

Rheumatology: 11. Evaluation of the patient with pain all over

Michael P.E. Puttick

The case

Over the last month, Mrs. S, an 80-year-old woman with a history of generalized osteoarthritis and osteoporotic fractures, has been experiencing increased pain and stiffness in her hands, wrists, upper arms, shoulders and calves and has had transient swelling at the wrists. She is frequently roused from sleep by pain. Morning stiffness lasts 3 hours, and she complains of marked fatigue. She denies having fevers, headache, jaw claudication or scalp tenderness. Investigations have shown mild normocytic anemia, a white blood cell count of $3.5 \times 10^9/L$ (polymorphonuclear leukocytes $1.8 \times 10^9/L$, lymphocytes $1.3 \times 10^9/L$) and a platelet count of $67 \times 10^9/L$. Her erythrocyte sedimentation rate was 75 mm/h. The results of tests for rheumatoid factor and antinuclear antibodies were negative. Her symptoms are not relieved by acetaminophen, and her tolerance of nonsteroidal anti-inflammatory drugs is poor because of stomach upset. Her response to prednisone, 10 mg/day, was prompt and marked but, because the dose could not be reduced below 5 mg/day without a flare-up of symptoms, she was referred for rheumatologic assessment.

Patients with widespread musculoskeletal pain are frequently encountered in clinical practice, but their assessment can be a formidable challenge because of the wide range of possible diagnoses: rheumatologic, endocrine/metabolic, neurologic, infectious, malignant or psychiatric disorders (Table 1). The most common cause is probably self-limited viral infection. A specific diagnosis is necessary before effective treatment can be recommended.

In most cases, a differential diagnosis can be established by clinical assessment (history and physical examination) and a few simple investigations (Table 2). The latter are recommended when symptoms are severe or have lasted longer than 1 or 2 weeks. Most patients will not require every test listed in Table 2; for example, younger patients with symptoms of fibromyalgia will probably need only the first 5. Extensive investigations should be reserved for situations when the clinical diagnosis is unclear.

Rheumatologic causes of widespread pain

Fibromyalgia

Fibromyalgia affects up to 2% of the population and can start at any age; it is at least 7 times more common in women than in men.¹ By the time the diagnosis is made, patients have often had symptoms for many years. Patients with fibromyalgia complain of pain all over and, by definition, have pain on both sides of the body, above and below the waist, and in both the trunk and extremities.²

Patients describe the pain in many different ways, often very emotionally. Muscular stiffness is a prominent complaint. Associated features include nonrestorative sleep, irritable bowel syndrome, headaches, paresthesias and a sensation of swelling of the hands and feet. Fibromyalgia is frequently associated with depression, memory and concentration difficulties, and anxiety, and it often accompanies other chronic painful disorders.

A diagnosis of fibromyalgia is made when there is widespread pain lasting for at least 3 months accompanied by tenderness at discrete locations (Fig. 1). Tender

Review

Synthèse

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The Arthritis Society salutes CMAJ for its extensive series of articles on arthritis. The Society believes that this kind of information is crucial to educating physicians about this devastating disease.

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points are palpated with the thumb, using sufficient force to cause blanching of the nailbed. To be eligible for research studies, patients must have at least 11 tender points of a possible 18 but, in practice, the diagnosis can be made in patients with fewer tender points if there is widespread pain and many of the other characteristic symptoms.³ Patients with fibromyalgia are often tender all over; the presence of tenderness other than at the classic locations does not exclude the diagnosis.

