The African Journal of MEDICINE and Medical Sciences

Volume 10
1981

BLACKWELL SCIENTIFIC PUBLICATIONS
Oxford London Edinburgh Boston Melbourne

Afr. J. Med. med. Sci. (1981) **10**, 33–38.

DISEASES OF PERIPHERAL NERVES AS SEEN IN THE NIGERIAN AFRICAN

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Summary

The anatomical and aetiological diagnoses of peripheral nerve disease excluding its primary benign and malignant disorders, as seen in 358 Nigerians are presented. There is a male preponderance and the peak incidence is in the fourth decade. Sensori-motor neuropathy was the commonest presentation (50%). Guillain-Barré syndrome was the commonest identifiable cause (15.6%), accounting for half of the cases with motor neuropathy. Peripheral neuropathy due to nutritional deficiency of thiamine and riboflavin was common (10.1%) and presented mainly as sensory and sensori-motor neuropathy. Diabetes mellitus was the major cause of autonomic neuropathy. Isoniazid was the most frequent agent in drug-induced neuropathy.

Migraine (20%) was not an uncommon cause of cranial neuropathy although malignancies arising from the reticuloendothelial system or related structures of the head and neck were more frequent (26%). In 26.5% of all the cases, the aetiology of the neuropathy was undetermined. Heredofamilial and connective tissue disorders were rare. Some of the factors related to the clinical presentation and pathogenesis of the neuropathies are briefly discussed.

Résumé

La diagnose anatomique et aetiologique de maladie de nerf peripherique à l'exclusion de ses desordres benins et malins, comme vu dans 358 Nigerians est presentée. Il y a une preponderance de male et l'incident maximum de la quatrième décade. La néuropathie — sensitivomotrice était la presentation la plus commune (50%). Le syndrome de Guillian Barré était la cause la plus reconnue (15.6%) et comptait pour la moitié des cas de neuropathie motrice. La neuropathie péripherique dûe aux insuffisances des vitamines du groupe B, thiamine et riboflavine était commune (10.10%) et se presentait surtout comme neuropathie sensorielle et sensitiromotrice. Le diabète-mellitus était la principale cause de neuropathie automatique. L'Isoniazid était la cause la plus commune dans le cas de neuropathie causae par medicament. La migraine (20%) est une cause pas mal commune de neuropathie craniene bien que les malignitiés lieés au système réticuloendothelique et à la structure de la tête et du cou soient plus fréquents (26%). L'aetiologie de la neuropathie était comprise dans 26.5% de cas. Les desordres de tissu cellutaire et heredofamiliale extaient rares. Certaines des factures concernant la presentation clinique et la pathogenié des neuropathies sont brevement discutées.

Introduction

Diseases of the peripheral nerves are fascinating in the multiplicity of the possible and probable aetiological factors, for the frequency by which no apparent cause is found and for the variability of therapeutic success. In the developing countries of the tropics, where leprosy (Hansen's disease) affects over 15 million people and nutritional deficiencies are common, the spectrum of diseases of the peripheral nerves could be different from that seen in developed countries and treatment of these diseases may be more rewarding

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0309-3913/81/0600-0033 $02.00

such as the good prognosis of Guillain-Barré syndrome (GBS) in Nigerians treated with corticosteroids (Osuntokun & Agbebi, 1973). This communication describes our experience of the pattern of diseases of peripheral nerves as seen in a teaching hospital in a developing country, Nigeria.

Patients and methods

The patients comprised Nigerians who presented primarily with clinical features of peripheral nerve disease and who were seen by us at the University College Hospital (UCH), Ibadan, mainly between 1964 and December 1976. The diagnosis of peripheral nerve disease was based on clinical grounds (presence of symptoms and signs of dysfunction of first sensory and motor neurones such as paraesthesiae, dysaesthesiae, stocking or glove sensory impairment, fasciculation, weakness and wasting of muscles in the limbs with diminished or absent tendon reflexes, with or without clinical neurophysiological corroboration. Absent ankle jerks alone were not accepted as adequate evidence of peripheral neuropathy in view of the fact that 25% of apparently normal Nigerians have absent ankle jerks (Osuntokun, 1969).

