was in good health and had no evidence of valvular disease or reduced immunity. It is unlikely that the small secundum atrial septal defect predisposed to infection of the aortic valve. Classical sodoku is transmitted by the bites of rats and small mammals, but this history is not usually obtained in other *Spirillum* infections (Kowal, 1961) and was not obtained in our patient. In view of his promiscuous homosexual behaviour it is possible that the infection was transmitted by venereal contact, but since the reservoir of the organism is unknown this must remain speculative.

Rat-bite fever normally responds to penicillin but the organism isolated from our patient was resistant to this drug *in vitro*, and treatment depended mainly on oxytetracycline. The MIC of metronidazole is sufficiently high for it to be unlikely to have affected the outcome in the dosage employed, though its use in the treatment of other anaerobic and fusospirochaetal infections is well recognized.

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References

- BREED, R.S., MURRAY, E.G.D. & SMITH, N.R. (1969) In: *Bergey's Manual of Determinative Bacteriology*, 7th edn. Williams and Wilkins, Baltimore.
- EDWARDS, C.E. & KRAUS, R. (1960) *Spirillum serpens* meningitis: report of a case. *New England Journal of Medicine*, **262**, 458.
- FINLAND, M. & BARNES, M.W. (1970) Changing etiology of bacterial endocarditis in the antibacterial era. *Annals of Internal Medicine*, **72**, 341.
- FONCANNON, F. (1930) Rat-bite fever. *Journal of the Kansas Medical Society*, **31**, 331.
- FUTAKI, K., TAKAKI, F., TANIGUCHI, T. & OSUMI, S. (1916) The cause of rat-bite fever. *Journal of Experimental Medicine*, **23**, 249.
- FUTAKI, K., TAKAKI, F., TANIGUCHI, T. & OSUMI, S. (1917) *Spirochaeta morsus muris*, n.sp., the cause of rat-bite fever. *Journal of Experimental Medicine*, **25**, 33.
- HITZIG, W.M. & LIEBESMAN, A. (1944) Subacute endocarditis associated with infection with a *Spirillum*. *Archives of Internal Medicine*, **73**, 415.
- HYLEMON, P.B., WELLS J.S., JR, KREIG, N.R. & JONNASCH, H.W. (1973). The genus *Spirillum*; a taxonomic study. *International Journal of Systemic Bacteriology*, **23**, 340.
- JOEKES, T. (1925) Cultivation of *Spirillum* of rat-bite fever. *Lancet*, **ii**, 1225.
- KOWAL, J. (1961) *Spirillum* fever, report of a case and review of the literature. *New England Journal of Medicine*, **264**, 123.
- LAMB, A.R. & PATON, F.W. (1913) A case of vegetative endocarditis caused by a hitherto undescribed *Spirillum*. *Archives of Internal Medicine*, **12**, 259.
- SHWARTZMAN, G., FLORMAN, A.L., BASS, M.H., KARELITZ, S. & RICHTBERG, D. (1951) Repeated recovery of a *Spirillum* by blood culture from two children with prolonged and recurrent fevers. *Pediatrics*, **8**, 227.
- SOPER, W.B. (1913) A case of *Spirillum* infection. *Archives of Internal Medicine*, **12**, 273.
- WEBSTER, A.D.B. for ASHERSON, G.L. (1973) *Spirillum* hepatitis in "acquired" hypogammaglobulinaemia with thyroiditis, pernicious anaemia and possible dermatitis herpetiformis. *Proceedings of the Royal Society of Medicine*, **66**, 1126.

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Hypertrophic osteoarthropathy associated with Fallot's tetralogy— a case report

B. OLU. GEORGE
M.R.C.P., L.M., L.R.C.S., L.R.C.P.

J. OLU. MABAYOJE
F.R.C.P., F.M.C.P.

*Department of Medicine, Lagos University Teaching Hospital,
Private Mail Bag 12003, Lagos, Nigeria*

Summary

A case of Fallot's tetralogy associated with hypertrophic osteoarthropathy in a young Nigerian female is described. The clinical spectrum of hypertrophic osteoarthropathy is reviewed. The rarity of this syndrome is stressed. Some other aspects of the clinical manifestation of cyanotic congenital heart disease which may mimic the skeletal syndrome are mentioned.

