“POLYMYALGIA ARTERITICA”*
FURTHER CLINICAL AND HISTOPATHOLOGICAL STUDIES
WITH A REPORT OF SIX AUTOPSY CASES

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During the last few years an increasing amount of evidence has accumulated, indicating that the well-defined clinical syndrome of “polymyalgia rheumatica” or “polymyalgia arteritica” is a manifestation of a generalized giant cell arteritis (Kogstad, 1965; Dixon, Beardwell, Kay, Wanka, and Wong, 1966; Bruk, 1967; Wilske and Healey, 1967), although criticism of this concept has also appeared (Gordon, Rennie, and Branwood, 1964; Andrews, 1965). In previous reports we presented series of clinical cases of this syndrome, in which arterial biopsies gave further support to this view (Hamrin, Jonsson, and Landberg, 1964, 1965). Angiographic and auscultatory studies suggested an involvement of the large arteries, and in one case autopsy confirmed the existence of giant cell arteritis in the aorta and right subclavian artery.

A clinical follow-up and a further study on the occurrence and distribution of arteritis in connexion with this syndrome, with special reference to the larger vessels, seemed desirable. In this paper we present the clinical and histopathological findings in six of our previously reported cases of “polymyalgia arteritica” in which autopsies were performed.

Clinical Material

The symptoms and signs and our diagnostic criteria have been reviewed previously (Hamrin and others, 1964, 1965). Of our recently reported 52 cases, eleven have died, and in six of these, material from the large arteries was obtained for histopathological examination at complete or partial autopsies. In all the cases the aorta, the common carotids, and the subclavian arteries were investigated, and in addition several other large arteries in most cases (Table I, overleaf). Their ages (1 male and 5 females) at death varied between 68 and 82 years and the intervals between the onset of clinical symptoms and death ranged from 2 to 7 years. Serological reactions for syphilis were negative in all the patients, as was the Waaler-Rose test on repeated examinations. In three cases out of five, in which a biopsy of the temporal artery had been performed, evidence of giant cell arteritis was obtained.

A survey of the clinical course of the disease as well as of the ESR and steroid therapy in each case is given in Fig. 1 (overleaf). The clinical activity is graded from 0 to 4, principally according to the system of Gordon (1960). It should be noted that Grades 3 and 4 mean a marked restriction of movements in the great joints. The time of diagnosing polymyalgia arteritica is also indicated in Fig. 1, and in these, as in most of our cases, the diagnosis was made before the biopsy.

Case Reports

Case 1, a woman aged 65 years, was taken ill acutely in May, 1964, with pain and stiffness in the back of the neck, the shoulders, and the hips, and 7 weeks later also in the right calf. She had no local symptoms from the temporal regions. She was admitted to the hospital with a diagnosis of calf-vein thrombosis.

Examination (June 27).—She was a thin woman in a fairly good general condition. In the right calf there was a tender, well-circumscribed swelling, measuring 12 × 6 cm. In spite of 3 weeks' adequate anticoagulant therapy she ran a persistent low-grade fever and the ESR rose from 34 to 75 mm. per hour. The diagnosis of thrombosis was considered unlikely and the therapy was discontinued. Movements of the large joints were painful and strongly inhibited, particularly in the right shoulder. Both temporal arteries felt normal. Over both the popliteal and femoral arteries whizzling murmurs were heard. Blood pressure in the right arm was 200/100 and in the left 190/90.

Biopsy of the right temporal artery on July 21 revealed a giant cell arteritis. After prednisolone therapy (10 mg./day initially), the ESR rapidly diminished and she
The symptoms and signs are graded by restriction of movements and degree of pain:

Grade 1: Slight inconstant symptoms.

Grade 2: Slight but constant symptoms.

Grade 3: Moderate pain and evident restriction of movements in one or several of the large joints.

Grade 4: Severe pain and marked restriction of movements in the neck, shoulders, and hip joints. The patient is seriously disabled.