A diagnosis of fibromyalgia does not preclude the need

Table 1: Differential diagnosis of pain all over

Type of problem	Diagnostic investigations
Rheumatologic	
Polymyalgia rheumatica/giant cell arteritis	Erythrocyte sedimentation rate
Connective tissue disease	Antinuclear antibodies
Rheumatoid arthritis	Rheumatoid factor
Fibromyalgia	Tender point count
Painful myopathies	Creatine phosphokinase
Endocrine/metabolic	
Thyroid disorders	Thyroid-stimulating hormone
Disorders of calcium, osteomalacia	Serum calcium, phosphorous, alkaline phosphatase
Adrenal insufficiency	Electrolytes, glucose, eosinophil count
Neurologic	
Painful peripheral neuropathies	Nerve conduction studies
Meningeal carcinomatosis	Lumbar puncture
Infectious	
Influenza and other viral illnesses	Viral serology
HIV infection	HIV test
Trichinosis	Eosinophil count
Malignant	
Multiple myeloma	Serum and urine protein electrophoresis, bone marrow biopsy
Metastatic carcinoma	Bone scan, alkaline phosphatase
Paraneoplastic syndromes	Variable
Psychiatric	
Depression, anxiety disorders, somatoform disorders, malingering	Psychometric testing

Table 2: Recommended initial investigations for persistent widespread pain

Complete blood count and differential count
Erythrocyte sedimentation rate
Rheumatoid factor
Antinuclear antibodies
Thyroid-stimulating hormone
Creatine phosphokinase
Alkaline phosphatase
Serum calcium and phosphorous
Serum protein electrophoresis

to investigate the presence of other conditions. The physician should make this diagnosis with reluctance in an older patient without a long history of musculoskeletal symptoms. The cause of fibromyalgia is unknown, and its relation to preceding trauma, such as motor vehicle accidents, is controversial.³ Some recent reports^{4,5} suggest an association with prior physical or sexual abuse.

Current approaches to treatment are often unsatisfactory (Table 3). When fibromyalgia is associated with another rheumatic disorder, treatment for the second disorder typically does not improve the fibromyalgia. Many patients can be helped by encouragement and reassurance, regular aerobic exercise and improvement of sleep. However, patients with fibromyalgia tend to remain symp-

