Arthritis Mutilans: A Report from the GRAPPA 2012 Annual Meeting

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ABSTRACT. Arthritis mutilans is often described as the most severe form of psoriatic arthritis. However, a widely agreed on definition of the disease has not been developed. At the 2012 annual meeting of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA), members hoped to agree on a definition of arthritis mutilans and thus facilitate clinical and molecular epidemiological research into the disease. Members discussed the clinical features of arthritis mutilans and definitions used by researchers to date; reviewed data from the ClASsification for Psoriatic ARthritis study, the Nordic psoriatic arthritis mutilans study, and the results of a premeeting survey; and participated in breakout group discussions. Through this exercise, GRAPPA members developed a broad consensus on the features of arthritis mutilans, which will help us develop a GRAPPA-endorsed definition of arthritis mutilans. (J Rheumatol 2013;40:1419–22; doi:10.3899/jrheum.130453)

Key Indexing Terms:

OSTEOLYSIS	ANKYLOSIS	PENCIL-IN-CUP
SUBLUXATION	FLAIL JOINT	ARTHRITIS MUTILANS

Psoriatic arthritis (PsA) is an inflammatory musculoskeletal disease specifically associated with psoriasis. Moll and Wright defined PsA as "psoriasis associated with inflammatory arthritis (peripheral arthritis and/or spondylitis) and usually a negative serologic test for rheumatoid factor."[1] In this seminal paper, they described 5 patterns of PsA: asymmetric oligoarthritis, symmetric polyarthritis, distal interphalangeal (DIP) joint-predominant arthritis, spondylitis, and arthritis mutilans[1]. Arthritis mutilans was described as the most severe form of PsA but was rare, affecting < 5% of patients with PsA[1,2]. It is now accepted that these patterns are not necessarily unique to a patient and they change over time; however, they do facilitate clinical description of a patient with PsA at the time of clinical assessment. One central question that remained, however, is whether arthritis mutilans is a unique PsA subtype or a manifestation of severe peripheral arthritis.

Although arthritis mutilans is recognized by rheumatologists as a severe destructive form of PsA, a precise definition has not yet been universally accepted. The earliest definition of arthritis mutilans was provided by Moll and Wright, who defined it as a subtype of PsA "often complicated by digital telescoping or *doigt en lorgnette* deformity resulting from severe osteolysis."[1] Subsequently, they included the following characteristic features in their definition: polyarticular disease, symmetrical distribution, long duration of disease, and radiological features (osteolysis, ankylosis)[2]. The first 3 of these features are likely to be interrelated, but it is the extreme radiological phenotype that is characteristic[3].

Others have used similar definitions. McGonagle, *et al* defined arthritis mutilans as "diffuse bone destruction of the small joints of the hands, especially DIP."[4] Marsal, *et al* stated that "mutilation was present when a metacarpal or a metatarsal head and the corresponding epiphysis of a phalanx or both epiphyses of an interphalangeal joint (IP) of a finger or toe were completely eroded."[5] This definition was extended by McQueen, *et al* and used in a series of radiologic and intervention studies[6,7,8], where they defined arthritis mutilans as pencil-in-cup deformities or bone lysis causing 30%–50% resorption of proximal and middle phalanges, manifesting clinically as digital shortening, or radiographically as complete erosion of bone on both sides of the joint(s). In their original study, Gladman, *et al* did not explicitly define arthritis mutilans but they described 8 distinct patterns[9]. More recently, they defined arthritis mutilans radiographically as the presence of ≥ 5 joints with grade 4 radiographic damage according to the modified Steinbrocker method[10,11]. Although the initial description by Moll and Wright and the definition by Gladman's group have included ankylosis, osteolysis is widely accepted as a defining feature of this condition[10].

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At the 2012 annual meeting of GRAPPA, members initiated an exercise to develop a precise definition of arthritis mutilans so that multicenter clinical, epidemiological, genomic, and biomarker research into this disease may be conducted. It is hoped that early identification of patients with psoriasis at risk for development of arthritis mutilans will lead to suitable intervention and prevent severe outcomes. The proceedings of the GRAPPA module are described here.