Introduction

Hypertrophic osteoarthropathy is a rare syndrome characterized by clubbing of the fingers and toes, chronic periostitis, with periosteal new bone formation involving especially the distal ends of the long bones, joint pain and swelling, signs of autonomic disorder (flushing and blanching, and profuse sweating), and gynaecomastia. It has been described in association with many varied conditions, of which

FIG. 1. Showing marked clubbing of the fingers and toes.

FIG. 2. Showing swelling of the knees and the 'elephant foot' appearance of the limb. The clubbing of the toes is also obvious.

it may be the presenting feature. In the pre-antibiotic era, most cases were associated with chronic suppurative conditions of the chest, such as bronchiectasis, lung abscess, and empyema. Primary intrathoracic neoplasms now represent the commonest associated diseases (Coury, 1960; Anderson, 1967). Although the association of clubbing of the fingers and toes occurs in cyanotic congenital heart diseases, hypertrophic osteoarthropathy is extremely rare in these conditions. The following case

report describes this predominantly skeletal syndrome in an African with the tetralogy of Fallot.

Case report

An 18-year-old Nigerian female first presented in October 1970, with a history of tiredness on slight exertion from about 2 years of age, and persistent swelling of both ankles over the preceding 2 years. Developmental milestones appeared to be normal. The parents observed that she was blue shortly after birth, and were told by the doctors that she had a 'hole in the heart'. The bluish discoloration of the lips and nails deepened on crying and, later on, exertion. There was no history of squatting, but she often got relief by stooping. The increasingly breathless attacks were associated with severe temporal headaches, pains in the eyes, retrosternal pain, and palpitation. There was no history of fainting attacks, cough, or haemoptysis. For years she had experienced widespread bone and joint pains, and swelling of her fingers and toes, and in the preceding 2 years, she had also noticed persistent swelling of the lower limbs.

The family history was non-contributory, and her mother had her after a normal pregnancy.

On clinical examination, the patient appeared well nourished—height 1.5 m, weight 37.3 kg. There was gross clubbing of the fingers and toes (Fig. 1), and marked cyanosis of the conjunctivae, tongue, lips, buccal mucosa, palms and fingers. She was afebrile. There were no tophi. The respiratory system was normal. In the cardiovascular system, there was a left lower parasternal heave but no palpable thrill. The first heart sound was normal, with accentuation and slight splitting of the second heart sound in the pulmonary area. There was also a soft mid-systolic

murmur in the pulmonary area and in the fourth left parasternal space. Blood pressure was 90/70 mm Hg. Radial pulses were of small volume, regular, rate 80/min. Apex beat was in the fourth left intercostal space, mid-clavicular line. There was no evidence of congestive cardiac failure. Other positive physical signs were found in the locomotor system. In addition to the marked digital clubbing, there was tender, non-pitting swelling of both legs, most marked distally. Both knees were swollen, warm, and tender, with positive patellar tap, indicating fluid (Fig. 2). The elbows, wrists, and shoulders were normal.

Investigations and management

Haemogram showed a consistent polycythaemia (Hb 20.8–21.4 g/100 ml; PCV 71), ESR was 0 mm/first hr (Westergren), and the Hb genotype was AA. White cell count was normal. Blood urea was 49 mg/100 ml and serum uric acid 8.5 mg/100 ml. Investigations on her blood were difficult because the blood either clotted in the syringe, or it was impossible to obtain plasma or serum from the clotted samples. Chest X-ray was normal. X-ray of the limbs showed periosteal reaction in the femora, tibiae, fibulae, radii, and ulnae (Fig. 3). ECG showed prominent P waves, right axis deviation (axis +150°), and right ventricular hypertrophy (Fig. 4). Diagnostic aspiration of the knee revealed a clear sterile aspirate.

A diagnosis of cyanotic congenital heart disease with hypertrophic osteoarthropathy was made. The patient was treated symptomatically with bed rest, intermittent oxygen and mild analgesics. She was later discharged home for outpatient follow-up. After defaulting for 11 months, she reported at the hospital with worsening of her symptoms and signs. The polycythaemia was more marked, Hb 22.0 g/100 ml, PCV 79, but the ECG remained unchanged. After several weeks' stay in hospital, at the request of the patient and her parents, she was discharged home. A few days later, she collapsed at home and died.