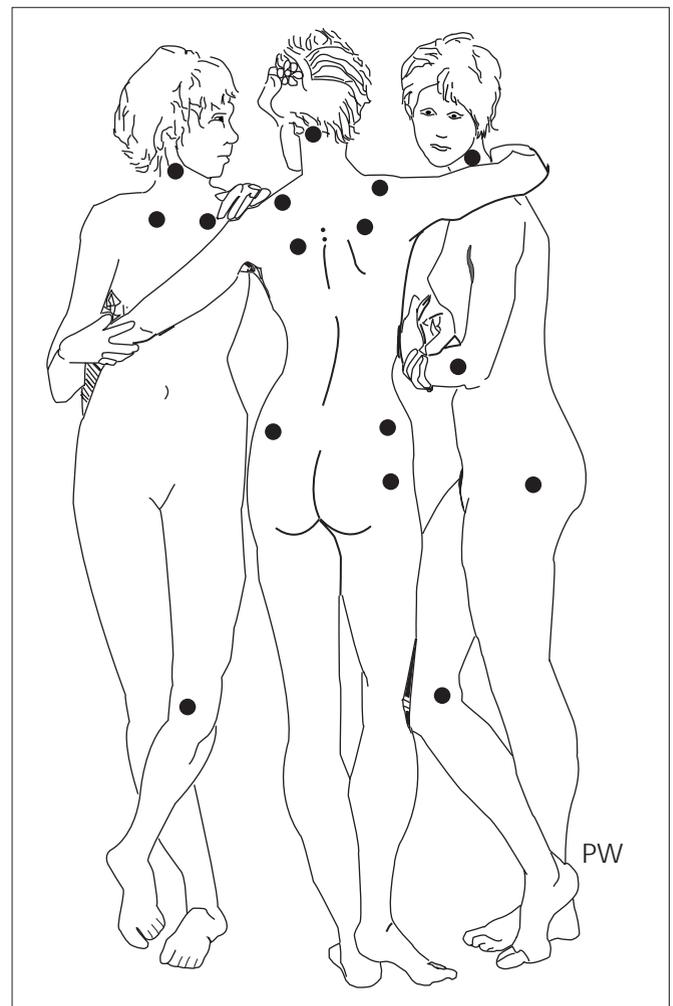


Fig. 1: Tender points in fibromyalgia are found at the following bilateral locations: suboccipital muscle insertion points; anterior aspects of the intertransverse spaces at C5-7; mid-point of the upper border of the trapezius; origin of the supraspinatus; second costochondral junction, superolateral aspect; lateral epicondyle, 2 cm distal; buttock, upper outer quadrant; greater trochanter, posterior aspect; medial fat pad of the knee. Reproduced with permission of *Arthritis Rheum* 1990;33:169,² Lippincott Williams & Wilkins.

tomatic at unchanged levels for many years. Most, if not all, should be encouraged to continue working and to maintain regular social activities despite their symptoms. Whether disability benefits should be granted for a diagnosis of fibromyalgia is an unresolved issue.³

Myopathies

Idiopathic inflammatory myopathies, such as dermatomyositis and polymyositis, typically cause proximal muscle weakness rather than pain, although pain is sometimes prominent, particularly if there is associated joint inflammation. A careful history and examination will usually permit the practitioner to distinguish between true muscle weakness and weakness due to pain. Muscle pain may be significant in myopathies secondary to toxins or drugs such as cholesterol-lowering agents or colchicine. Hypothyroidism sometimes presents as a myopathy, with proximal muscle weakness and an elevated creatine phosphokinase level, or as generalized myalgia with normal muscle enzymes.

Connective tissue diseases and rheumatoid arthritis

These conditions are discussed more fully in a previously published article in this series by Alice Klinkhoff.⁶ In the elderly, rheumatoid arthritis may start with typical polymyalgia rheumatica symptoms (see later). Symmetrical synovial swelling may then appear weeks or months later.

Polymyalgia rheumatica

Polymyalgia rheumatica (PMR) is an idiopathic disorder affecting people over the age of 50 years. It is characterized by the presence of inflammation in joints⁷ and other synovial structures.⁸ Patients with PMR have widespread pain and stiffness (as was the case for Mrs. S), which is most severe at the limb girdles, neck and low back. Constitutional symptoms such as fatigue, malaise, fevers and weight loss are often prominent and may occasionally obscure the musculoskeletal complaints. Fatigue and malaise may lead to a diagnosis of depression. Physical findings include pain at the extremes of movement of the shoulders, hips and knees; some patients cannot raise their arms over their head because of the pain. There may be synovial swelling or effusions at fingers, wrists and knees and, occasionally, pitting edema of the hands or feet.

Laboratory tests will reveal normocytic anemia, an elevated platelet count, an erythrocyte sedimentation rate (ESR) of over 40 mm/h, an elevated level of α_2 globulins and elevated liver enzymes in up to one-third of patients. Results will be negative for rheumatoid factor and antinuclear antibodies (Table 4). Although most patients will have a markedly elevated ESR, depending on the duration of symptoms, in a recent retrospective study,⁹ 22% of patients had a pretreatment ESR of 30 mm/h or lower.

Giant cell arteritis

Giant cell arteritis (GCA) is a vasculitis of medium and large vessels that typically involves arteries of the head and neck, although its distribution may be more general.¹⁰ GCA and PMR are related disorders that may develop together, or one may precede the other.¹¹ In addition to the constitutional symptoms associated with PMR, symptoms of GCA include headache, swelling of the temporal artery, scalp tenderness, jaw claudication, tongue or throat pain and visual disturbances.

Physical findings are variable for this condition. The physician should examine the patient for thickening, nodularity or tenderness of the temporal arteries¹² and scotomata (areas of lost or reduced vision within the visual field), should listen for bruits at the temporal and occipital arteries, and should inquire about pain associated with brushing hair, difficulty in chewing meat and pain when swallowing.