The module began with a general description of arthritis mutilans by Dafna Gladman (Toronto, Canada), followed by further description by Vinod Chandran (Toronto, Canada) and a presentation of the results of a pre-meeting electronic survey of GRAPPA members on the defining features of the condition. This was followed by a description of data from the ClASsification for Psoriatic ARthritis (CASPAR) study[12] by Philip Helliwell (Leeds, UK) and a brief report on the Nordic psoriatic arthritis mutilans study[13] by Björn Gudbjörnsson (Reykjavik, Iceland). The module ended with breakout group discussions and a followup survey on items of the pre-meeting survey in which consensus was not obtained.

Dafna Gladman reviewed arthritis mutilans as described by Moll and Wright and showed a number of clinical and corresponding radiographic pictures of the condition. She raised the question whether ankylosis and lysis should be considered as features of arthritis mutilans since both lead to severe destruction of the joint(s). She also asked whether there was a temporal relationship between joint lysis and ankylosis, pointing out that some patients have ankylosis and lysis in the same digit.

Vinod Chandran then reviewed the definitions of arthritis mutilans used by investigators to date[1,4,5,8,10]. Key terminologies have included digital telescoping, severe osteolysis, diffuse bone destruction, involvement of small joints of the hands, involvement of DIP joints, digital shortening, pencil-in-cup deformities, complete erosion of both sides of a joint of the hands or feet, subluxation, and ankylosis. Although the numbers of joints have not been explicitly mentioned except more recently by Chandran, *et al*, Moll and Wright described polyarticular disease as being important[1,10]. The following 5 key questions were identified: (1) Should arthritis mutilans be defined radiographically or clinically? A radiographic definition is likely to be more sensitive than a definition based on features elicited by clinical examination alone. (2) What should the radiographic definition include? Should it be defined as erosion involving the entire joint margin of small joints or pencil-in-cup change or ankylosis? (3) Should the definition be made on a defined number of affected joints or would involvement of a single joint suffice? (4) What should the clinical definition include? Is shortening of digits or flail joints (not due to subluxation) sufficient? (5) Since rapidity of joint destruction was also deemed important by some experts, should a timeframe to development of severe joint damage also be included in the definition?

GRAPPA electronic survey on arthritis mutilans

Members reviewed the results of an electronic survey conducted prior to the meeting. One hundred eleven GRAPPA members responded to the survey; 72 (70%) of the respondents were from Europe or North America; 99 (89%) were rheumatologists; and 77 (76%) of them had been practicing for > 10 years. Eighty (82%) respondents saw ≥ 10 patients with PsA each month, although 88 (87%) reported that they saw < 5 patients with arthritis mutilans in a month. Ninety-four (86%) agreed that the term "arthritis mutilans" should be used specifically to denote a severe form of PsA and not other arthritides. A majority of the respondents believed that involvement of the metacarpophalangeal (MCP), proximal interphalangeal (PIP), DIP, and IP joints of the toe should be included in the definition of arthritis mutilans; < 2% believed that axial joints should also be included. The opinion on the number of joints involved was variable: 46 (42%) believed that involvement of even a single joint is sufficient, whereas 31 (28%) expressed that ≥ 5 joints should be involved. Sixty-five (60%) believed that rapidity of joint damage should not be considered in the definition. Fifty-eight (53%) thought that the definition of arthritis mutilans should be based on features elicited on both clinical and radiographic evaluation. Members held similar opinions that the radiographic definition of arthritis mutilans should include (1) erosion involving entire articular surfaces on both sides of the joint (73; 67%); (2) pencil-in-cup change where one articular surface is eroded creating a pointed appearance and the other articular surface is concave, resembling an upside down cup (77; 71%); and (3) evidence of resorption of adjacent bone (70; 64%). Only 17 (16%) considered bony bridging across the joint line leading to ankylosis as a feature. Ninety-nine (91%) and 96 (88%) agreed that (1) shortening of finger or toe or (2) digital telescoping were important clinical features. Other features considered important by varying numbers of respondents were flail joint not due to subluxation (64; 59%), ankylosis (19; 17%), and asymmetry (11; 10%). High acute-phase response was regarded as feature of the disease by 62 (86%). Interestingly, small numbers of respondents agreed on laboratory features of arthritis mutilans: anti-cyclic citrullinated protein antibodies (11; 15%) positivity, presence of the shared epitope (9; 13%), and rheumatoid factor positivity (5; 7%). Only 15 (21%) considered HLA-B*27 positivity a feature.