Broken lines indicate periods in which information about the state of the patient was uncertain.

Black columns represent prednisolone dosage (or equivalent dosage of triamcinolone) in Case 3.

* = Date of diagnosis.

Fig. 1.—Clinical course in six cases of polymyalgia arteritica.
became quite free of symptoms except for the right arm, which gradually developed into a "frozen shoulder". On October 21 there was a cerebro-vascular episode with a left-sided hemiplegia. Because of her mental confusion it was difficult to evaluate whether the patient had any polymyalgic symptoms. The ESR remained low even after cessation of the steroid therapy. 22 months after beginning of her illness she died from a further cerebral catastrophe with a right-sided hemiplegia.

Autopsy.—The findings included, in addition to bilateral broncho-pneumonias, a recent massive haemorrhage in the left cerebral hemisphere as well as a small cavity containing yellowish semi-fluid material in the right internal capsule, representing the remains of an old haemorrhage. The examined arteries showed moderately advanced atherosclerosis and histologically no clear-cut picture of arteritis (Table I). The small vessels of the myocardium, the left deltoid muscle, and the right gastrocnemius had a normal appearance. The myocardium showed a slight fibrosis but no signs of inflammation.

**Case 2, a 74-year-old woman,** fell ill subacutely in June, 1962, with stiffness and pain on movement around the large joints. During the following year her condition gradually deteriorated and she became completely confined to bed. She lost 5 kg. in weight. At times she complained of itching over the trunk. Her temperature was about 38°C. After an illness of one year she was admitted to the hospital with a diagnosis of rheumatoid arthritis.

**Examination** (June 17, 1963).—She was very thin and her appearance was suggestive of malignant disease. Temperature 38°C. ESR 126 mm./1st hour. The muscles of the shoulders were markedly wasted and the
clinical picture was that of "frozen shoulders". She denied pain in the temporal regions either on admission or previously. The temporal arteries were normally pulsating. At a later stage, a murmur could be heard over the right axillary artery.

Biopsy of the left temporal artery showed a giant cell arteritis (Fig. 2a).

Recovery.—After 2 months' steroid treatment (prednisolone 5 mg./day) she considered herself as healthy as before the disease and after 4 months the ESR had fallen to 20 mm./1st hour.

Progress.—2 years later she was admitted to the surgical department with intestinal obstruction. She had then been free from myalgic symptoms for more than 2 years and had had no steroid therapy for 17 months. After a colonic resection for an adenocarcinoma she died 3 days post-operatively (43 months after the onset of the polymyalgic disease).

Autopsy.—There were signs of acute circulatory insufficiency with stasis in the abdominal organs and pulmonary oedema. The myocardium showed a moderate diffuse fibrosis. Rather pronounced atherosclerosis was found in the aorta and its large branches as well as in the coronary arteries. Microscopical investigation revealed an arteritis of giant cell type, most pronounced in the abdominal aorta but also in the thoracic aorta as well as in the left common and internal carotid and the left subclavian artery (Table I). Thus, in addition to more or less heavy round cell exudates in the adventitia, often concentrated around the vasa vasorum, granulomatous infiltrates could be followed into the media, containing lymphocytes, plasma cells, macrophages, and multinuclear giant cells (Fig. 2b). There was a more or less pronounced destruction of the elastica. Discrete inflammatory changes of a non-specific appearance were found in the right brachial artery. The small vessels of the myocardium and deltoid muscles were normal. There were no signs of residual cancer or any remote metastases. The small bowel was moderately dilated.

Case 3,* a 74-year-old man, became ill in January, 1962, with stiffness and pain on movement in the back of the

*Reported as Case 6 in our first communication on this subject (Hamrin and others, 1964).
POLYMYALGIA ARTERITICA

The disease affected the neck, calves, thighs, hips, shoulders, and brachial regions, in that order. One month later his physician diagnosed temporal arteritis. The ESR was 133 mm./1st hour. The patient was given steroid therapy (triamcinolone 4 mg. three times a day), but noted transitory diplopia 2 weeks later.

