

Diagnostic approach in a patient presenting with polymyalgia

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Polymyalgia rheumatica (PMR) is a common syndrome in the elderly, consisting of pain, aching and morning stiffness involving the neck, hip girdle, and shoulder girdle, and which is generally associated with an elevated erythrocyte sedimentation rate (ESR) (1). Although the cause is unknown, its diagnosis is relatively straightforward when the typical symptoms are present. In addition, in some instances the response to corticosteroids is used to support the diagnosis. Isolated PMR is generally a benign and self-limiting condition. However, despite recent observations (2), none of the clinical and laboratory findings in PMR are specific (3). In this regard, polymyalgia manifestations may occur in patients with infections, neoplasms or other rheumatic diseases.

For these reasons several points can be made about the diagnosis of this syndrome:

1. In the presence of the typical clinical manifestations, PMR can be diagnosed in a straightforward fashion.
2. In series of patients with PMR, no association with other diseases has been observed except for giant cell arteritis (GCA).
3. Polymyalgia rheumatica is remarkably predictable in its rapid and complete or nearly complete improvement after the initiation of low-dose prednisone therapy.
4. In the typical case an extensive work-up for tumors or infections is not needed.
5. Nevertheless, in view of the lack of specific diagnostic tests, the clinician should remain alert to the possibility of other diseases mimicking PMR, and should follow up clues to the presence of another disease when present.

It has been widely observed that up to 50% of patients with biopsy-proven GCA may have classical PMR (4, 5). In addition, a positive temporal artery biopsy for GCA has been reported in almost 20% of patients with primary PMR (1, 5). Apart from this common association between PMR and GCA, there are several clues that may alert the clinician to the possible presence of other entities in patients with polymyalgic symptoms.

For example, a subset of elderly patients

with late onset rheumatoid arthritis (RA) may present with polymyalgic symptoms that sometimes are difficult to differentiate from PMR (6). Furthermore, some patients initially presenting with PMR may later during their follow up develop findings more clearly consistent with seronegative RA and thus meet the 1987 ACR criteria for RA (7-10). Complicating this picture is the fact that peripheral synovitis may be present in up to 25% of patients with PMR (11). Polymyalgia rheumatica synovitis is frequently asymmetric and non-erosive with knee and wrist involvement. These manifestations generally resolve completely after corticosteroid therapy is started or the corticosteroid dose is increased (11). In addition, the distal swelling and edema observed in PMR patients (12) is often similar to that found in patients with RS3PE syndrome (remitting seronegative symmetrical synovitis with pitting edema) (13).

Late onset seronegative spondyloarthropathy (SpA), which is characterized by oligoarthritis, distal pitting edema (particularly of the lower limbs), minimal involvement of the axial skeleton, constitutional symptoms and an elevated ESR, may also mimic PMR (14-16). A detailed clinical history showing the presence of other manifestations of SpA, such as peripheral enthesitis and/or dactylitis, an association with HLA-B27, and radiological evidence of sacroiliitis, may help to differentiate late onset SpA from PMR.

Among the connective tissue diseases, systemic lupus erythematosus (SLE) in the elderly can sometimes present as PMR (17, 18). A positive antinuclear antibody (ANA) test alone is not sufficient to exclude PMR. Indeed, in general the frequency of positive ANA is higher in the elderly. A detailed clinical history may be of help in eliciting symptoms related to SLE, where present. In these cases the physical examination may disclose features such as pleuritis or pericarditis, which are common in late-onset SLE; the presence of hematological abnormalities such as leukopenia or thrombocytopenia should also raise the suspicion of this condition. Moreover, the finding of unexplained high titers of ANA should lead to a more complete

analytical study, including anti-nDNA, anti-ENA, C3, and C4 determinations. In a patient presenting with PMR symptoms where muscle weakness outweighs the symptoms of pain in the shoulder and hip girdles, the possibility of a myopathy should be considered (19). In these cases elevated muscle enzyme levels and a typical myopathic pattern in the electromyogram, together with the presence of chronic inflammatory infiltration in the muscle, may support the diagnosis of polymyositis.