Arthritis mutilans in the CASPAR study

Philip Helliwell reviewed data on arthritis mutilans from the CASPAR study, a large international collaboration to define new classification criteria for PsA[12]. Clinical characteristics were collected on almost 600 patients with PsA and a

similar number of control patients, 70% of whom had rheumatoid arthritis. During data collection, investigators could tick a box called "arthritis mutilans," which was checked in 21 cases. The clinical characteristics of these cases are compared to the 567 other cases of PsA in Tables 1 and 2.

The CASPAR data have shown that arthritis mutilans cases are usually polyarticular, of long duration, and symmetrical with characteristic radiological features (osteolysis, ankylosis, entheseal abnormalities, and spinal involvement). Cases have more (low titer) anti-CCP antibodies, slightly more disability, and are more likely to have had joint surgery.

The Nordic Psoriatic Arthritis Mutilans Study

Björn Gudbjörnsson briefly reported the prevalence and clinical characteristics of PsA mutilans in the Nordic study[13], in which 59 patients (age ≥ 18 yrs) have been included to date. The female to male ratio was about 1:1. The mean age at skin disease onset was 25 years and at onset of joint disease was 30 years. At study start, the mean duration of arthritis was 27 ± 11 years for males and 33 ± 11 years for females.

This study showed that the prevalence of PsA mutilans in the adult Nordic population is low, 3.69 per 1,000,000 inhabitants (95% CI 2.75–4.63). PsA mutilans was most frequently seen in the DIP joints of the toes, followed by the IP joint of the thumb. Female and male patients had similar numbers of painful and swollen joints. Of the 38 patients (64%) who had a history of dactylitis, 23 (61%) had a history of dactylitis in the same finger/toe as they had arthritis mutilans. At the time of inclusion, 45% of the patients had clear or almost clear skin.

Summary of breakout group discussions

GRAPPA attendees were divided into 11 breakout groups and tasked with discussing the following questions: (1) When defining arthritis mutilans, involvement of which joints should be considered? (2) Should number of joints involved be a criterion? (3) Should rapidity of joint damage be considered? (4) Should the definition of arthritis mutilans be based on features elicited on clinical examination only, radiographic evaluation only, or both? (5) What are the radiographic criteria for arthritis mutilans: erosion involving entire articular surfaces on both sides of the joint and/or pencil-in-cup change? What about ankylosis? (6) What are the clinical criteria for defining arthritis mutilans: shortening of digits, digital telescoping, and/or flail joint not due to subluxation?

The consensus of the breakout groups was that the definition of arthritis mutilans should involve peripheral joints, especially of the hands and feet, but not axial joints. Involvement of one joint was considered sufficient. Rapidity of joint destruction was not considered important. Both radiographic and clinical features were important, but radiographic features were believed to be more sensitive. The proposed clinical and radiographic features described above were generally agreed upon. However, osteolysis was considered to be the defining feature. Although ankylosis was a feature of severe joint destruction, most groups agreed to place joint ankylosis into a different category distinct from arthritis mutilans.

Results of postdiscussion voting

After the breakout group discussion, a postdiscussion survey was conducted in an attempt to obtain consensus on some of the areas of disagreement. One hundred twenty-two

Table 1. Clinical and laboratory features of cases of arthritis mutilans, compared to other cases of psoriatic arthritis.

	RF+, %	Anti-CCP+, %	HAQ	Any Joint Surgery, %	Axial, %	Symmetry No.
AM	0	25	0.90	48	14	0.80
Others	5	7	0.81	13	8	0.56

AM: arthritis mutilans; CCP: cyclic citrullinated protein; HAQ: Health Assessment Questionnaire; RF: rheumatoid factor. Symmetry number: range 0–1, where 1 is perfectly symmetrical[3].

Table 2. Radiological features of arthritis mutilans compared to others.

	Ankylosis on Radiograph %†	Juxtaarticular Bone on Radiograph, %*	Entheseal New Bone, %	Entheseal Erosion, %†	Osteolysis, %†
AM	43	38	29	43	57
Others	9	16	13	4	9

AM: arthritis mutilans. * $p < 0.05$; † $p < 0.0001$.