When this diagnosis is suspected, the patient should be started on high doses of corticosteroids (1 mg/kg per day) immediately because of the risk of sudden blindness associated with untreated GCA.¹³ Controversy exists about whether a biopsy is needed in all patients with suspected GCA.^{11,14} In my practice, patients with typical symptoms and findings, an elevated ESR and a prompt response to high doses of corticosteroids are not subjected to biopsy. A biopsy is carried out for all other patients with suspected

Table 3: Treatment of fibromyalgia

Nonpharmacologic
Education*
Exercise programs
Aerobic: walking, swimming, bicycling
Stretching: yoga, Tai Chi
Pharmacologic
Nonnarcotic analgesics
Acetaminophen
Low-dose NSAIDs
Sleep medications
Low-dose amitriptyline or trazodone
Cyclobenzaprine
Zopiclone
Antidepressants (in patients with concomitant depression)

Note: NSAIDs = nonsteroidal anti-inflammatory drugs.

*In addition to local resources, patients may be directed to the Arthritis Society (800 321-1433, www.arthritis.ca).

Table 4: Diagnostic criteria* for polymyalgia rheumatica⁴

1. Age > 50 yr
2. Three of the following:
 - Pain in the neck, shoulder or pelvic girdle
 - Marked morning stiffness for > 1 h
 - Elevated erythrocyte sedimentation rate
 - Rapid response to prednisone (20 mg/d)
3. Negative tests for rheumatoid factor and antinuclear antibodies

*All 3 criteria must be met to confirm a diagnosis of polymyalgia rheumatica.

GCA. It is sometimes necessary to do bilateral temporal artery biopsies to prove the diagnosis. A temporal artery biopsy can be performed within 7–14 days of starting treatment without compromising the histopathologic findings.¹⁵

Management of polymyalgia rheumatica and giant cell arteritis

Occasionally, a patient with mild symptoms of PMR may be successfully treated with nonsteroidal anti-inflammatory drugs (NSAIDs). However, a patient's rapid, substantial response to low doses of corticosteroids (10–20 mg/day) is included in some sets of criteria for the diagnosis of PMR (Table 4). Patients with PMR often describe their response to corticosteroids as “magic” or “miraculous.”

A usual course of therapy for PMR begins with prednisone, 5 mg, twice daily. If the response is insufficient after 2 or 3 days, the dose is increased to 10 mg twice daily. Almost all patients respond to prednisone, 5 mg, twice a day, or their dose can be tapered off to this level within a month or so.¹⁶ Patients with PMR usually require treatment with corticosteroids for extended periods, often for at least 18 months. For example, they may be maintained on a stable dose of prednisone for several months, before the dose is gradually reduced by 1 mg every month or two, depending on changes in symptoms and ESR. Attempts to reduce prednisone doses more quickly may lead to a flare-up of symptoms, if the diagnosis is correct; thus, it is best to taper it off at a rate that will have patients off the drug in no less than 1 year. Alternate-day corticosteroids are usually poorly tolerated, and symptoms increase on the “off” day.

In many patients, tapering off prednisone is difficult or impossible, and rheumatologic consultation may be helpful. Sometimes the use of NSAIDs will facilitate tapering off the steroid, but the combination of prednisone and NSAIDs is associated with an increased risk of gastrointestinal toxicity. Use of prophylactic misoprostol or proton pump inhibitors should be considered. The efficacy of steroid-sparing agents such as methotrexate and hydroxychloroquine has not been well established.

The treatment of GCA usually requires higher initial doses of prednisone, usually 40–60 mg daily in divided doses, to reduce the risk of sudden blindness.¹³ A response is generally obtained within a few days when patients are treated with prednisone, 25 mg, twice daily (or 20 mg twice daily for frail elderly patients or patients with multiple medical problems). If symptoms are not controlled, the daily prednisone dose is increased by 10–25 mg. The starting dose is maintained for 4–6 weeks then, if symptoms are controlled and the ESR has fallen, tapering off is started.