In this study, we have excluded:

(i) patients who suffered from the tropical ataxic neuropathy of which peripheral neuropathy constitutes an inconstant feature, though in combination with myelopathy, bilateral atrophy and perceptive deafness constitutes a nosological entity in Nigerians which has been described in detail elsewhere (Osuntokun, 1968, 1971).

(ii) patients who developed peripheral neuropathy during treatment of diabetes mellitus or who presented with combined symptoms of diabetes mellitus and peripheral neuropathy, and are described elsewhere (Osuntokun, 1970; Osuntokun *et al.*, 1971). However, we included patients whose primary presentation of diabetes mellitus was peripheral neuropathy.

(iii) patients with primary neoplastic disease of the nerves such as neurofibromatosis.

Clinical assessment of nutritional status (as described by Jelliffe, 1966) was supplemented by laboratory tests which included the following: haematological indices (haemoglobin concentration, packed cell volume, total and differential white cell count); estimation of serum protein (including total albumin and globulin fractions), cholesterol, calcium, phosphorus, alkaline phosphatase, red blood cell transketolase activity as a measure of thiamine nutritional status using the method of Brin (1965), Nicotinic acid by microbiological assay using *Lactobacillus plantarum* (Freed, 1967), Ribofalvin (Burch, Bassey & Lowry, 1948); Vitamin B_{12} by microbiological assay using *Lactobacillus casei* (Spray, 1964); Pyridoxine activity in serum was estimated by the yeast method of Atkin *et al.*, (1943) as modified by Saubeilich (1967) using *Saccharomyces uvarum*, and serum Pathothenic levels determined by microbiological assay using *Lactobacillus plantarum* (Bird & Thompson, 1967).

Other investigations, carried out to establish the anatomical and aetiological diagnoses in all patients in which no obvious cause was apparent, included: erythrocyte sedimentation rate, cerebrospinal fluid (CSF), examination for cellular pleocytosis and protein analysis (repeated two or more times when necessary especially in the diagnosis of GBS), blood and CSF Wasserman and veneral disease research laboratory (VDRL) serology tests, lupus erythematosus (LE) cells test, rheumatoid factor, estimation of plasma thiocyanate (Aldridge, 1944), tests for liver function (serum transaminases, bromosulphathalein retention tests, thymol flocculation and turbidity tests), thyroid function tests (triiodothyronine, T_3, red cell T_3 resin uptake and thyroxine), xylose excretion test and a 3-day faecal fat estimation, glucose tolerance tests with and without steroid priming (Jackson, 1961) and interpreted according to WHO (1965) criteria, and examination of urine for porphobilinogen.

Additional tests performed included biopsies of the skin, liver and lymph nodes for histological examination when necessary. Peripheral nerve biopsy (anterior, tibial or sural) were done for light microscopy histology and single nerve fibre preparation by the method of Thomas & Lascelles (1965) in some patients. Electrophysiological studies done comprised electromyography of the weak muscles using coaxial needle electrodes, determination of motor conduction velocities of the medium ulnar and lateral popliteal nerves, with measurement of the peak to peak amplitude and latency to inflexion of the sensory action potentials.

In a number of patients, virological studies

were carried out on blood, CSF and liver biopsy specimens.

Plain radiographs of the chest were performed in all the patients.

Results

Age and sex distribution

This is shown in Table 1. Males predominate with the male:female ratio being 3:2. The peak incidence occurred in the fourth decade. None of the patients with diabetic and alcoholic neuropathy was under 30-years-old. Carpal tunnel syndromes was three times more common in females than males.