Fever may be a symptom of primary PMR in up to 35% of patients (1). Although the fever in PMR is usually low grade, the possibility of other diseases should be considered. In this respect, it is of particular importance to rule out an underlying infection. Among these, the possibility of bacterial endocarditis is especially ominous; up to 30% of patients with this infection may show musculoskeletal manifestations (20). Therefore, in the presence of inappropriate malaise and low-grade fever along with musculoskeletal manifestations, a careful attempt should be made to exclude bacte-

rial endocarditis, and blood cultures and echocardiogram should be requested. Furthermore, in some parts of the world the presence of chronic infectious diseases should be taken into account. For example, brucellosis and tuberculosis are common in northwestern Spain (21), and in our experience polymyalgic symptoms may be present in patients with long-term infections caused by *Brucella abortus* or *Mycobacterium tuberculosis* (unpublished data).

Finally, malignancy may occasionally be present with proximal aching and stiffness (22). Indeed, rheumatologists need to consider hematologic malignancies, such as multiple myeloma (23, 24) and primary systemic amyloidosis (25), in elderly patients who have long-standing asthenia, aching, and muscle pain, especially if there are atypical symptoms of PMR such as the lack of accentuation of symptoms with movement, minimal morning stiffness, and a more diffuse continuous aching. In addition, solid malignancies in the kidney, ovary or stomach may present with PMR-like symptoms (26-29). The absence of im-

provement following treatment with low doses of prednisone (< 20 mg/day) and in many cases the presence of atypical symptoms of PMR should alert the physician to the possibility of such conditions.

In view of the above, we would suggest the following work-up in a patient presenting with polymyalgic symptoms (Fig. 1):

A. A clinical history should be taken. The interview should elicit data concerning the following:

1. The duration of symptoms (> 4 weeks duration of polymyalgia symptoms can exclude the majority of viral diseases).
2. Clinical symptoms of GCA (GCA may be associated with PMR, and requires a higher prednisone dose to prevent visual complications).
3. The absence of symptoms of SpA (particularly late onset SpA) and connective tissue diseases (mainly SLE).
4. Possible infections, undulant fever, contacts with persons with active tuberculosis, or a possible epidemio-

