UNILATERAL RHEUMATOID ARTHRITIS FOLLOWING HEMIPLEGIA

BY

MALCOLM THOMPSON AND E. G. L. BYWATERS

From the Royal Victoria Infirmary, Newcastle-on-Tyne, and the Postgraduate Medical School, London

Hemiplegia may sometimes give rise to peculiar and painful syndromes affecting the paralysed side: these include what has been described as the "shoulder hand syndrome" (Swan, 1954) as well as a "hemi-arthropathy" (Euzière, Pages, Lafon, Mirouze, and Salvaing, 1949) similar in some ways to that seen in Parkinsonism (Perrin and Louyot, 1939). Perhaps even less well known and of great scientific interest are the protective effects which hemiplegia may confer. Coste and Forestier (1935) described two hemiplegic patients who developed Heberden's nodes 9 and 10 years respectively after their strokes, and in both cases the nodes appeared on the fingers of the unaffected hand only. Forestier (1935) also reported that, in a 55-year-old woman who had suffered a stroke 7 years previously, Heberden's nodes developed 8 months after the stroke and remained restricted to the normal hand. Winter (1952) observed a similar case. Protection against the development of Heberden's nodes by lower motor neurone lesions was seen by us in a woman of 59 with Erb's palsy and contralateral Heberden's nodes, as previously noted by Hench (1940), McEwen (1940), and Stecher and Karnosh (1947). The last-named authors also reported that apparent regression of established Heberden's nodes on the paralysed side in a hemiplegic patient was due to soft-tissue wasting only, since the radiological appearances were not improved.

In regard to the protection afforded by a previous hemiplegia against subsequent inflammatory arthritis, Jacqueline (1953), described a man who had sustained a right hemiplegia in childhood, who developed multiple joint pains at the age of 41 years and severe rheumatoid arthritis at the age of 51 years. The interesting feature was that the arthritic process attacked the joints on the left or non-hemiplegic side, alone, and remained restricted to the left side during 2 years' further observation.

This phenomenon is clearly of interest and importance for the understanding of the factors responsible for the localization of rheumatoid arthritis. We have seen four such patients, whose case histories are given below.

Case Reports

Case 1, a man, aged 48 years, gave a history of rheumatic fever when aged 9 years and had a mid-thigh amputation of the right leg necessitated by septicaemia when aged 18 years. He developed right-sided Jacksonian epilepsy at the age of 35 years and his right arm became paralysed at the age of 47 years, when investigations revealed a meningioma of the left parietal lobe. Spastic paralysis of the right arm persisted after surgical removal of the tumour and deep x-ray therapy. 15 months after the operation (in June, 1950) the patient developed rheumatoid arthritis. He was first seen by one of us at the Hammersmith Hospital in September 1950, when arthritic changes were noted in the left ankle, knee, shoulder, elbow, and wrist, and in several joints in the left hand, but in no joints on the right side. He later developed typical rheumatoid nodules on the left elbow and on the fingers of the left hand. In 1953 and 1954 the differential agglutination test was positive to a titre of 1 : 128 and 1 : 256, and the erythrocyte sedimentation rate was raised to 22 mm. in one hour (Westergren) on one occasion.

The arthritis has remained restricted to joints on the left (non-hemiplegic) side, a total of fourteen joints being involved on this side during a period of observation extending over 5 years. The arthritis has never been severe and has not prevented him from working, but between 1958 and 1960 he became progressively dysarthric, dysphasic, and disabled through post-radiation cortical atrophy and stenosis of the left internal carotid artery.

Radiology.—Radiographs of the hands were taken in 1950, 1951, and 1956. The right hand showed osteoporosis but no soft-tissue swelling or erosions. The left hand showed soft-tissue swellings only in 1950, but in 1951 progressive erosions involved the ulnar styloid and 2nd and 5th metacarpophalangeal joints, and there was slight periostitis on 5th metacarpal shaft. In 1956, the radiograph of the left hand showed healed erosions of the ulnar styloid and at the bases of the 2nd and 5th metacarpals, with gross erosion and homogenization of the carpus (Fig. 1, opposite).

Arteriogram.—As in many rheumatoid arthritics with nodules and circulating macroglobulin (Scott, Hourihane, Doyle, Steiner, Laws, Dixon, and Bywaters, 1961) a brachial arteriogram showed multiple digital arterial occlusions: these were just as marked on the paralysed as on the normal side (Fig. 2, opposite).

Fig. 1.—Case 1. Left and right (paralysed) carpus, showing erosions on left and osteoporosis on right. Dorsal aspect.

Fig. 2.—Case 1. Digital arteriogram of left and right (paralysed) hands, showing blocks and impaired pulp filling on both sides with uniformly smaller calibre main vessels on the right. Palmar aspect.