Autopsy findings were as follows: severe and generalized cyanosis of all organs. The specific cardiovascular lesions were pulmonary trunk hypoplasia with organized fibrin at the base of the pulmonary trunk, right ventricular hypertrophy, high VSD, overriding aorta, and widely patent foramen ovale, i.e. tetralogy of Fallot plus patent foramen ovale (Figs 5 and 6).

Discussion

Finger clubbing was first described by Hippocrates in the fifth century B.C. Hypertrophic osteoarthropathy was, however, first recognized and described independently by Bamberger (1889) and Marie (1890) in the late nineteenth century. The clubbing associ-

FIG. 3. X-ray of the radius and ulna showing the periosteal thickening.

ated with hypertrophic osteoarthropathy is usually gross and there is a tendency to regard the osteoarthropathy as a more advanced stage of clubbing. Clubbing is, however, not an essential feature of this condition (Holling, Brodey and Boland, 1961) and the two may occur independently.

The arthropathy is symmetrical and can be extremely painful, with hot swollen joints. The joints affected are the ankles (88%), wrists (82%), knees (75%) and, less commonly, elbows, shoulders, fingers, and other joints (Coury, 1960). There may be hydrarthrosis. Radiologically, the joints show soft tissue swelling only. The course of the arthropathy reflects the activity of the underlying disease. The periostitis begins and is most marked at the distal ends of the extremities, resulting in painful, tender non-pitting swelling over the distal ends of the

FIG. 4. ECG showing peaked P waves, marked right axis deviation (axis $+150^\circ$) and right ventricular hypertrophy.

FIGS. 5 and 6. Showing the anatomical findings in the heart.

FIG. 5. Patent foramen, ovale and V.S.D.

FIG. 6. Fallot's tetralogy.

TABLE 1. Documented reports of hypertrophic osteoarthropathy associated with cyanotic congenital heart disease

Author(s)	No. of cases reported	Associated cardiac lesion(s)	Age of onset in years
1. Bamberger (1891)*	1	Pulmonic stenosis with VSD	7
2. Shaw and Cooper (1907)*	1	Tetralogy of Fallot	21
3. Means and Brown (1947)*	1	Tetralogy of Fallot	26
4. Kahn (1957)*	1	Eisenmenger's complex	32
5. Trever (1958)	2	(i) Transposition of great vessels	16
		(ii) Eisenmenger's complex	18
6. Wahi and Bawa (1961)	1	?	?
7. Dailey, Genovese and Behnke (1962)*	1	Patent ductus arteriosus with reversal of flow	?20
8. Williams <i>et al.</i> (1963)*	1	Patent ductus arteriosus with reversal of flow	26
9. Robinson, Kahn and Syed (1965)*	1	Tetralogy of Fallot	20
10. McLaughlin <i>et al.</i> (1967)	2	(i) Transposition of great vessels	20
		(ii) Tricuspid atresia	7
11. George and Mabayoje (present report)	1	Tetralogy of Fallot with patent foramen ovale	?16

* As quoted by McLaughlin *et al.* (1967).

long bones—'elephant foot' (Fig. 2). It spreads proximally as the disease progresses.

Gynaecomastia was first noted in patients with hypertrophic osteoarthropathy by Bamberger (1891). This association has been confirmed by other observers. It occurs in about 8% of cases of hypertrophic osteoarthropathy (Semple and McCluskie, 1955).

Our patient presented with clinical features of long standing polyarthropathy and bone pains in association with cyanotic congenital heart disease. Gouty arthritis was considered because of the joint pains, the raised serum uric acid level, and the fact that it is a recognized complication of secondary polycythaemia and has been described in relation to

cyanotic congenital heart disease (Somerville, 1961). In such cases, the cyanosis had been present for at least 10 years, and the haemoglobin level was 130% or more at the time of the first attack of gout. Somerville (1961) also observed some correlation between haemoglobin and serum uric acid in certain of her adult patients with secondary polycythaemia. The age of the patient with secondary polycythaemia appeared to influence the development of hyperuricaemia. Hyperuricaemia was uncommon under the age of 16, and gout was not seen below the age of 18. Fallot's tetralogy, the commonest cyanotic congenital heart disease found in patients who survive to adult life, was the commonest cyanotic congenital heart disease associated with gout. In our