Schedules for tapering off corticosteroids are empirical, but, in general, rapid or large dose reductions should be avoided. The following schedule has proven effective; each number represents the total daily prednisone dose expressed in milligrams and is given for a month: 50, 40, 30, 25, 20, 15, 10, 7.5, 5, 2.5. Thereafter, the patient takes 2.5 mg every

Key points

- Assessment of patients with widespread musculoskeletal pain is a challenge because of the wide range of possible diagnoses.
- In most cases, a differential diagnosis can be established by clinical assessment and a few simple investigations.
- A diagnosis of fibromyalgia is made when the patient has experienced widespread pain for at least 3 months, accompanied by tenderness at discrete locations.
- Myopathies typically cause muscle weakness rather than pain, although pain is sometimes prominent, particularly if there is joint inflammation.
- Polymyalgia rheumatica is common in patients over 50 years of age; patients have widespread pain and stiffness, especially at the limb girdles, neck and low back, and may experience fatigue, malaise, fevers and weight loss.
- Polymyalgia rheumatica responds readily to low doses of corticosteroids, but treatment may be complicated by the development of giant cell arteritis.
- Because giant cell arteritis carries a risk of sudden blindness, it requires immediate treatment with higher doses of corticosteroids.
- The prolonged use of corticosteroids can lead to significant morbidity; interventions to prevent corticosteroid-induced osteoporosis should be initiated at the start of therapy.

other day for a month, then 2.5 mg every third day for a month, and then the drug is discontinued. In this schedule, prednisone is taken once daily after the first 3–4 months. Some practitioners like to convert patients to an alternate-day regimen, but this change should not be made until disease symptoms are well controlled and the ESR is stable.

As with PMR, patient symptoms and changes in the ESR are used to guide tapering off. The ESR commonly rises gradually as the prednisone dose is reduced. A sudden rise in the ESR should prompt an evaluation for the recurrence of disease signs and symptoms, as well as for alternative causes, such as infection. An asymptomatic rise in the ESR is not an indication for increasing the dose of corticosteroid, but may necessitate delaying further dose reductions. Clear evidence of disease flare-ups should prompt an increase in the prednisone dose by about 50% or sufficient to suppress symptoms and reduce the ESR. Corticosteroid treatment is usually continued for at least 1 year. Steroid-sparing agents such as azathioprine or methotrexate are occasionally helpful in patients who are unable to tolerate reductions in prednisone.

The prolonged use of corticosteroids is typically associated with multiple side effects, including weight gain, hypertension and glaucoma. Osteoporosis is a particular problem in the elderly, predominantly female population affected by PMR and GCA. (Its management is discussed in an upcoming article in this series by John P. Wade.) Ef-

fective interventions for the prevention of corticosteroid-induced osteoporosis are available and should be initiated at the onset of corticosteroid treatment.¹⁷⁻¹⁹

Treatment for Mrs. S

At the time of the initial rheumatologic assessment, 4 months after the onset of symptoms, the results of the physical examination were notable only for osteoarthritic changes in Mrs. S's fingers and knees. The differential diagnosis was believed to include PMR, rheumatoid arthritis and systemic lupus erythematosus (SLE). On further investigation, the patient's complete blood count and ESR were found to be normal. Specific serology for SLE (levels of complement, anti-DNA antibodies and antibodies to extractable nuclear antigens) was negative. Mrs. S was started on vitamin D, calcium and cyclic etidronate for osteoporosis, and slow tapering off the dose of prednisone was begun.

Four months later, when this dose was 2 mg daily, the patient visited her physician complaining of scalp pain and tenderness, swollen scalp "veins" and pain in her throat, neck and clavicles. Physical examination revealed marked thickening and tenderness of the temporal arteries. The ESR was 55 mm/h. A temporal artery biopsy showed changes attributable to GCA. The prednisone dose was increased to 20 mg twice daily, resulting in prompt resolution of all symptoms. It has since been tapered off over the last year to 2.5 mg daily. The course of Mrs. S's treatment has been complicated by an episode of herpes zoster, but she has remained free of further osteoporotic fractures and the temporal arteritis has been well controlled. The cytopenias have not recurred and remain unexplained.

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