Examination.—On March 3, 1962, the right eye was amaurotic and despite an increased steroid dose the left eye became amaurotic 2 days later. During the following year, steroid therapy (triamcinolone maximum 4 mg. three times a day) relieved his muscle and joint symptoms fairly well. When he discontinued this therapy on two occasions the symptoms grew worse and also involved the elbows, wrists, and knee joints.

In March, 1963, after a short interruption of steroid therapy, he had bilateral "frozen shoulders". There was a slight reduction of movement in both elbows and the cervical spine. He was completely blind. The temporal arteries, which one year earlier had been prominent, hard, and pulseless, could now neither be seen nor palpated, but weak pulsations could be felt in front of the tragus.

Biopsy of a temporal artery disclosed giant cell arteritis, while the circumflex scapular artery showed no signs of inflammation. Biopsy of the teres major muscle was normal.

Progress.—In September, 1963, prostatectomy revealed an adenocarcinoma of the prostate.

Termination.—2 years later the patient died of pulmonary oedema in the surgical ward, 43 months after onset of the polymyalgic disease.

Autopsy.—The prostatic carcinoma had invaded the pelvic walls and the urinary bladder and produced a right-sided hydrolephrosis. Except for a number of pleural metastases no evidence of distant metastasis was found. The heart showed a moderate left-sided hypertrophy and dilatation, but no evidence of rheumatic valvular disease. The myocardium was pale with numerous small fibrous scars. The coronary vessels showed a fairly advanced, partially obstructive atherosclerosis but no thrombi. The vessels of the circle of Willis were sclerotic and the brain stem contained multiple foci of softening. The aorta was the site of an advanced atherosclerosis, with moderate macroscopical changes in the carotids and subclavian arteries. Microscopical investigation revealed an arteritis of giant cell type in the aortic arch, right subclavian, and superior mesenteric arteries (Table 1). In the right subclavian artery small necroses were found, surrounded by granulation tissue with giant cells. In addition, inflammatory exudates of a non-specific appearance were seen in the media, often lying longitudinally, separating the muscle bundles and sometimes presenting as small collections of neutrophil leucocytes. More discrete inflammatory changes were found in the walls of the right coronary artery and the left common carotid. The myocardium was the site of an interstitial myocarditis with focal granulomatus infiltrates with the appearance of Aschoff bodies with a central necrosis of fibrinoid type, often with an admixture of neutrophil leucocytes (Figs 3a and b, overleaf).

Some of these granulomata seemed to arise in the small interstitial vessels as small lumina persisted in the centres of the lesions. The rest of the interstitial vessels showed no inflammatory changes.

Case 4, a 77-year-old woman, became ill in May, 1962, with fever and influenza-like diffuse pain without any catarrhal symptoms. The pain soon localized to the shoulders, the brachial regions, and the back of the neck. After a temporary improvement the symptoms deteriorated 9 months later and she suffered from similar stiffness and pain in the hips and pelvic muscles.

Examination.—In May, 1963, she had again improved a little. She was a thin, aged woman with generally wasted muscles and a more pronounced muscular atrophy around the shoulders. Movements of the large joints were painful and the mobility in the shoulders was slightly restricted. The left hip was ankylosed after tuberculous coxitis in her youth. Both temporal arteries were pulsating.

Biopsy of the parietal branch of the right temporal artery showed pronounced sclerotic vascular changes with a fibrous thickening of the intima. In the adventitia a few discrete round cell collections were observed, which, however, were not thought sufficient to justify a diagnosis of arteritis.

As steroid therapy was considered to be contraindicated because of her old tuberculous infection, she received only physiotherapy; she improved little by little, though rather severe pain persisted in the right shoulder. During 1965 she developed cardiac failure and there were repeated small cerebro-vascular episodes. She died in March, 1966, 2 months after a new episode and 46 months after the onset of the polymyalgic disease. During the last year she had presented a prominent soft swelling of the right subdeltoid bursa.