TABLE 1. Age and sex distribution of patients with peripheral nerve disease

Age (years)	Male	Female	Total	Percentage
0– 9	5	5	10	3.0
10–19	22	14	36	10.0
20–29	31	31	62	17.0
30–39	44	34	78	22.0
40–49	42	26	68	19.0
50–59	35	21	56	16.0
60–69	25	10	35	10.0
70 and above	10	2	12	3.0
Total	214	144	358	100.0
Percentage	60.0	40.0	100.0	

TABLE 2. Anatomical diagnosis of peripheral nerve disease in Nigerians

Anatomical diagnosis	Number		Percentage	
Peripheral neuropathy		268		69.0
Sensori-motor	194		50.0	
Sensory	52		13.0	
Motor	22		6.0	
Mononeuritis		64		17.0
Simplex	29		8.0	
Multiplex	35		9.0	
Cranial Neuropathy		46		12.0
Autonomic Neuropathy		8		2.0

Clinical features

The anatomical diagnoses are shown in Table 2. Sensori-motor neuropathy was the commonest form (50%). Autonomic neuropathy as the initial presentation of peripheral nerve disease was rare (2%). Table 3 shows the aetiological diagnosis. No aetiological factor was identified in 26.5% of the cases. GBS was the most frequent identifiable cause (15.6%). The mode of presentation in patients with GBS was sensori-motor in 70%, motor neuropathy in 20% and 11% had associated cranial nerve involvement, sensory (5%) and autonomic neuropathy (2%) were unusual. Sixty-seven percent of patients with diabetes mellitus presented with sensori-motor neuropathy. Isoniazid (INH) was incriminated in 80% of the patients with drug-related neuropathy; vincristina and nitrofuradantin were the other drugs encountered in this study. The causes of sensory, and motor neuropathy are shown in Tables 4 and 5 respectively. Nutritional

TABLE 3. Aetiological diagnosis of peripheral nerve disease in Nigerians

Aetiology	Number	Percentage
Undetermined	95	26.5
Guillain-Barré Syndrome	56	15.6
Diabetes mellitus	39	10.9
Nutritional deficiencies	36	10.1
Malignancy	24	6.7
Hansen's disease	22	6.2
Pressure and trauma	16	4.5
Drugs	13	3.6
Alcohol	12	3.4
*Infections	9	2.5
Migrane	9	2.5
†Other edocrine disturbances	5	1.4
Porphyria	4	1.1
Amyloidosis	3	0.8
‡Miscellaneous	15	4.2

*Postmeningitis, 4; Herpes zoster, 3; Typhoid fever, 2.
†Thyrotoxicosis, 2; Acromegaly, 2; Hypothyroidism, 1
‡Includes Charcot-Marie-Tooth disease, ureamia, botulism, serogenic brachial amyotophy, lead poisoning, rheumatoid arthritis.

TABLE 4. Causes of sensory neuropathy

Cause	Number	Percentage
Undetermined	17	32.7
Nutritional	8	15.4
Diabetes mellitus	6	11.5
Hansen's disease	5	9.6
Drugs	4	7.7
Alcohol	3	5.8
Herpes zoster	3	5.8
Guillain-Barré syndrome	3	5.8
Typhoid fever	2	3.8
Amyloidosis	1	1.9

TABLE 5. Causes of motor neuropathy

Cause	Number	Percentage
Guillain Barré Syndrome	11	50.0
Undetermined	4	18.0
Nutritional deficiency	2	9.0
*Others	5	23.0

*Diabetes mellitus, porphyria, lead poisoning, infantile neuropathy and botulism — 1 each.

deficiency, the most frequent identifiable cause of sensory neuropathy (15.4%) was more common in females. It was due mainly to thiamine and riboflavin deficiency. The major predisposing factors in them were pregnancy and lactation. None of the patients had clinical or biochemical evidence of vitamin B_{12} deficiency. Predominant motor neuropathy was uncommon (6%); GBS, accounting for 50% of the cases, was the commonest cause. Autonomic neuropathy was encountered in only eight patients, of which six (75%) were related to diabetes mellitus, one to amyloidosis and the aetiology was undetermined in the last case.

