Psoriatic Arthritis

Importance of diagnosis to long-term outcomes

Paolo Gisondi

Overview

• Epidemiology of PsA
• Dermatologist as sentinel of PsA, the importance of early diagnosis
• Therapy of PsA

Definition of Psoriatic Arthritis

Psoriatic arthritis can be defined as an “inflammatory entheso-arthro-osteopathy”, occurring in subjects with psoriasis or with a predisposition to psoriasis, which may involve both peripheral and axial osteo-articular compartment and may be responsible for extra-articular manifestations

Psoriatic disease

Psoriatic disease is a disorder that involves several different compartments in the same patient:
- skin
- enthesis-joint-bone
- nail
- gut
- uvea
- liver
- endothelium

Scarpa R. et al. JEADV 2010

Psoriatic Arthritis: Epidemiology

- Equally prevalent in men and women; peak onset in the late 30s to 50s
- Prevalence of PsA in the general population is 0.16-0.45%
  - The worldwide prevalence of PsA is higher in northern Europe and lower in Japan
- Prevalence of PsA varies greatly in patients with psoriasis from 2% to 42%


Prevalence of PsA in psoriatic patients in Italy

<table>
<thead>
<tr>
<th>First Author</th>
<th>Criteria</th>
<th>Prevalence</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Marco G.</td>
<td>CASPAR</td>
<td>39.7%</td>
<td>Arch Dermatol Res 2012</td>
</tr>
<tr>
<td>Salvarani C.</td>
<td>Moll and Wright, Amor</td>
<td>22%, 24%</td>
<td>J Rheumatol 2005</td>
</tr>
<tr>
<td>Gisondi P.</td>
<td>ESSG</td>
<td>7.7%</td>
<td>Eur J Dermatol 2005</td>
</tr>
<tr>
<td>Scarpa R.</td>
<td>Wright and Moll</td>
<td>34.4%</td>
<td>Br J Rheumatol 1984</td>
</tr>
</tbody>
</table>
PsA most often develops in patients with pre-existing psoriasis

<table>
<thead>
<tr>
<th>Symptomatic Progression</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin Symptoms</td>
<td>Joint Symptoms</td>
</tr>
<tr>
<td>Up to ≈84%</td>
<td></td>
</tr>
<tr>
<td>Joint Symptoms</td>
<td>Skin Symptoms</td>
</tr>
<tr>
<td>≈3%–15%</td>
<td></td>
</tr>
<tr>
<td>Skin and Joint Symptoms</td>
<td>≈13%</td>
</tr>
</tbody>
</table>

Verona outpatients Clinic (June 2006-April 2013)

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Number of patients</td>
<td>2046</td>
</tr>
<tr>
<td>Male</td>
<td>63%</td>
</tr>
<tr>
<td>Age</td>
<td>55.2 ± 12.5</td>
</tr>
<tr>
<td>BMI</td>
<td>26.9 ± 4.8</td>
</tr>
<tr>
<td>Prevalence of PsA</td>
<td>43%</td>
</tr>
<tr>
<td>Age at diagnosis of psoriasis</td>
<td>39.3 ± 13.1</td>
</tr>
<tr>
<td>Age at diagnosis of PsA</td>
<td>49.4 ± 9.2</td>
</tr>
</tbody>
</table>

The dermatologist plays a pivotal role in the early diagnosis of PsA

- Identification of possible PsA in patients with psoriasis.
- Appropriate referral to the rheumatologist.
- Early diagnosis prevents joint damage and may improve long-term outcome.
The risk of PsA remains constant following the initial diagnosis of psoriasis

Incidence and cumulative prevalence of PsA over time in a population of psoriasis patients

The risk of PsA remains constant following the initial diagnosis of psoriasis.

Underdiagnosis of PsA in Psoriasis Patients

Two observational studies assessed the prevalence of PsA among patients with plaque-type psoriasis who were seen by dermatologists:

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients with plaque type PsO, n</th>
<th>Patients with PsA, %</th>
<th>Of the total number of patients with PsO evaluated, percentage of patients that were newly diagnosed with PsA, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reich et al</td>
<td>1,511</td>
<td>20.6</td>
<td>17.6</td>
</tr>
<tr>
<td>Radtke et al</td>
<td>2,009</td>
<td>19</td>
<td>4.2</td>
</tr>
</tbody>
</table>

PsO=psoriasis; PsA=psoriatic arthritis.

PsA=psoriatic arthritis; PsO=psoriasis.

Do patients with psoriatic arthritis who present early fare better than those presenting later in the disease?

