Current Practice

Polymyalgia Rheumatica

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Polymyalgia rheumatica is an important condition today for a number of reasons. Although usually not serious and only rarely fatal, it causes great distress in elderly patients over periods of many months or some years: such patients are often thought to be merely osteoarthrotic and unduly complaining and are considered rather a nuisance by relatives and even sometimes by their physicians. The discovery of a sedimentation rate over 80 mm. in 1 hour (Westergren) may sometimes come as something of a revelation and surprise to the latter. It is important also because it is a condition fairly common and very often missed or misdiagnosed; and, lastly, it is important because it is so eminently treatable.

Before discussing the management of any particular rheumatic disorder it is as well to look at it critically and to decide what it is one is trying to treat and control. This is particularly so in the case of polymyalgia rheumatica. What is it? What is this condition? It was first described by Bruce¹ in 1888 under the title "senile rheumatic gout," and many years later Barber² coined the term polymyalgia rheumatica. Horton, Magath, and Brown³ had meantime described temporal (giant cell or cranial) arteritis, and in the last few years many articles have drawn attention to the close similarity or apparent identity of these two conditions⁴⁻⁷ so much so that Hamrin, Jonsson, and Landberg⁸ suggested the alternative title "polymyalgia arteritica." Olhagen in 1963⁶ had considered polymyalgia rheumatica to be a form of senile arteritis. Bruk⁹ studied 80 cases and did arterial biopsies in 33 of them. Fifteen had inflammatory changes histologically, 9 having giant cells present: only 6 of the 15 biopsy-positive cases had clinical evidence of inflammation in the artery biopsied, a fact noted also by Bevan, Dunnill, and Harrison,¹⁰ for in their study of proved cases of giant cell arteritis one in four arteries histologically positive were clinically entirely normal. In Bruk's series no abnormalities were found in muscle enzyme tests in 21, muscle biopsies in 17, and electromyographic studies in 18 patients. Four of five biopsies of the sternoclavicular joint showed a histological picture of chronic non-specific synovitis and capsulitis. A year previously Dixon and his colleagues⁷ had found temporal artery biopsies positive in 10 of 28 cases of so-called polymyalgia rheumatica, though in 1964 Gordon, Rennie, and Branwood¹¹ found no evidence of arteritis in their series of patients. In a three-year follow-up of 32 acute cases of polymyalgia rheumatica Andrews¹² found one case each of bronchial carcinoma, sero-negative polyarthritis, and probable rheumatoid arthritis, and three of peripheral scleroderma: 26 cases made satisfactory recoveries. Turning to necropsy evidence, Hamrin¹³ reported that all of three necropsies showed disseminated giant cell arteritis of the aorta and some of the great vessels arising from it, and in a more recent publication Hamrin, Jonsson,

and Hellsten¹⁴ reported six cases followed up to necropsy: four had giant cell arteritis in the aorta and its large branches, one had no necropsy evidence of arteritis, though a previous temporal artery biopsy in life had been positive, and one had a granulomatous myocarditis.

There seems on present evidence, therefore, to be a good case for considering many of these late-middle-aged and elderly patients as having an acute or subacute arteritis. Though some turn out to have sero-positive or sero-negative rheumatoid arthritis, a few some other connective tissue disorder such as scleroderma, and a few carcinomatosis, most recover after a duration of anything from a few months to two or three years. Some cases last considerably longer. The more arterial biopsies and angiograms that are done, the more often is a positive diagnosis of arteritis made. One can therefore usually give an optimistic prognosis as regards cure, pointing out at the same time that, though eventually complete recovery will occur, these patients are elderly and sometimes frail and are prone to cross-infection and arteriosclerotic complications, and that many months or even years may pass before they are completely better.

Investigations

The sedimentation rate is usually elevated, over 80 mm. in 1 hour, though rarely it is normal. A normal sedimentation rate does not completely negative the diagnosis, but it makes it unlikely. A careful examination of the affected vessels should be made for thickening and tenderness, diminished or absent arterial pulsation, and bruits. Biopsy of a suitable superficial vessel or vessels should be done; the temporal artery is the most accessible. Dixon¹⁵ describes, as an early diagnostic sign, undue sensitivity of one or both carotid sinuses, shown by marked slowing or stopping of the pulse for a few beats on light pressure over the carotid artery under the angle of the jaw, the test being always done with the patient recumbent. Angiograms may be useful in revealing the extent and localization of the disease in the affected arteries: pulsation may disappear in a vessel narrowed but not obliterated by the disease process. In the differential diagnosis one should always consider the other connective tissue disorders, rheumatoid arthritis, systemic lupus erythematosus, polyarteritis nodosa, scleroderma, and dermatomyositis, and also malignant conditions, including myeloma and leukaemia.