The causes of sensori-motor neuropathy are shown in Table 6. The aetiological factor was

TABLE 6. Causes of sensori-motor neuropathy

Cause	Number	Percentage
Undetermined	61	31.0
Guillain-Barré syndrome	39	20.0
Nutritional deficiency	26	13.4
Diabetes mellitus	26	13.4
Malignancy	13	6.7
Drugs	9	5.0
Alcohol	9	5.0
Porphyria	2	1.0
Uraemia	2	1.0
Charcot-Marie-Tooth disease	2	1.0
Hansen's disease	2	1.0
Amyloidosis	2	1.0
Rheumatoid arthritis	1	0.5

undetermined in 31% of the cases. Diabetes mellitus (13.4%) and nutritional deficiencies (13.4%) were not uncommon causes. Seven of the thirteen patients with associated malignancies had non-Hodgkin's lymphoma and the remaining six had carcinoma arising from intra-abdominal structures, the liver, stomach and ovary. Table 7 shows the causes of the cranial

TABLE 7. Causes of cranial neuropathy excluding isolated facial nerve paresis in Nigerians

Cause	Number	Percentage
Malignant tumours	12	26.0
Migrane	9	20.0
Guillain-Barré syndrome	6	13.0
Undetermined	4	9.0
Postmeningitis	4	9.0
Thyrotoxicosis	2	4.0
Subdural haematoma	2	4.0
Diabetes mellitus	1	2.0
Hansen's disease	1	2.0
*Others	5	11.0

*Includes typhoid fever, porphyria, diptheria, botulism and posterior communicating artery aneurysm.

neuropathy. Malignant tumours related to structures around the head and neck were the major causes; the mechanism of the neuropathy in the majority of the cases was either by direct infiltration or compression of the cranial nerves. Migraine with associated ophthalmoplegia accounted for 20% of the cases. Thyrotoxicosis (two cases) presented as an isolated abducens paresis in one patient and bilateral but asymmetrical ophthalmoplegia in the other; conjunctival oedema with prolapse, lid-lag and exophthalmos were not seen in these patients.

The causes of mononeuritis multiplex and simplex are shown in Tables 8 and 9 respectively.

TABLE 8. Causes of mononeuritis multiplex in Nigerians

Cause	Number	Percentage
Hansen's disease	10	40.0
Trauma	7	28.0
Pressure	3	12.0
Undetermined	2	8.0
*Serogenic brachial amyotrophy	1	4.0
Diabetes mellitus	1	4.0
Prostatic carcinoma	1	4.0

*Sequel to antitetanus serum injection.

TABLE 9. Causes of mononeuritis simplex in Nigerians

Cause	Number	Percentage
Undetermined	11	38.0
Hansen's disease	6	21.0
Trauma	6	21.0
Acromegaly	2	7.0
Diabetes mellitus	2	7.0
Hypothyroidism	1	3.0
Non-specific granuloma	1	3.0

Leprosy affecting mainly the lateral popliteal and ulnar nerves was the commonest cause of mononeuritis multiplex. Sensory (23%) and sensori-motor (9%) neuropathy were not uncommon in patients with leprosy and none had predominant motor neuropathy. Trauma to the brachial plexus following injuries to the neck and arm and 'saturday night' palsy were not uncommon. The other nerves commonly involved in trauma were the ulnar at the elbow or in the forearm, lateral popliteal around the neck of the fibula and the median nerve in forearm lacerations. Compression of the median at the wrist presenting as carpal tunnel syndrome was the most frequent form of mononeuritis simplex (seventeen out of twenty-nine cases). The aetiology was undetermined in nine patients (53%); leprosy was

incriminated in three patients, diabetes mellitus and acromegaly in two cases each and hypothyroidism in only one patient. None of the patients with carpal tunnel syndrome was pregnant or on oral contraceptives. Meralgia paraesthetica was encountered in a 45-year-old obese but non-diabetic male. In a patient who presented with an isolated ulnar nerve disease at the elbow without other features of leprosy or parasitic infections and antecedent history of trauma, histology of the nerve biopsy revealed a non-specific granuloma.