Case 2, a married woman, aged 71 years, was seen at the Royal Victoria Infirmary, Newcastle upon Tyne, in May, 1958, suffering from an acute exacerbation of rheumatoid arthritis. She had previously sustained two attacks of cerebral thrombosis in 1956 with residual left-sided hemiplegia. Motor function was restored in the left leg with only slight residual foot-drop and peroneal weakness, but there was little recovery in the left arm and none in the left hand. In November, 1957, 18 months after the second attack of cerebral thrombosis, the patient developed acute polyarthritis, which involved the right hand, wrist, elbow, sterno-clavicular joint, and knee-joint. The arthritis was initially severe but improved with rest in bed. In March, 1958, she had a laparotomy for acute volvulus and in May, 1958, sustained an acute exacerbation of the arthritis, the right foot, ankle, and hip becoming involved in addition to the joints previously affected. The arthritis was classically rheumatoid in type, with the erythrocyte sedimentation rate raised to 60 mm. in one hour (Westergren), and the Rose-Waaler test repeatedly positive to titres of 1 : 256.

The arthritis improved considerably with treatment by initial complete bed rest, the fitting of plaster splints, physiotherapy, calcium aspirin gr. 72 daily, and local steroid injections into the most severely involved joints. The arthritic lesions remained restricted to the joints on the right, or non-hemiplegic side (Fig. 3).

Fig. 3.—Case 2, showing involvement of joints of the right side.

Radiology.—The arthritic lesions were restricted to the right side. On September 30, 1958, the bones of the left elbow were found to be osteoporotic, but otherwise normal, while those of the right elbow, although well calcified, showed early erosions on the external epicondyle and a detached fragment of bone. Periostitis was noted over the right radial head. By May, 1959, there was further decrease in the thickness of the articular cartilage and progression of erosions, now on the medial epicondyle.

The left knee showed rarefaction only, but the right knee showed marginal erosions in the tibia, which progressed with loss of joint space. The lateral views showed pocketed erosions of the patella and by May, 1959, there were also posterior erosions on the femoral condyles.

The left hand showed rarefaction only, compatible with atrophy of disuse, but the right hand showed soft tissue swelling, local rarefaction near joints, erosions on the 2nd, 3rd, 4th, and 5th metacarpal heads, loss of joint space, and adjacent periosteal reaction.

Biopsy.—Specimens were taken from both knee joints and both quadriceps muscles in March and April, 1959.

The findings in the right quadriceps suggested slight recent atrophy with increase in sarcolemmal nuclei, but no gross loss of muscle fibre. One paravascular focus of lymphocytes was seen (Fig. 4, opposite).

The left quadriceps showed longstanding atrophy without much recent sarcolemmal proliferation, some increase in connective tissue and no lymphocytic foci (Fig. 4, opposite).

The appearance of the synovial membrane from the right knee was compatible with rheumatoid arthritis, with synovial cell hyperplasia, gross proliferation of fibroblasts and ground substance, some sub-synovial lymphocytes diffusely scattered and a little pigment. No plasma cells were seen (Fig. 6, opposite).

The histological examination of the left knee showed mild synovitis with slight hyperplasia of synovial cells, slight increase in sub-synovial ground substances, and some paravascular lymphocytic infiltrations. No plasma cells were seen (Fig. 7, opposite). The changes in the left synovial membrane were much less evident than those in the right knee.

Fig. 4.—Case 2. Muscle biopsy of rheumatoid thigh (right), showing slight atrophy and paravascular lymphocytic focus.
(Haematoxylin and eosin. $\times 140$.)

Fig. 5.—Case 2. Muscle biopsy of paralysed thigh (left), showing severe chronic atrophy.
(Haematoxylin and eosin. $\times 140$.)

Fig. 6.—Case 2. Biopsy of right knee.
(Haematoxylin and eosin. $\times 140$.)

Fig. 7.—Case 2. Biopsy of left knee.
(Haematoxylin and eosin. $\times 140$.)

The radiographic and biopsy evidence confirmed the major involvement of the joints on the right side, with virtually complete sparing of those on the hemiplegic side. This pattern has continued for 4 years since the onset of the polyarthritis, the only joint involved on the left side being the left knee, and that only slightly. The patient is now bedridden as a result of two attacks of volvulus requiring operation, and a further episode of cerebral thrombosis. Her present arthritic symptoms are restricted to the *right* shoulder, hip, elbow, and knee joint.

Studies undertaken to elicit defective circulation or circulatory response on the affected side were negative. The levels of capillary resistance, as determined by a negative pressure method, were found to be comparable on both sides. The responses to cutaneous vasodilators (Trafuril), estimated when the patient was not taking salicylates, were also found to be similar in both limbs as were the responses to an erythema dose of ultra-violet radiation. Rise of temperature in response to warming showed little difference between the two sides.

