CONCISE REPORT

Laboratory and imaging studies used by French rheumatologists to determine the cause of recent onset polyarthritis without extra-articular manifestations

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Background: The cause of recent onset polyarthritis can be difficult to identify.
Objective: To determine which laboratory and imaging studies French rheumatologists recommend, not taking cost into account, for the diagnosis of recent onset polyarthritis without extra-articular manifestations.
Methods: From the list of the French Society for Rheumatology, a random sample of 210 rheumatologists was selected, who were asked to complete a questionnaire on the laboratory and imaging studies they would recommend in two fictional cases of recent onset polyarthritis (possible rheumatoid arthritis (RA)—case 1 and probable RA—case 2).
Results: In case 1, the following were recommended by over 75% of respondents: hand radiographs, rheumatoid factors (RFs), and antinuclear antibodies (ANA) (92%, 98%, and 98%, respectively). 50–74% of respondents recommended radiographs of the feet, knees, and chest (50%, 57%, and 66%, respectively); blood cell counts, erythrocyte sedimentation rate (ESR), serum assays of C reactive protein (CRP), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) (65%, 74%, 67%, and 62%, respectively). 25–49% recommended determination of creatinine and proteinuria, HLA-B27, antikeratin antibody, radiographs of the pelvis, and synovial fluid analysis. Several investigations were recommended less often in case 2 than in case 1. Nevertheless, some laboratory and imaging studies (radiographs of hand, feet, knees, chest *x* rays, blood cell counts, ANA, RF, antikeratin antibody, CRP, ESR, creatinine, AST and ALT, proteinuria, and joint aspiration) were recommended by more than 25% of respondents in both cases.
Conclusion: Wide variations were found among rheumatologists, indicating a need for standardisation. Some laboratory and imaging studies are recommended by at least 25% of respondents in recent onset polyarthritis with or without clues suggesting RA. In contrast, many tests were considered useful by fewer than 25% of the respondents in both cases.

The cause of recent onset polyarthritis can be difficult to identify.[1] Yet, early diagnosis is essential, for at least two reasons. Firstly, polyarthritis can indicate the presence of a serious disease requiring urgent attention, such as an infection, a metabolic disorder, or a systemic disease. Secondly, a need for treatment with one or more disease modifying antirheumatic drugs (DMARDs) should be identified early, as there is strong evidence that early DMARD treatment improves the outcome of rheumatoid arthritis (RA).[2–4]

The chances of identifying the cause of early polyarthritis may depend on the combination of clinical, imaging, and laboratory tests used. However, the diagnostic efficacy of the many possible test combinations has not been determined, so that there is no scientific basis for developing a consensus on this point. Consequently, there may be substantial variations among rheumatologists in the tests used to evaluate recent onset polyarthritis.

In patients without extra-articular manifestations, clinicians request the tests that they feel are most likely to have an impact on decisive treatment, their main goal being to distinguish RA from other conditions.

We conducted an observational survey of the laboratory tests and imaging studies recommended by rheumatologists, without taking cost into account, for the diagnosis of recent onset polyarthritis without extra-articular manifestations.

PATIENTS AND METHODS

Respondent selection

From the list of the French Society for Rheumatology, we selected at random a sample of 210 rheumatologists. We mailed an invitation to participate in the study and a questionnaire to each of these rheumatologists. All the rheumatologists who did not answer our request were contacted by phone or sent a second letter, or both.

Questionnaires

The questionnaire was developed as follows. Two fictional case scenarios (appendix 1) were written in the study investigators' workshop which were submitted to all the members of the Inflammatory Joint Disease Committee (Club Rhumatisme et Inflammation) of the French Society for Rheumatology, and finally modified during a second meeting of the investigators' study. The two scenarios described patients presenting recent onset polyarthritis. Case 1 described a patient with few clues suggesting RA ("possible RA"), and case 2 described a patient with several features that pointed to RA ("probable RA"). All the items in the questionnaire were open ended questions to replicate the situation of the clinician evaluating a patient and to avoid bias by suggestion.

The rheumatologists were asked to indicate which laboratory tests and imaging studies they would use in each case to identify the cause of the polyarthritis.

