Localized Clubbing and Hypertrophic Osteoarthropathy Due to Infection in an Aortic Prosthesis

J. O. KING

British Medical Journal, 1972, 4, 404-405

One of the most interesting and yet unexplained signs in clinical medicine is hypertrophic osteoarthropathy. Most commonly due to carcinoma of the bronchus (Hammarsten and O'Leary, 1957), this entity consists of periosteal new bone formation at the distal ends of the long bones, peri-arthritis, sometimes with effusions, and usually digital clubbing.

Localized clubbing has been reported on many occasions, and the commonest cause of this has been aneurysmal dilatation of the aorta or great vessels (Mendlowitz, 1942). Localized hypertrophic osteoarthropathy, on the other hand, is extremely rare, and in the few cases where it has been described the changes have been confined to the lower limbs in patients with patent ductus arteriosus and reversed shunt (Williams *et al.*, 1963; Dailey *et al.*, 1962). The case is reported here of a woman who developed clubbing of the toes and hypertrophic osteoarthropathy of the lower limbs after infection in an abdominal aortic prosthesis.

Case Report

In April 1968 a 50-year-old married woman had a Dacron prosthesis inserted for a leaking abdominal aortic aneurysm. The graft extended from below the renal arteries to both common femoral arteries. Soon afterwards she developed intermittent claudication, and in May 1969 a further operation was required to replace the original graft, which had thrombosed. Six months later she developed a small-bowel obstruction and required a laparotomy for freeing adhesions.

In May 1970 she complained of night sweats, rigors, swelling and tenderness of her legs, and pigmentation and thickening of the skin of her feet. Examination showed fever, clubbing of the toes but not of the fingers (Fig. 1) diffuse swelling of both legs, and bilateral knee effusions. The heart and lungs were normal. Investigations showed a microangiopathic haemolytic anaemia with a haemoglobin of 8.0 g/100 ml. Blood cultures from both arms and legs failed to grow any organism, except for two bottles on the same day which grew *Staphylococcus albus*. This organism was also cultured from the urine and a liver biopsy specimen. The chest x-ray appearances were normal but films of the lower limbs showed the changes of hypertrophic osteoarthropathy in all bones, including the femora (Fig. 2 and 3). Radiological examination of the bones of the upper extremities showed nothing abnormal.

Over the next six months she received several prolonged courses of intravenous antibiotics, which produced appreciable symptomatic relief from her fever and night sweats. The haemoglobin rose to 11.5 g/100 ml, but her legs remained the same, clinically and radiologically.

Later, despite oral penicillin, the leg swelling, pain, and joint stiffness slowly increased and she was confined to bed in March 1971. In May bilateral axillofemoral arterial bypasses were constructed using bovine heterografts, with ligation of the lower ends of the Dacron prosthesis. On the day after the operation she was free of pain in the legs and over the next two weeks all soft-tissue swelling resolved. Definitive removal of the old graft was postponed because of the remarkable improvement and the formidable nature of the operation. The circulation in the legs was well maintained by the axillofemoral anastomoses.

In July 1971 she suddenly collapsed and died after a massive gastrointestinal haemorrhage. At necropsy an aortoduodenal fistula

was found at the junction of the abdominal aorta and the old Dacron prosthesis. In this area the aorta was necrotic and infiltrated with polymorphs. The tibiae showed subperiosteal bone formation. No cardiac or pulmonary lesions were found.

FIG. 1—Clubbing of toes and swelling of feet seen on clinical examination in May 1970.

FIG. 2—Radiographic changes of hypertrophic osteoarthropathy in a femur.

FIG. 3—Radiographic appearances of the feet.

Comment

This patient developed localized clubbing of the toes and hypertrophic osteoarthropathy of the lower extremities after infection in an abdominal aortic prosthesis. As *Staph. albus* was cultured from three sites and the fever and night sweats responded to penicillin it seems likely that this organism was responsible.

The localized nature of the hypertrophic osteoarthropathy and the dramatic relief of symptoms after interruption of the blood flow through the infected prosthesis provide further support for the existence of a humoral mechanism in the pathogenesis of this lesion.

University of Melbourne Department of Medicine, Royal Melbourne Hospital, Victoria 3050, Australia

J. O. KING, M.B., M.R.A.C.P., Thwaites Research Fellow

Although the importance of humoral agents has been suggested (Marie, 1890; Mendlowitz, 1942; Hall, 1959; Ginsberg and Brown, 1961), the neurogenic theory for the production of hypertrophic osteoarthropathy is currently favoured. This arose after finding in man and in dogs that when the osteoarthropathy occurred in association with lung neoplasms thoracic vagotomy produced an immediate fall in blood flow to the affected limbs, with subsequent relief of symptoms (Flavell, 1956; Holling *et al.*, 1961).

The evidence from this case report suggests that the substance which causes hypertrophic osteoarthropathy either is produced by vascular tissue in response to specific infections or tumours or is present in the blood in a precursor state and is activated by contact with abnormal vascular tissue. For the effect of this substance to be localized it must be metabolized in the periphery or in the lungs.