Treatment and General Management

Treatment, for once in the rheumatic disorders, is more important than general management, for dramatic results usually follow the administration of quite small amounts of

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corticosteroids, such as 2.5 mg. prednisolone three or four times a day. The condition usually starts to come under control within 24 to 48 hours, when corticosteroids should be continued at the lowest effective dose, only very gradually being withdrawn when the condition is well controlled. The dose should be reduced by no more than 0.5 or 1 mg. at a time, and two to four weeks should elapse between each dose reduction. If symptoms or signs reappear the dose should be adjusted a step higher and an attempt to reduce made again a few weeks later. Prednisone and prednisolone are available in 1 mg. tablets and for this reason are to be preferred to other equally effective corticosteroid preparations which are issued only in larger-strength tablets. Overdosage, as throughout the field of corticosteroid therapy, must be sternly avoided. Only very rarely is it necessary to exceed an oral dose of 10 mg. prednisone a day, and then only for short periods. More than 7 mg. a day will produce signs of overdosage of Cushingoid type if continued for several weeks or months. Should there be symptoms suggesting that the retinal vessels are affected the dosage should be quickly increased, though amaurosis may still occur. Occasionally signs appear in the central nervous system which also demand an increase in dosage. On no account should treatment be delayed in such cases for arterial biopsy or for any other reason, or permanent sequelae may occur in eye or brain. The patient has to be very thoroughly instructed in the art of his or her own treatment, and the dangers of stop-start therapy emphasized. Ordinary analgesics such as aspirin or paracetamol may be taken as required, but other anti-inflammatory agents such as phenylbutazone, oxyphenbutazone, indomethacin, or mefenamic and flufenamic acids are much less effective than the corticosteroids and may not prevent progress of the disease while under treatment. Biopsy of a temporal artery will usually relieve the severe headache which may be present in this area. Although there may be signs of inflammation in some joints, as shown by Gordon *et al.*¹¹ and Bruk,⁹ these respond more effectively to corticosteroid therapy than to other agents. Physical measures, heat and exercises, and rehabilitation are necessary only in certain cases—for instance,

where corticosteroid therapy has been delayed and immobility has caused aggravation of co-existent osteoarthritis, or where joints have become stiff and "frozen" during the earlier stages of the disorder—shoulders rather than hips being more commonly affected in this way. Pain and stiffness in shoulder and hip girdles are so effectively and rapidly relieved by corticosteroid therapy that the diagnosis should be queried if there is no real improvement within a few days. The patient must be warned that the disease may not burn out for two or three years or more, and that no quick permanent cure will result from a few days' treatment, but that therapy must continue probably for very many months. The steroids may be only very gradually reduced when the condition comes under adequate control, pain being relieved and function restored. Too rapid reduction of dosage will result in a rapid return of symptoms, sometimes with signs of extension of the disease to areas unaffected previously. The best measure of progress is the patient's own statement regarding the easing of previously distressing symptoms, but the sedimentation rate will usually fall towards or into the normal range as the disease comes under control. Iron and vitamin supplements may be necessary in individual patients.

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TODAY'S TESTS

With the help of expert contributors we print in this section notes on drugs in common use.

Histidine Loading (FIGlu Excretion) Test

This test was first used as a biochemical index of abnormal folate metabolism in leukaemic children who were being treated with folic acid antagonists,¹⁻³ but it has had a much wider application in recent years in the investigation of folate deficiency in general. Active folate (tetrahydrofolate) is required for the catabolism of histidine to glutamic acid (Fig. 1). In folate deficiency there is a block to the further metabolism of formimino-glutamic acid (FIGlu), which accumulates and is excreted in the urine. This pathway can be stressed by giving a loading dose of histidine, and this is the basis of the FIGlu excretion test.⁴

Methods

Clinical application of the FIGlu test was limited initially by the complexities of the methods required for the detection of FIGlu in urine.⁵ However, more recent techniques have simplified the procedure. Electrophoresis using high voltage,⁶

or preferably conventional voltage on cellulose acetate,^{7,8} is a useful screening method which can be calibrated to give semi-quantitative results. A simplified quantitative assay has been described by Chanarin and Bennett,⁹ which is a combination of previously used spectrophotometric¹⁰ and enzymatic methods.³ In principle, this method uses a crude liver enzyme preparation to convert folic acid to its active form, tetrahydrofolate (FH₄). The formimino-transferase present in the liver extract transfers the formimino-group of FIGlu to FH₄, and the addition of HCl converts the resulting end-product to 5,10-methenyl-FH₄, which can be read spectrophotometrically.

Furthermore, the liver extract also contains urocanase, which converts urocanic acid to FIGlu (Fig. 1), so that the method measures the combined excretion of these two compounds. The amount of urocanic acid can be estimated separately by the differential destruction of FIGlu by boiling the urine at alkaline pH.

Histidine Loading Dose.—A loading dose of histidine is given to stress the normal metabolic pathway (Fig. 1). In practice, 15 g. of *l*-histidine monohydrochloride monohydrate given as a single oral dose is satisfactory, although Luhby and Cooperman⁵ have recommended that it should be given in three divided doses. This dosage may lead to false positive results