Autopsy.—In addition to bronchopneumonia there was very pronounced atherosclerosis of the aorta and its branches as well as of the coronary and cerebral vessels. The aortic ostium was the site of a moderate calcifying stenosis, and the myocardium showed a moderate diffuse fibrosis. There was mural thrombotic material on the wall of the thoracic aorta with signs of multiple embolization with old and recent infarcts of the spleen, kidneys, and cerebrum, including a large fresh softening of the left temporal and parietal lobes. Histologically, the large vessels showed, in addition to atherosclerosis, only very discrete adventitial round cell infiltrates of uncertain significance (Table 1). No inflammatory changes could
be detected in the vessels of the deltoid muscles or in the right subdeltoid bursa.

Case 5,* a 75-year-old woman, was taken ill in January, 1959, with “pain all over the body”. The pain soon localized to the shoulders, the back of the neck, and hips, and quite disabled the patient. For a short period she felt pain on chewing, and she also complained of itching over her back. She became anorexic and noticed that sugary foods tasted either sour or bitter. She had diabetes mellitus, requiring insulin, with an increasing instability during the spring of 1959. The ESR was 64 mm./1st hour. Because of a provisional diagnosis of

*Reported as Case 2 by Hamrin and others (1965). A sister of this patient has also had polymyalgia arteritica, and was reported as Case 13 by Hamrin and others (1964).
POLYMYALGIA ARTERITICA

The patient received steroid therapy (prednisolone 10 mg./day) with excellent effect on the mobility of the joints. A trial with oxypHENbutazone resulted in exanthema and bilateral sialadenitis.

Termination.—After repeated attacks of cholelithiasis with pancreatitis the patient died of a fulminating pancreatitis in December, 1966, about 7 years after the onset of the polymyalgic disease.

Autopsy.—The clinical diagnosis of an extensive acute hemorrhagic necrosis of the pancreas was confirmed, with extensive tissue necroses and cholelithiasis with an occluding stone in the papilla of Vater; there was also bile stasis and slight icterus. The aorta and its branches showed a fairly pronounced atherosclerosis and a coronary sclerosis with an old infarct in the back and lateral walls of the left ventricle. Discrete changes indicative of giant cell arteritis were found in the left common carotid, the right axillary artery, and the right external iliac arteries, while non-specific inflammation was seen in the abdominal aorta, and the left subclavian and left femoral arteries (Table I).

Discussion

In all patients the diagnosis was made on clinical grounds. Only Case 3 presented clinical signs of temporal arteritis, and giant cell arteritis could be confirmed in this and two other cases, in which the inflammation in the temporal arteries had thus run its course without any local symptoms.

The arteries showed macroscopically no characteristic changes apart from the more or less pronounced atherosclerosis. The histopathological findings in the arteries are summarized in Table I.
It was possible to demonstrate in four out of six autopsies clear, although rather discrete, changes representing giant cell arteritis in the aorta and its main branches. In two of these (Cases 2 and 3), a giant cell arteritis had been verified by biopsy, while one biopsy had given a negative result (Case 6); no biopsy had been performed in Case 5.

In Case 1, with a positive temporal biopsy, no arteritic changes could be found at autopsy. It should be noted that in this case the clinical signs and the normal ESR indicated absence of disease activity at time of death.

In Case 4 neither biopsy nor autopsy revealed any arteritis. This patient was seriously disabled by repeated vascular episodes, and the degree of the polymyalgic symptoms was difficult to evaluate. Yet it is noteworthy that during the last months of her life she suffered a large indolent swelling of the subdeltoid bursa.

The unpredictable distribution of the arteritis (Table I) is in accordance with earlier investigations (Sproul, 1942; Heptinstall, Porter, and Barkley, 1954). The demonstration of arteritis must therefore be somewhat haphazard and this may help to explain the negative autopsy findings in two cases. The rather discrete and quiescent nature of the lesions (except in Case 3) could be in accordance with the long duration of the process and its tendency to heal.