I would like to acknowledge the support of Ormond College, University of Melbourne, during the tenure of the Thwaites Research Fellowship. I would also like to thank Professor R. R. H. Lovell for his helpful advice and permission to report this case.

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Brain Stem Encephalitis Caused by *Herpesvirus hominis*

A.D. DAYAN, WILLIAM GOODDY,
M. J. G. HARRISON, PETER RUDGE

British Medical Journal, 1972, 4, 405-406

Herpesvirus hominis (herpes simplex) encephalitis typically presents in the adult as a temporal lobe disturbance and it is not generally known as a cause of brain-stem disorders. The recent introduction of antiviral preparations such as idoxuridine has made it important to delineate the clinical effects of this virus as an aid to its speedy diagnosis and treatment. We wish to report two cases of brain-stem encephalitis due to herpes simplex infection in which we used an immunofluorescent technique to help in the rapid identification of the pathogenetic agent.

Case 1

Three weeks before admission to hospital a 14-year-old schoolboy had had a febrile illness with a sore throat and mild nasal congestion from which he rapidly recovered. Ten days later he complained of mild headache which increased during the course of the day. By evening he was vomiting and had great difficulty in remembering the earlier part of the day. The next day he was lethargic and delirious, with a temperature of 102°F (38.9°C); he complained of double vision and his speech was slurred. He was admitted on the third day. By then he was unable to clear his throat; he dribbled saliva, tended to choke and cough while eating, was very restless, and failed to recognize members of his family.

Neurological examination showed a confused, febrile boy with a slurring dysarthria and incontinence of urine. There was first-degree nystagmus to right and left. The palate elevated very poorly. There was no definite limb weakness or ataxia. All the tendon reflexes were depressed. Both planter responses were flexor. There was no sensory loss.

Over the next 48 hours, as his level of consciousness fell, he developed mild bilateral facial weakness and his tendon reflexes

disappeared. He had two brief episodes of coma associated with divergent upward gaze, very small pupils, and flaccidity of the limbs. Two days later his respiration became irregular and periodic and there were frequent extensor spasms. After tracheostomy his spontaneous respiratory pattern varied between central neurogenic hyperpnoea, Cheyne-Stokes, and regular breathing. After nine days a flaccid right hemiplegia appeared. His conditions then deteriorated, he became hypotensive, and he died on the 16th day of the illness.

The cerebrospinal fluid contained 50 lymphocytes/mm³. 55 mg protein/100 ml, and 62 mg glucose/100 ml; culture was sterile. Serum complement-fixing antibody titres to *H. hominis* rose from 1:4 on the day of admission to 1:128 on day 15. The electroencephalogram showed diffuse, irregular, slow-wave background activity with anterior left hemisphere and mid-temporal focal slow-wave abnormalities. The slow waves had a repetitive pattern which changed in periodicity between day 4 and day 10.

Intravenous idoxuridine 3 g daily was given without discernible clinical effect between day 10 and day 15 of the illness.

At necropsy there was extensive patchy haemorrhagic infarction of both cerebral hemispheres, maximal in the temporal lobes, and small haemorrhagic softenings were scattered throughout the cerebral peduncles, pons, and medulla. Microscopical examination showed necrotizing encephalitis in the cerebral cortex, more severe and diffuse throughout the tegmentum, pes pontis, and floor of the fourth ventricle. Inclusion bodies were not seen.

Cryostat sections from many areas of the brain were examined by the indirect immunofluorescent technique, using rabbit anti-herpes and swine anti-rabbit sera. Neurones and glial cells in the cerebral cortex and brain stem contained herpes-virus antigens, and so did a few macrophages in the perivascular infiltrates.

Case 2

A 48-year-old pattern cutter was admitted to a regional hospital with a one-week history of progressive vertigo, headache, hiccup, and photophobia. He was febrile and had a stiff neck. Over the next week he became increasingly drowsy and developed dysarthria before transfer to this hospital.

On admission he was afebrile, drowsy, and confused. He had neck stiffness. His speech was so disturbed that conversation was impossible. Both pupils were pin-point in size but reacted to light and accommodation. There was bilateral ptosis, gaze paresis, first-degree nystagmus to the right, and failure of adduction of the left eye. Upward gaze was limited and convergence absent. There was weakness of the right masseter. The right corneal reflex was absent. Pin-prick sensibility was impaired over the left side of the face. A lower motor neurone facial weakness was present on the left. He had mild left pyramidal signs with ataxia and was unable to stand because of severe dysequilibrium. Adequate sensory testing was not possible.

Over the next two days his condition deteriorated and he became more drowsy and developed some limitation of abduction of the left eye. Thereafter his condition remained static and then began gradually to improve. He became more alert, and many of the

Institute of Neurology and National Hospitals for Nervous Diseases, London W.C.1

A. D. DAYAN, M.D., M.R.C.PATH., Consultant Neuropathologist
 WILLIAM GOODDY, M.D., F.R.C.P., Physician
 M. J. G. HARRISON, D.M., M.R.C.P., Senior Registrar
 PETER RUDGE, M.B., M.R.C.P., Senior Resident House Physician