Abbreviations: ALT, alanine aminotransferase; ANA, antinuclear antibodies; AST, aspartate aminotransferase; CRP, C reactive protein; DMARD, disease modifying antirheumatic drug; ESR, erythrocyte sedimentation rate; RA, rheumatoid arthritis; RF, rheumatoid factor

In France, a large proportion (70–100%) of all laboratory and imaging investigations are reimbursed by the national health insurance system, and most patients have additional health insurance to cover the residual cost. Thus, the diagnostic investigation is not constrained by the possibility that the patient may be unable to pay for some tests. Consequently, we asked the rheumatologists to disregard cost considerations when replying to the questionnaire items.

All answers were qualitative except the certainty rating in the first diagnosis, which was expressed on an 11 point scale (0–10).

Statistical analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS 9.0, 1999). Comparisons of investigations recommended for both cases (intra-investigators comparison) were done using the McNemar test[5] and the Wilcoxon test for paired series,[6] for qualitative and quantitative items, respectively.

To summarise the results, investigations proposed by the respondents were separated into four groups according to the proportion of rheumatologists recommending their use (0–24%, 25–49%, 50–74%, 75–100%). The statistical threshold for significance was set at $\alpha=0.001$ to prevent significance occurring by chance because of multiple testing.[7]

Sample size calculations

Sample size calculations showed that 100 rheumatologists would have to be included in the study to obtain >10% precision, with the α risk set at 5% and good feasibility, in determining the proportions of rheumatologists who recommended each investigation in the case with few diagnostic clues. According to the proportion of rheumatologists expected to fail to return the questionnaire (about 50%), a panel of 210 rheumatologists (representing 10% of French rheumatologists) was randomly invited to participate in the study.

RESULTS

Population of respondents

Of the 210 rheumatologists invited to participate in the study, three were excluded because they had stopped practising rheumatology, 19 because they had no clinical practice, and 17 because they had no patients with inflammatory joint disease. In addition, six declined to participate in the study and 46 accepted but failed to return the questionnaire. Thus, 119 rheumatologists participated in the survey. All of them saw inflammatory arthritis over the years.

Validity of the scenarios

One hundred and two (86%) and 117 (98%) respondents considered that RA was the most probable diagnosis in cases 1 and 2, respectively. The certainty rating was higher, equal, and lower for 90 (76%), 16 (13%), and 2 (1%) respondents (mean rating 8, range 3–10) in the second than in the first scenario (mean 6, range 2–9), respectively (certainty was not specified by 11 rheumatologists). This significant difference (Wilcoxon test for paired data $p<0.0001$) indicated that the two scenarios differed in their tendency to suggest RA. Similarly, among the 97 (82%) rheumatologists who considered that RA was the most probable diagnosis in both scenarios, the certainty rating was higher, equal, and lower for 80 (82%), 15 (15%), and 1 (1%) of the respondents in the second scenario than in the remainder, respectively (data were not specified in one case). In both scenarios, connective tissue diseases and spondyloarthropathies were considered as the main differential diagnosis of RA, but the number of suspected diagnoses was significantly lower in the second (mean 2, range 1–6) than in the first scenario (mean 4, range 1–9) ($p<0.0001$).

Investigations recommended by the respondents (table 1)

In fictional case 1, at least 75% of respondents indicated that they would obtain hand radiographs, rheumatoid factors (RFs), and antinuclear antibodies (ANA) (92%, 98%, and 98%, respectively). A total of 50–74% recommended radiographs of the feet, knees, and chest (50%, 57%, 66%, respectively); blood cell counts, erythrocyte sedimentation rate (ESR), serum assays of C reactive protein (CRP), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) (65%, 74%, 67%, and 62%, respectively). A total of 25–44% indicated that they would look for creatinine, proteinuria, and antikeratin antibodies, examine the synovial fluid and, in patients with little evidence of RA, test for HLA-B27. Other investigations were considered useful by fewer than 25% of the respondents.