- METHODS: Patients followed prospectively were divided into those first seen within 2 years of diagnosis (group 1; 436 patients) and those seen with more than 2 years of disease (group 2; 641 patients).
- RESULTS: Patients in group 2 were older, had longer duration of psoriasis and PsA, more joint damage and were less likely to be treated with DMARDs. After adjusting for age, sex, education level, clinical joint damage at first visit and treatment, group 2 had significantly greater rate of clinical damage progression compared with group 1.
- CONCLUSIONS: These results suggest that patients with PsA should be treated earlier in the course of their disease.

Dermatologist and rheumatologist combined consultation

- Dedicated to
  - patients with psoriasis who complain articular symptoms like pain or morning stiffness.
  - patients with a definite rheumatological diagnosis and skin lesions
- Optimise accuracy both in diagnosis and treatment.

Gisondi P et al (to be documented)

Shared clinics facilitate PsA diagnosis and offer more comprehensive treatments

- Multidisciplinary "shared care" clinic opened in 2003 at the Brigham and Women's Hospital (Boston, MA)
  - Patients were simultaneously examined by attending dermatologist and attending rheumatologist

<table>
<thead>
<tr>
<th>Management class</th>
<th>Taking medication (PsA ≥ 10%)</th>
<th>Taking medication (PsA &lt; 10%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topical therapy alone</td>
<td>30.0</td>
<td>30.0</td>
</tr>
<tr>
<td>Systemic medicationa</td>
<td>14.9</td>
<td>23.4</td>
</tr>
<tr>
<td>PsA (n = 167*c)</td>
<td>18.8</td>
<td>33.8</td>
</tr>
<tr>
<td>Biologic medicationc</td>
<td>31.7</td>
<td>36.7</td>
</tr>
<tr>
<td>PsA (n = 167*c)</td>
<td>22.7</td>
<td>24.0</td>
</tr>
</tbody>
</table>

aSystemic medication includes any traditional DMARDS, and excludes biologic agents
bPercentage of psoriasis-alone patients on corresponding therapy
cPercentage of PsA patients on corresponding therapy


Clinical case

- 25 years old patient with severe psoriasis and HCV + infection.
- CsA therapy was effective in controlling skin psoriasis.
- She complains pain at DIP joints of right hand
Rheumatologist consultation

- Ultrasonography reveals edema and power doppler positive signal

Since only one digit is involved, peritendineal steroid injection was performed.

Baseline  After 2 months of steroid injection
PsA - Moll & Wright Classification Criteria

- Predominantly axial spondylitis
- Polyarticular (symmetric)
- Oligoarticular, asymmetric (4 or less joints)
- Combined variants
- Peripheral variants
- Enthesitis (dactylitis)
- Polyarticular RA-like

PsA - Moll & Wright Classification Criteria

ClAssification Criteria for Psoriatic ARthritis (CASPAR Criteria)

To meet the CASPAR criteria, a patient must have inflammatory articular disease (joint, spine or enthesial) plus ≥3 points from the following 5 categories:

1. Evidence of current psoriasis*, a personal history of psoriasis or a family history of psoriasis
2. Typical psoriasis nail dystrophy
3. A negative test result for rheumatoid factor
4. Either current dactylitis, defined as swelling of an entire digit, or a history of dactylitis
5. Radiographic evidence of juxta-articular new bone formation appearing as ill-defined ossification near joint margins (but excluding osteophyte formation) on plain radiographs of the hand or foot

*score 2
Taylor M et al. Arthritis and Rheumatism 2008

Diagnosis of PsA in daily practice

- Psoriasis
  - Skin, nail
  - Current and/or positive history of psoriasis
  - Family history of psoriasis
- Inflammatory articular involvement (clinical or by imaging)
  - Peripheral arthritis
  - Spondylitis
  - Enthesitis
  - Dactylitis
- Other rheumatic conditions excluded

Marchesoni A. et al. J Rheumatol 2012
How Can Psoriatic Arthritis Be Diagnosed Early?

- Periodic screening of patients with psoriasis and their relatives.
- Refer to rheumatologist for evaluation.
- Strategies for screening should include questionnaires and biomarkers (genetic, soluble, cellular, imaging).
  - Soluble: CRP, IL-6, RANKL, MMP-3, osteoprotegerin, circulating osteoclast precursors.


Risk Factors for Psoriatic Arthritis

- Obesity

- Scalp and intergluteal/perianal lesions

- Nail distrophy

- Subclinical enthesopathy

Scalp and inverse psoriasis
Nail psoriasis

- 50% of adults patients and 10% of children with skin psoriasis.
- Up to 30% of cases the only manifestation of psoriasis.
- Significant disease burden:
  - Functional impairment
  - Recalcitrant to treatment

Thickening of the nail is a common feature in nail psoriasis also in patients without clinically apparent nail involvement

Nail anchored by enthesis

Extensor tendon
Superficial and deep lamina
Nail
Lateral lamina
Flexor tendon
Psoriasis patients with nail disease have a greater magnitude of underlying systemic subclinical enthesopathy than those with normal nails

Comparison of median ultrasound (US) scores related to inflammation and chronicity in psoriasis patients with and without nail disease and healthy controls.