(64%) of the participants were rheumatologists. More than 70% of the respondents agreed that the involvement of PIP, DIP, and IP joints of the toes be included in the definition, and more than 65% opined that MCP and metatarsophalangeal (MTP) joints also be included. Ninety-seven (87%) agreed that involvement of a single joint was sufficient. One hundred seven (95%) did not want rapidity of damage included. Fifty-seven (50%) expressed that both clinical and radiographic features be included, and 42 (37%) were comfortable with using either. More than 85% of the respondents agreed that erosion involving entire articular surfaces on both sides of the joint or pencil-in-cup change were sufficient radiographic features, but only 16 (8%) agreed that bony bridging across the joint line leading to ankylosis should be included. More than 80% agreed that shortening of finger or toe, digital telescoping, or flail joint not due to subluxation should be included in the clinical definition.

Future plans

Through this exercise, GRAPPA has developed a broad consensus on the features of PsA mutilans, which will help us develop a GRAPPA-endorsed definition of arthritis mutilans. Proper disease definition will facilitate studies to identify clinical predictors, genes, and other biomarkers for arthritis mutilans and will set the gold standard for developing magnetic resonance imaging criteria. Therapeutic intervention trials may then be conducted, with the ultimate goal of preventing arthritis mutilans and its associated severe disability.

REFERENCES

1. Moll JM, Wright V. Psoriatic arthritis. Semin Arthritis Rheum 1973;3:55-78.
2. Wright V, Moll JM. Seronegative polyarthritis. Amsterdam: North Holland Publishing Co.; 1976.
3. Helliwell PS, Hetthen J, Sokoll K, Green M, Marchesoni A, Lubrano E, et al. Joint symmetry in early and late rheumatoid and psoriatic arthritis: Comparison with a mathematical model. Arthritis Rheum 2000;43:865-71.
4. McGonagle D, Conaghan PG, Emery P. Psoriatic arthritis: A unified concept twenty years on. Arthritis Rheum 1999;42:1080-6. Erratum in: Arthritis Rheum 1999;42:997.
5. Marsal S, Armadans-Gil L, Martinez M, Gallardo D, Ribera A, Lience E. Clinical, radiographic and HLA associations as markers for different patterns of psoriatic arthritis. Rheumatology 1999;38:332-7.
6. Ly J, Pinto C, Doyle A, Dalbeth N, McQueen FM. Axial bone proliferation causing cervical myelopathy in the mutilans form of psoriatic arthritis despite peripheral bone erosion. Ann Rheum Dis 2009;68:443-4.
7. Tan YM, Ostergaard M, Doyle A, Dalbeth N, Lobo M, Reeves Q, et al. MRI bone oedema scores are higher in the arthritis mutilans form of psoriatic arthritis and correlate with high radiographic scores for joint damage. Arthritis Res Ther 2009;11:R2.
8. McQueen F, Lloyd R, Doyle A, Robinson E, Lobo M, Exeter M, et al. Zoledronic acid does not reduce MRI erosive progression in PsA but may suppress bone oedema: The Zoledronic Acid in Psoriatic Arthritis (ZAPA) Study. Ann Rheum Dis 2011;70:1091-4.
9. Gladman DD, Shuckett R, Russell ML, Thorne JC, Schachter RK. Psoriatic arthritis (PSA) — an analysis of 220 patients. Q J Med 1987;62:127-41.
10. Chandran V, Thavaneswaran A, Pellett FJ, Gladman DD. The association between human leukocyte antigen and killer-cell immunoglobulin-like receptor gene variants and the development of arthritis mutilans in patients with psoriatic arthritis [abstract]. Arthritis Rheum 2011;63 Suppl:S532.
11. Rahman P, Gladman DD, Cook RJ, Zhou Y, Young G, Salonen D. Radiological assessment in psoriatic arthritis. Br J Rheumatol 1998;37:760-5.
12. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H. Classification criteria for psoriatic arthritis: Development of new criteria from a large international study. Arthritis Rheum 2006;54:2665-73.
13. Gudbjornsson B, Ejstrup L, Gran J, Iversen L, Lindqvist U, Paimela L. Psoriatic arthritis mutilans (PAM) in the Nordic countries: demographics and disease status. The Nordic PAM study. Scand J Rheumatol 2013 Mar 21. [Epub ahead of print]