The following investigations were recommended less often in case 2 than in case 1 ($p\leqslant0.001$): radiographs of the pelvis and chest, RF (in the case with diagnostic clues the history of a positive test for RF was known), HLA-B27, and viral serologies (hepatitis C, hepatitis B).

DISCUSSION

The indication for laboratory tests and imaging studies in determining the cause of recent onset polyarthritis has not been specifically evaluated. Some of them may be proposed in detecting extra-articular injuries, others in identifying specific diseases such as RA, connective tissue diseases, or spondyloarthropathy, which are the most likely diagnoses evoked by rheumatologists.

Agglutination tests for RF, such as the Waaler-Rose and latex tests, are widely used and have proved valuable in diagnosing RA,[8 9] but other autoantibody-antigen systems may be useful in diagnosing RA (see review by Saraux *et al*[10]). In our study we found that most French rheumatologists recommended RF and that some recommended antikeratin antibody testing to rule in or to rule out RA.

Very few studies have evaluated laboratory tests aimed at identifying joint diseases other than RA, such as infection, metabolic disorders, or systemic disease. In our study we found that blood cell counts, the erythrocyte sedimentation rate, and ANA were considered useful by at least 75% of respondents; and CRP, AST, ALT, and proteinuria by at least 50%. This suggests that an important objective in the opinion of many rheumatologists was to look for autoimmune disease and for organ involvement. Fewer than 25% of respondents considered that viral serologies were useful, probably because some viral diseases, such as hepatitis B, hepatitis C, or mononucleosis, may be detected in most cases from extra-articular clinical signs and AST and ALT, which are recommended by at least 50% of respondents.

The sensitivity of hand *x* ray findings was nearly 20% and specificity about 90% for the diagnosis of RA.[11] In this study, at least 75% of respondents felt that hand radiographs were useful, and at least 50% that radiographs of the feet, knees, and chest were useful. These results suggest that rheumatologists use radiographs not only for the diagnosis of RA but also to look for evidence of other diseases, including chondrocalcinosis, spondyloarthropathies, and sarcoidosis.

In conclusion, we found wide variations in the opinions of the rheumatologists about which laboratory and imaging studies are useful for identifying the cause of recent onset polyarthritis. Standardisation would help to reduce these differences. Nevertheless, this study suggests that a limited panel of laboratory and imaging studies (radiographs of hand, feet, knees, blood cell counts, ANA, RF, antikeratin antibody, CRP, ESR, creatinine, AST, ALT, proteinuria, and joint aspiration) are considered useful by at least 25% of respondents in recent onset polyarthritis.

Table 1 Diagnostic imaging studies and laboratory tests recommended by French rheumatologists in two fictional cases of early polyarthritis. Results shown as number (%) of rheumatologists