It is thus apparent that the arteritis which can be verified by biopsy in many cases of the polymyalgic syndrome is not confined to the temporal and other cranial arteries but many also involve the aorta and its great branches. This supports the view that the syndrome is a manifestation of a generalized giant cell arteritis. Clinically the development of an aortic arch syndrome has been observed in an increasing number of cases (Hamrin and others, 1965; Strachan, Wigzell, and Anderson, 1966) and our previous auscultatory studies have also suggested such an involvement. Like Serre, Labauge, Simon, and Barjon (1966) we wish to call attention to the value of systematic auscultation of the great peripheral vessels in cases of polymyalgia arteritica.

The concept of polymyalgia arteritica as a clinical entity is now widely accepted, but there is not much agreement on the subject of differential diagnosis. Meulengracht (1945) and Holst and Johansen (1945), who probably were the first modern authors to describe the disease, regarded it as a more serious form of periarthritis humeroscapularis, but French and English authors have tended to look upon it as a form of rheumatoid arthritis, typical of old age. The preliminary diagnosis on admission to hospital in more than half our cases (58 cases up to January 1, 1966) was rheumatoid arthritis, and humeroscapular periarthritis was considered at some time or other in at least one-third of them (Hamrin, 1966).

There are, however, several points of difference between the arteritis in these cases and that described in rheumatoid arthritis in both distribution and histological character (Sokoloff, Wilens, and Bunim, 1951; Schmid, Cooper, Zilt, and McEwen, 1961). Whether the granulomatous myocarditis in Case 3, which presented as a classical case of temporal arteritis (Hutchinson, 1890), but also fulfilled the criteria of polymyalgia arteritica, was due to the arteritis or represented a rheumatic or rheumatoid affection can not be definitely decided. The absence of serological evidence favours the former. As far as we know, myocarditis has not been previously reported in cases of giant cell arteritis or polymyalgia arteritica, but it is known to occur in other arteritis processes, e.g. polyarteritis nodosa. The new concept of polymyalgia arteritica may assist in solving the problem of specific cardiac changes in rheumatoid arthritis (Garrod, 1876).

Summary

In six cases from previously reported series of polymyalgia arteritica, the clinical course and autopsy findings were followed up. Four showed giant cell arteritis in the aorta and its large branches, and another had no arteritis at autopsy in spite of a previous biopsy finding of arteritis in the temporal artery. One patient had granulomatous myocarditis.

The definition of this condition is discussed.

REFERENCES


POLYMYALGIA ARTERITICA


Études cliniques et histopathologiques supplémentaires de la polymyalgie artéritique. Rapport de six cas d’autopsie

RÉSUMÉ

Six cas de polymyalgie artéritique, appartenant à une série déjà décrite, furent suivis plus longtemps et on rapporte ici leur évolution clinique et les résultats d’autopsie. Dans quatre de ces cas on trouva une artérite à cellules géantes dans l’aorte et ses grandes branches; dans un autre cas l’autopsie ne révèla pas d’artérite, bien que, antérieurement une biopsie de l’artère temporaire en ait montré une. Le sixième cas eut une myocardite granulomateuse.

On discute la définition de cette affection.

Estudios clínicos e histopatológicos adicionales de la “polymyalgia arteritica” relato de seis casos de autopsia

SUMARIO

Seis casos de “polymyalgia arteritica”, perteneciendo a una serie ya descrita, fueron seguidos más adelante y se relatan aquí su evolución clínica y los resultados de autopsia. En cuatro casos se halló una arteritis a células gigantes en la aorta y sus ramos mayores, en un otro caso no se encontró evidencia de arteritis en la autopsia aunque una biopsia anterior hubiese revelado su presencia en la arteria temporal. En el sexto caso se descubrió una miocarditis granulomatosa.

Se discute la definición de esta afección.