patient, although the serum uric acid level was as high as 8.6 mg/100 ml, the radiological appearances were not those of gouty arthritis. Other differential diagnoses of articular and bone manifestations in patients with heart diseases, e.g. infective endocarditis, rheumatic fever, or in this environment, sickle cell disease, were considered, but not entertained for long in the light of the laboratory and X-ray findings. The definitive diagnosis of the cardiac lesion was confirmed at autopsy to be Fallot's tetralogy.

There are only a few published cases of hypertrophic osteoarthropathy associated with cyanotic congenital heart disease (Table 1). In a review of over 3000 cases of cyanotic congenital heart disease seen at the Johns Hopkins Hospital, Trever (1958) encountered only three patients with associated hypertrophic osteoarthropathy. More recently, McLaughlin, McCarthy and Downing (1967) reported two cases. These reports emphasize the low frequency of this association. Our report is another example.

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References

- ANDERSON, G. (1967) Clubbing and hypertrophic osteoarthropathy. *Hospital Medicine*, **1**, 698.
- BAMBERGER, E. VON (1889) *Wiener Klinische Wochenschrift* (Berlin), **2**, 226.
- BAMBERGER, E. (1891) Über knochenveränderungen bei chronischen Lungen- und herzkrankheiten. *Zeitschrift für Klinische Medizin* (Berlin), **18**, 193.
- COURY, C. (1960) Hippocratic fingers and hypertrophic osteoarthropathy. A study of 350 cases. *British Journal of Diseases of the Chest*, **54**, 202.
- DAILEY, F.H., GENOVESE, P.D. & BEHNKE, R.H. (1962). Patent ductus arteriosus with reversal of flow in adults. *Annals of Internal Medicine*, **56**, 865.
- HOLLING, H.E., BRODEY, R.S. & BOLAND, H.C. (1961) Pulmonary hypertrophic osteoarthropathy. *Lancet*, **ii**, 1269.
- KAHN, D. (1957) Clubbing and hypertrophic osteoarthropathy. *Archives of Internal Medicine* (Chicago), **100**, 147.
- MARIE, P. (1890) De L'ostéo-arthropathie hypertrophique pneumonique. *Revue de médecine* (Paris), **10**, 1.
- MEANS, M.G. & BROWN, N.W. (1947) Secondary hypertrophic osteoarthropathy in congenital heart disease. *American Heart Journal*, **34**, 262.
- MCLAUGHLIN, G.E., MCCARTHY, D.J. & DOWNING, D.F. (1967) Hypertrophic osteoarthropathy associated with cyanotic congenital heart disease: A report of two cases. *Annals of Internal Medicine*, **67**, 579.
- ROBINSON R.D., JR, KAHN, A.H. & SYED, S.A. (1965) Hypertrophic osteoarthropathy in congenital heart disease. *Journal of Pakistan Medical Association*, **15**, 246.
- SEMPLE, T. & MCCLUSKIE, R.A. (1955). Generalised hypertrophic osteoarthropathy in association with bronchial carcinoma: Review based on 24 cases. *British Medical Journal*, **1**, 754.
- SHAW, H.B. & COOPER, R.H. (1970) Pulmonary hypertrophic osteoarthropathy occurring in a case of congenital heart disease. *Lancet*, **i**, 880.
- SOMERVILLE, J. (1961) Gont in cyanotic congenital heart disease. *British Heart Journal*, **23**, 31.
- TREVER, R.W. (1958) Hypertrophic pulmonary osteoarthropathy in association with congenital heart disease: Report of two cases. *Annals of Internal Medicine*, **48**, 660.
- WAHI, P.L. & BAWA, Y.S. (1961) Hypertrophic osteoarthropathy in congenital cyanotic heart disease: Case Report. *Indian Journal of Medical Sciences*, **15**, 453.
- WILLIAMS, B., LING, J.T., LEIGHT, L. & MCGAFF, C.J. (1963) Patent ductus arteriosus and osteoarthropathy. *Archives of Internal Medicine* (Chicago), **111**, 346.