Case 3, a man, aged 61 years, sustained a left hemiplegia in 1927 when aged 29 years, probably caused by neuro-vascular syphilis for which he was subsequently treated. He had persistent signs of a slight left-sided hemiplegia with residual slurring of speech, stiffness of the left arm and leg, and a slight limp. 32 years later (in December, 1959) he was referred to the Royal Victoria Infirmary, Newcastle upon Tyne, for investigation of an acute polyarthritis of 3 months' duration. This arthritis had commenced abruptly in the right knee and had gone on to involve the right ankle, wrist, hand, fingers, and shoulder. The arthritis was classically rheumatoid in type, the erythrocyte sedimentation rate being raised to 90 mm. in one hour (Westergren), and the Rose-Waaler test positive to a titre of 1 : 512 on three occasions. The patient subsequently developed rheumatoid nodules, tendon lesions, and bursitis, in addition to arthritis of the right ankle and foot. During further observation of this patient over a 30-month period, it was noted that the arthritis remained restricted to joints on the right or non-hemiplegic side (Fig. 8).

Radiology.—The hands, knees, and feet showed characteristic rheumatoid erosions in the joints on the right side, but no erosions were seen in any joints on the left side.

Case 4, a married woman, aged 49 years, seen at the Hammersmith Hospital on October 23, 1961, had sustained a cerebral vascular accident when aged 36 years with residual left-sided hemiplegia. The left arm remained spastic and paretic, but there had been substantial recovery in the left leg, and from 6 months after the stroke the patient was able to walk with the aid of a caliper. In 1954, when aged 42 years, she developed a ganglion on the right wrist and noted that the knuckles

Fig. 8.—Case 3, showing swelling of right ankle and no involvement of left ankle.

of her right hand were thickened. One year later she developed florid polyarthritis involving the right metacarpophalangeal and interphalangeal joints, the right shoulder, and the left ankle. The arthritis improved on treatment with salicylates and physiotherapy, but relapsed in April, 1960, when it was particularly severe in the right hand and right shoulder.

Physical Examination.—There was swelling of the right 3rd proximal interphalangeal joint; the right 1st, 2nd, and 3rd metacarpophalangeal joints, the right wrist, and the right 2nd, 3rd, 4th, and 5th metatarsophalangeal joints. The right elbow and shoulder were painful with limited range of movement, and the right knee showed painless thickening of the tissues with a normal range of movement. The left ankle, which showed swelling, pain, and limitation of movement, was the only joint clinically involved on the left side.

The left arm showed spastic paresis with flexor contraction, but passive straightening was possible. There was also sensory loss in the left arm and leg. The left leg showed no voluntary movement except for iliopsoas and weak dorso-plantar flexion. Erythrocyte sedimentation rate was raised to 38 mm. in one hour (Westergren), the differential agglutination test was positive to titres of 1 : 32 and 1 : 64, and the latex-fixation test was positive.

Radiology.—There were extensive changes of rheumatoid type in the right elbow and hand, but the joints on the left were spared (Fig. 9a, b, opposite).

Fig. 9.—Case 4. Metacarpophalangeal joints. Dorsal aspect. (a) Right hand, showing erosions; (b) Left hand, showing atrophy only.

The right foot was severely involved and showed severe lesions in the tarsus and 4th metatarsophalangeal and 3rd interphalangeal joints; on the left side there were

slight lesions only of the 4th and 5th metatarsophalangeal joints, and of the first terminal interphalangeal joint (Fig. 10a, b).

Fig. 10.—Case 4. Foot x rays. (a) Right foot, showing erosions in tarsus, metatarsophalangeal, and interphalangeal joints; (b) Left foot, showing erosions of 4th and 5th metatarsophalangeals and of terminal big toe joint.

Discussion

These four case histories substantiate the observation that the joints of hemiplegic limbs are much less liable to develop rheumatoid arthritis than the joints on the non-paralysed side. In all our patients the diagnosis of rheumatoid arthritis was evident clinically, radiologically, and serologically. The arthritis was particularly severe in Cases 2, 3, and 4, yet the only joints in the hemiplegic limbs to become involved were the left knee joint in Case 2 and the left ankle and two toes in Case 4. Nevertheless, the finding of arthritis in these few joints is sufficient to demonstrate that the protective effect against development of arthritis afforded by hemiplegia, although impressive, is not absolute.

