PsA/Pso</th>
<th>PsA/healthy group</th>
<th>Pso/healthy group</th>
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<tbody>
<tr>
<td>TMJ dx pain</td>
<td>0.87632</td>
<td>0.02712</td>
<td>0.02198</td>
</tr>
<tr>
<td>TMJ sn pain</td>
<td>0.67353</td>
<td>0.14367</td>
<td>0.09291</td>
</tr>
<tr>
<td>Brachialgia dx</td>
<td>0.06655</td>
<td>0.00239</td>
<td>0.33443</td>
</tr>
<tr>
<td>Brachialgia sn</td>
<td>0.25560</td>
<td>0.09579</td>
<td>0.55490</td>
</tr>
<tr>
<td>Headache dx</td>
<td>0.67731</td>
<td>0.00357</td>
<td>0.00025</td>
</tr>
<tr>
<td>Headache sn</td>
<td>0.26706</td>
<td>0.01287</td>
<td>0.00004</td>
</tr>
<tr>
<td>Neck pain dx</td>
<td>0.86289</td>
<td>0.13334</td>
<td>0.09130</td>
</tr>
<tr>
<td>Neck pain sn</td>
<td>0.99513</td>
<td>0.05612</td>
<td>0.12122</td>
</tr>
<tr>
<td>Max mouth opening</td>
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<td>0.00000</td>
<td>0.00005</td>
</tr>
<tr>
<td>Deviation dx</td>
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<td>0.00000</td>
<td>0.00000</td>
</tr>
<tr>
<td>Deviation sn</td>
<td>0.45725</td>
<td>0.00000</td>
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</tbody>
</table>

Compared to a sample of healthy subjects [22, 23].

Analysing our sample 65% of Group 1 patients and 100% of Group 2 presented TMJ involvement.

This surprising result is more than a mere coincidence as shown by the statistic comparison with the healthy group. Observing the ANOVA results for the comparisons of all variable means between Group 1 and 2 there is no significant difference (P>0.05).

Group 1 patients are traditionally considered “cutaneous”. If we look at the association with TMDs (65% of cases) these patients might require a different diagnosis. TMJ involvement might be considered the first sign of arthropatic involvement of PsA. A careful evaluation of the symptoms shows a strong relation between local TMJ pain, headache and mandibular kinetics thus indicating a significative difference (p<0.05).

If we consider the whole number of TMJ positive patients and the radiological results we found an impressive series of bone erosion and remodelling of the mandibular condyle. This phenomenon, in PsA is a characteristic feature mediated by TNF-alpha over expression within the joint, leading to the increased production of MMPs and cartilage destruction.

These documented bone modifications of the mandibular condyle are commonly observed in the other joints of patients affected by PsA. Moreover considering the particular anatomy and biomechanical restrictions of the TMJ, the articular damage is expressed by DDWR or DDWOR that represents the irreversible joint damage. In association to the radiological findings both Group patients complained of symptoms such as headache, neck pain and brachialgia, vertigo and tinnitus. The difference between healthy controls and the overall prevalence of these clinical and radiological features (Groups 1 and 2 together) is highly significant (p<0.05).

These clinical symptoms alone are usually underestimated by clinicians as isolated records. If we consider all these symptoms globally in association with the condition of a systemic inflammatory disease they might represent the key to the beginning of an arthropatic involvement.

This kind of patients represents a challenge for dermatologists and
rheumatologists that, together with the maxillo-facial surgeons, have the duty of considering an early and sub-clinic articular damage. If underestimated the TMJ damage evolves to its natural history and this process might spread and involve the other joints commonly reported in literature for PsA.

Like other destructive forms of arthritis, PsA responds well to treatment with conventional disease-modifying antirheumatic drugs such as methotrexate (MTX) or leflunomide, as well as biologic agents such as tumor necrosis factor alpha (TNF-alpha) inhibitors, to reduce pain and inflammation and ideally achieve protection from structural damage. During the last decade, considerable progress has been made in the diagnosis, monitoring, and treatment of PsA in the course of multiple clinical trials, which have particularly studied the efficacy and safety of TNF-alpha inhibitors in PsA.

Comparing the TMJ damage to the PsA the systemic treatment for TMDs should be taken into account to prevent and to limit PsA progression.

References