Discussion

Peripheral nerve disease excluding primary neoplastic lesions appears to be a disease of adults in this environment for only 13% of the cases were less than 20-years-old. The male preponderance observed in this study is similar to the usual pattern of our hospital attendance and is unlikely to suggest a male predilection. Similar to the experience of others, carpal tunnel syndrome appears to be a disease restricted mainly to females in Nigerians (Staal, 1970).

In this study, neuropathy as the presenting feature of diabetes mellitus was common, similar to the experience of others although presentation as diabetic amyotrophy and mononeuritis simplex was rare (Rundles, 1945; Ellenberg, 1958; Garland, 1960). Paresis of the cranial nerves and individual nerve lesions in diabetics have been related to microangiopathy (Greenbaum *et al.*, 1964; Asbury *et al.*, 1970). The rarity of these clinical types in our study confirms previous impressions that the pathogenesis of symmetrical peripheral neuropathy in the African diabetic is predominatly metabolic in origin (Osuntokun, 1970). Pregnancy and lactation which are known predisposing or precipitating factors of vitamin deficiency in females, were the major factors in our female patients with nutritional neuropathy (Ironside, 1939; King, 1950). Although the true incidence of peripheral nerve disease as part of neurological paramalignant syndromes was not the objective of this study and as such could not be ascertained, the nature and site of malignancies encountered conforms to the pattern in other series (Henson & Urich, 1972; Anderson, 1973). The low incidence of Hansen's disease in this series probably reflects selection bias as the majority of such patients are seen primarily at Leprosaria in this environment (G.O. Alabi, 1976, personal communication). The absence of predominant motor neuropathy in our patients with leprosy is similar to the findings of Karat, Rao & Karat (1972) that motor paralysis alone is rare without sensory disturbances in leprosy. The low incidence of isoniazid-induced peripheral neuropathy in our series despite the endemic nature of tuberculosis in this environment confirms recent reports suggesting that Nigerians are predominantly fast acetylators (Afonja, *et al.*, 1977; Salako & Aderounmu, 1977).

This study confirms previous impressions that acute intermittent porphyria is rare in Nigerians although its clinical presentation conforms to the pattern described from other environments (Greenwood, 1967; Ridley, 1969; Makanjuola, Osuntokun & Boroffka, 1973). This rarity suggests genetic differences rather than clinical unawareness in the Nigerian African as the disease has been described in the African Bantu (Dean, 1969). The female predilection and clinical presentation of carpal tunnel syndrome encountered in this series conforms to the well-documented pattern (Murray & Simpson, 1958; Staal, 1970). The rarity of hypothyroidism as an aetiological factor in this limited study is difficult to explain. The role of other factors such as fatty infiltration and episodic microtraumata to the wrist in the pathogenesis of the carpal tunnel syndrome in Nigerians requires further study.

This study further confirms the impression that connective tissue disorders are uncommon in Nigerians as only one patient in the entire series had neuropathy related to rheumatoid arthritis (Greenwood, 1968). The scarcity of the heredofamilial and metabolic forms of peripheral nerve disease is difficult to explain but may be related to the slow progression of such conditions. Conceivably, it may suggest that their clinical disability is functionally acceptable such that the patients need not report in the hospital.

Similar to the experience of others, the aetiological factor was undetermined in a large percentage of the patients in this series (Miller, 1966; Prineas, 1970). The role of other factors such as microtraumata to unshod feet and infections in the pathogenesis of peripheral nerve disease in the African requires further study.

Acknowledgment

We are indebted to our medical colleagues within and outside the Department of Medicine for

referring some of the patients, and to Dr A. Aladetoyinbo and Mrs O. Osanyintuyin for the biochemical analysis in particular the microbiological assays of the vitamins, and to members of the Department of Morbid Anatomy for the histopathological reports. The secretarial assistance of Mrs E.O. Bamgbelu and Miss I. Ogunseye is acknowledged.

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(*Received* 19 *December* 1980; *accepted* 2 *January* 1981)