The explanation for this protection is not clear, and several mechanisms may be involved. The first possibility to be considered is that lack of movement and pressure in the joints of the hemiplegic limbs, had exerted a protective effect analogous to that of therapeutic rest and splinting. This theory is partially but not completely supported by the findings in our patients. Case 3 had been fully ambulant for 32 years since his stroke yet the protection against arthritis was complete. Similarly, Jacqueline's patient had been fully ambulant for 50 years since his stroke.

The involvement of the left knee in Case 2 and of the left ankle and foot in Case 4 did, however, represent examples of rheumatoid arthritis developing in hemiplegic limbs in joints which were still subject to locomotor and weight-bearing strains. Furthermore, in all instances of completely hemiplegic limbs (*i.e.* the arms in Cases 2, 3, and 4), the protection afforded against the development of arthritis in these limbs proved to be complete. There are therefore grounds for believing that the failure of arthritis to develop may be entirely due to the disuse of the hemiplegic limb, and that the degree of protection is approximately proportional to the severity of the paralysis.

No other explanation (*e.g.* in vasomotor or neurological terms) can at present be provided to explain these findings. Studies of capillary resistance; response to application of cutaneous vasodilators; temperature gradients from direct and indirect heating; and responses to erythema doses of ultra-violet radiation were made in Case 2, but no striking differences between the responses in the two sides were noted. Winter (1952) found no significant difference in blood flow, as estimated calorimetrically, in the limbs of his hemiplegic patient.

The arteriogram in Case 1 showed the uniformly diminished calibre of the main vessels on the

paralysed side as might be expected, but blocks and failure of digital pulp filling were seen on both sides. This is consistent with the close correlation between digital lesions and high-titre sheep cell agglutination (Bywaters, 1957), and with the observation of Hess and Ziff (1960) that rheumatoid macroglobulin can localize on vascular endothelium. This may in effect be a change mediated in the blood vessels by rheumatoid macroglobulin and therefore unaffected by lack of movement in the joints.

There is also the possibility of some direct change being induced in joint tissues, exerting a protective effect, when the nerve supply to the joint is interrupted. In degenerative joint disease the protective effect is seen with both upper and lower motor neurone lesions, but in rheumatoid arthritis we have no information as to the possible suppression of lesions in limbs when the lower motor neurone has been damaged.

Despite these speculations, it is clear that a good measure of protection against the rheumatoid process is conferred by a hemiplegia, irrespective of the mechanism of this benefit. No beneficial effect, in our experience, is seen when hemiplegia develops in a patient already suffering from rheumatoid arthritis, the joints in the affected limbs remaining painful and tender. Indeed, Nava (1953) described a patient suffering from mild rheumatoid arthritis who had a fierce exacerbation of arthritis following a stroke, the symptoms being limited to the joints of the paralysed limbs.

It is likely that further examples of this peculiar protective effect of hemiplegia will be reported. Studies of the factor or factors operating in hemiplegic limbs modifying tissue reactions may shed light on modes of pathogenesis and methods of prevention of rheumatoid arthritis.

Summary

Four cases are described in which classical rheumatoid arthritis supervened following hemiplegia. All the joints in the completely hemiplegic limbs were spared, but in two ambulant cases five joints were involved in the used but hemiplegic limbs. Histological and radiological studies confirmed the clinical findings, but an arteriogram showed changes in both the paralysed and the contralateral rheumatoid hand. It is concluded that the most reasonable explanation for the immunity of the paralysed side to the development of rheumatoid changes is the relative lack of use and function.

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Arthrite rhumatismale unilatérale après une hémiplégié

RÉSUMÉ

On décrit quatre cas où une arthrite rhumatismale

classique survint après une hémiplégié. Toutes les articulations dans les membres complètement hémiplégiés furent épargnées, mais dans deux cas ambulants cinq articulations des membres hémiplégiés, mais en service, furent impliquées. Les faits cliniques furent confirmés par des examens histologiques et radiologiques, mais un artériogramme révéla des lésions dans la main paralysée de même que dans la main rhumatismale opposée. On conclut, que l'explication la plus logique de l'immunité du côté paralysé au développement des lésions rhumatismales est l'absence relative d'usage et de fonction.

Artritis reumatoide unilateral después de hemiplegia

SUMARIO

Se describen cuatro casos en que una artritis reumatoide clásica ocurrió después de una hemiplegia. Todas las articulaciones en los miembros enteramente hemiplegicos fueron respetadas, pero en dos casos ambulatorios articulaciones de los miembros hemiplegicos, pero usados, se vieron implicadas. Los hechos clinicos fueron confirmados histológica y radiológicamente, pero un arteriograma reveló alteraciones tanto en la mano paralizada como en la otra, reumática. Se concluye que la explicación más lógica de la inmunidad del lado paralizado contra un desarrollo de lesiones reumatoides es la ausencia relativa de uso y de función.