	Case 1 (possible RA)	Case 2 (probable RA)	p Value
Radiographs			
Hands	109 (92)	113 (95)	>0.05
Chest	78 (66)	55 (46)	0.001
Knees	68 (57)	66 (55)	>0.05
Feet	59 (50)	60 (50)	>0.05
Pelvis	54 (45)	28 (24)	0.0001
Other imaging studies			
Radionuclide bone scanning	8 (7)	3 (3)	>0.05
MRI hand-wrist	2 (2)	0 (0)	>0.05
Echocardiography	2 (2)	0 (0)	>0.05
Joint ultrasonography	0 (0)	0 (0)	>0.05
HLA			
B27	33 (28)	9 (8)	0.0001
A, B, DR	14 (12)	9 (8)	>0.05
Routine laboratory tests			
Erythrocyte sedimentation rate	88 (74)	93 (78)	>0.05
C reactive protein	80 (67)	86 (72)	>0.05
Blood cell counts	77 (65)	94 (79)	0.01
AST/ALT	74 (62)	32 (27)	0.05
Proteinuria	47 (39)	32 (27)	0.01
Creatinine	41 (34)	46 (39)	>0.05
Serum uric acid	17 (14)	14 (12)	>0.05
Ferritin	14 (12)	5 (4)	0.01
Iron	11 (9)	5 (4)	0.02
Fibrin	4 (3)	4 (3)	>0.05
Creatine kinase	4 (3)	1 (1)	>0.05
Iron binding capacity	2 (2)	0 (0)	>0.05
APTT	1 (1)	1 (1)	>0.05
Aldolase	1 (1)	0 (0)	>0.05
Lactic dehydrogenase	0 (0)	0 (0)	>0.05
Microbiological studies			
Genital tract	2 (2)	0 (0)	>0.05
Stool	0 (0)	0 (0)	>0.05
Blood	0 (0)	0 (0)	>0.05
Serology			
Hepatitis C	23 (19)	11 (9)	0.0001
Hepatitis B	21 (18)	10 (8)	0.001
Lyme	15 (13)	2 (2)	0.01
HIV	13 (11)	3 (3)	>0.05
Parvovirus B19	10 (8)	1 (1)	0.01
Chlamydiae	8 (7)	0 (0)	0.01
Antistreptolysin O	3 (3)	1 (1)	>0.05
Mycoplasma	1 (1)	0 (0)	>0.05
Salmonella	0 (0)	0 (0)	>0.05
Immunology			
Antinuclear factor	117 (98)	104 (87)	>0.05
Rheumatoid factor	117 (98)	87 (76)	0.0001
Latex test	103 (87)	47 (39)	0.0001
Waaler-Rose test	97 (82)	72 (61)	0.001
Antikeratin antibodies	49 (41)	35 (29)	>0.05
Complement	15 (13)	12 (10)	>0.05
Antiperinuclear factor	12 (10)	8 (7)	>0.05
Antiphospholipid antibody	2 (2)	1 (1)	>0.05
Cryoglobulinaemia	2 (2)	0 (0)	>0.05
Antineutrophil cytoplasmic antibody	1 (1)	0 (0)	>0.05
Joint aspiration (synovial fluid analysis)	43 (36)	31 (26)	>0.05
Biopsy			
Salivary gland	3 (3)	1 (1)	>0.05
Synovial membrane	2 (2)	0 (0)	>0.05
Ophthalmological examination	10 (8)	15 (13)	>0.05

Abbreviations: MRI, magnetic resonance imaging; AST, aspartate aminotransferase; ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; HIV, human immunodeficiency virus.

Appendix 1

Case without diagnostic clues (case 1)

A 32 year old woman presents with a complaint of joint symptoms of three months' duration. Her medical history is unremarkable, and she is not taking drugs regularly. Her first symptoms were inflammatory pain and swelling in the right knee. The ESR and CRP level were normal. Non-steroidal anti-inflammatory drug treatment was given for one month, to no effect. A corticosteroid was injected into the knee. Symptoms during the past month were inflammatory pain (with night pain and two hours of morning stiffness) in the knees, wrists, right 2nd and 3rd metacarpophalangeal joints, and right ankle.

She denies any intercurrent or precipitating event, and neither does she report any cutaneous, stomatological, ophthalmological, gastrointestinal, or urinary symptoms. The physical examination shows arthritis of the wrists, right 2nd and 3rd metacarpophalangeal joints, and knees, with no extra-articular abnormalities.

Case with diagnostic clues (case 2)

A 48 year old woman presents with a three month history of inflammatory pain with swelling in the wrists; 1st, 2nd, 3rd, and 4th metacarpophalangeal joints of both hands; 2nd, 3rd, and 4th proximal interphalangeal joints of both hands; and right knee. She has no history of significant disease and is not taking drugs regularly. She denies any intercurrent or precipitating event and says she has no history of cutaneous, stomatological, ophthalmological, gastrointestinal, or urinary symptoms. The physical examination shows marked arthritis of the above-listed joints, with no extra-articular abnormalities. She shows you a laboratory report indicating that a latex test for RF was positive with a titre of 1/160.

Please answer the following questions for each of these cases

(1) List the diagnoses you suspect, in decreasing order of likelihood. On an 11 point scale (0–10), rate your degree of certainty that the patient has the first diagnosis on your list.

(2) Would you obtain imaging studies? If yes, which ones?

(3) Would you obtain laboratory tests? If yes, which ones?

(4) Would you obtain other diagnostic tests? If yes, which ones?

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