Ash ZR et al. Ann Rheumatic Dis 2012

Preliminary Evidence That Subclinical Enthesopathy May Predict Psoriatic Arthritis in Patients with Psoriasis

Table 2: Independent predictors of the development of PoA in the study population (n = 26).

<table>
<thead>
<tr>
<th>Development of PoA</th>
<th>Standardized &amp; Coefficient</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>age: years</td>
<td>~0.001</td>
<td>0.91</td>
</tr>
<tr>
<td>Male vs Female</td>
<td>-0.04</td>
<td>0.96</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.2</td>
<td>0.12</td>
</tr>
<tr>
<td>Psoriasis Area and Severity Index</td>
<td>0.09</td>
<td>0.2</td>
</tr>
<tr>
<td>Thickness of quadriceps tendon</td>
<td>1.4</td>
<td>0.02</td>
</tr>
</tbody>
</table>

PoA: psoriatic arthritis.

Tinazzi I et al. J of Rheumatology 2011

Questionnaires for Patients with Psoriasis

- The Toronto Psoriatic Arthritis Screen (ToPAS) 12 questions on skin and articular complaints, including pictures of psoriasis.1
- Pilot-testing a Psoriatic Arthritis Screening and Evaluation tool (PASE) articular symptoms (7 questions) and function score (8 questions).2
- The Psoriasis Epidemiology Screening Tool Questionnaire (PEST) only five simple questions and a homunculus.3
- Early ARthritis for Psoriatic patients questionnaires (EARP) 10 simple questions.4

4Tinazzi I et al. Rheumatology 2012;51:2058
The Early ARthritis for Psoriatic patients questionnaire (EARP-10) screening questionnaire

- 10-item questionnaire
- Easy to administer and understand
- Faster to complete (2±1.5 min)
- Peripheral and axial disease
- Sensitivity 91.6%
- Specificity 85.2%

A score ≥3 correlated with clinically identified PsA by a rheumatologist.

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do your joints hurt?</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Have you taken anti-inflammatory more than twice a week for joint pain in the last 3 months?</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Do you wake up at night because of low back pain?</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Do you feel stiffness in your hands for more than 30 minutes in the morning?</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Do your wrists and fingers hurt?</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Do your wrists and fingers swell?</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Do your finger hurt and swell for more than 30 minutes in the morning?</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Do your Achilles tendon swell?</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Do your feet or ankles hurt?</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Do your elbow or hips hurt?</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

The first 10 items of the EARP questionnaire were chosen after the psychometric analysis. Each positive answer is scored as one, and the final score is calculated by summing the positive answers.

The piramid of PsA management

Early diagnosis
Disease and patient characterization
Assessment of disease severity
Tailored treatment
Treat-to-target and tight control
Remission or minimal disease activity

Drugs for Psoriatic Arthritis

- Corticosteroids
  - systemically
  - locally
- NSAIDs
- DMARDs (Disease Modifying Anti-Rheumatic Drugs)
  - traditional (synthetic)
  - biotechnological (anti-TNF)
  - new small molecules
Synthetic DMARDs for PsA

- Commonly used
  - Methotrexate
  - Sulphasalazine
  - Cyclosporine
  - Leflunomide

- Rarely used (now)
  - Anti-malarials
  - Azathioprine

Anti-TNF Agents in Psoriatic Arthritis

- Infliximab
- Etanercept
- Adalimumab
- Golimumab

Psoriatic Arthritis Clinical Subgroups

- Poly-arthritis
- Oligo-arthritis
- Axial predominant
- Enthesitis predominant

Typical features
- Dactylitis
- Mutilans
- Distal invovl.
GRAPPA recommendations for treatment of patients with psoriatic arthritis

Efficacy of systemic treatments on the different components of PsA

Conclusions

• The dermatologist plays a pivotal role in the early diagnosis of PsA.

• Strategies for screening of PsA could include the following:
  – Questionnaires
  – Combined consultation with rheumatologist
  – Hs-CRP, IL-6, RANKL, MMP-3, osteoprotegerin
  – Detection of enthesopathy

• Treatment of PsA with TNF-α blockers prevent joint irreversible damage

GRAPPA - Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

From Paolo Gisondi, Verona (Italy)