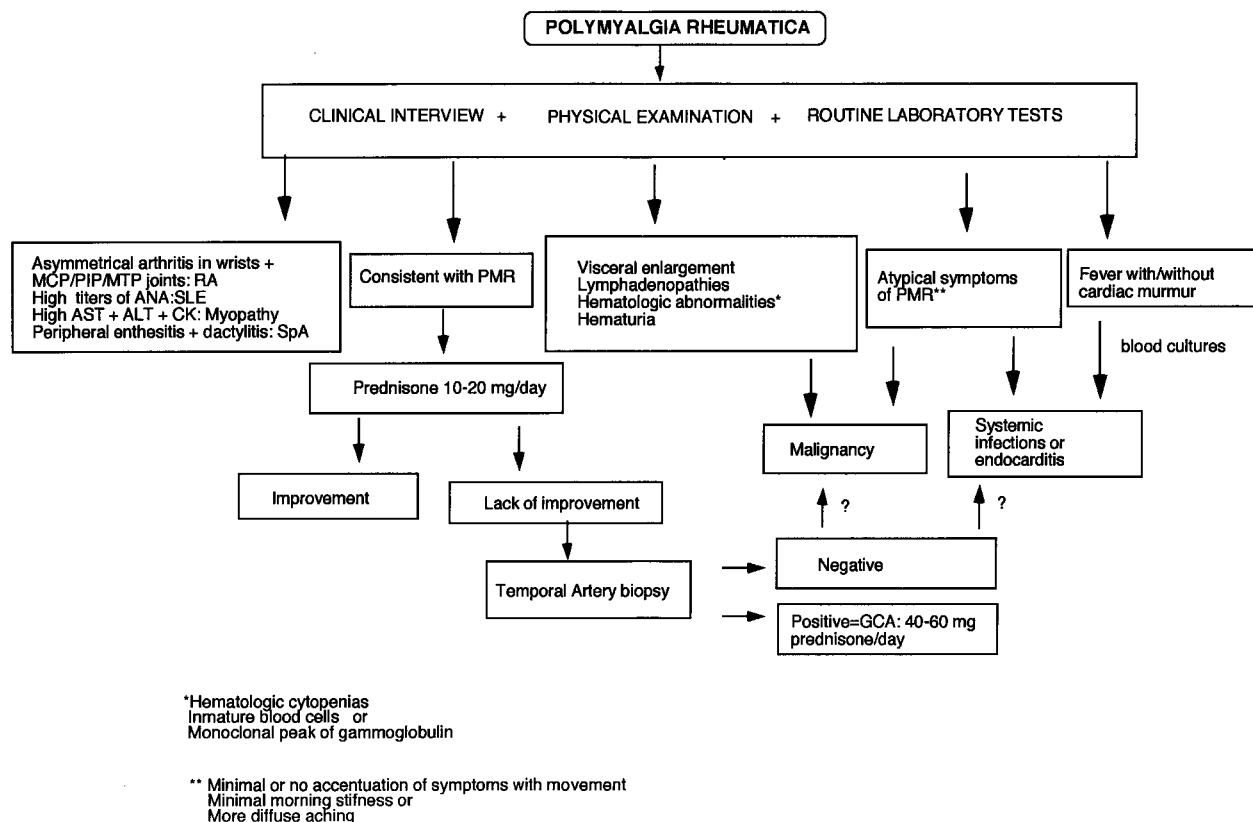


Fig. 1. Work-up of a patient presenting with clinical features of polymyalgia rheumatica.

logic context involving other infectious diseases.

B. Physical examination:

1. The fever may not be due to PMR and in these cases the possibility of systemic infections, including bacterial endocarditis, should be excluded.
2. The presence of arthritis: In general asymmetric and non-erosive arthritis involving the knee or wrist may be found in PMR, but in these cases the 1987 ACR criteria for RA are usually not fulfilled.
3. The presence of a cardiac murmur may be a reason to perform an echocardiogram, especially if no previous history of murmur has been recorded. In addition, visceral enlargement or lymphadenopathies should instigate a search for either solid or hematologic malignancies.

C) Routine analyses should include full blood count tests and ESR or C-reactive protein determinations, blood biochemistry analyses (including liver and function tests, protein electrophoresis, rheumatoid factor, and antinuclear antibodies) and a urinalysis.

1. The presence of bicytopenia or severe anemia (< 100 g/l hemoglobin) should lead to an evaluation for hematologic malignancies.
2. An abnormally high ALT/AST ratio with a normal ALP should lead to tests for myopathy, i.e. a creatine kinase (CK) determination and possibly an electromyogram.
3. In cases of unexplained hematuria tests for kidney or urinary collecting system malignancies should be carried out.
4. Unexplained high titers of ANA should lead to tests for other connective tissue diseases, especially SLE.
5. If a monoclonal immunoglobulin is present in the serum or urine, multiple myeloma or primary amyloidosis need to be excluded.
6. If the dipstick proteinuria level is 1+ or more, the 24-hr urine protein excretion should be measured. If the result is greater than 150 mg, urine

electrophoresis should be performed to measure the levels of albumin and other proteins and to eliminate the possibility of light chain myeloma.

- D. If all of the possible secondary causes of PMR are excluded, treatment with prednisone at a dosage between 10 - 20 mg/day is mandatory. However, if no improvement is obtained after 7 days, the possibility of GCA should be considered. In this regard, if a temporal artery biopsy is negative for GCA, a more exhaustive study to exclude solid malignancies should be considered.

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