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Primary Neuro-ophthalmological Presentation of Burkitt's Lymphoma*

B. O. Osuntokun, O. Osuntokun, A. Adeloye† and E. L. Odeku†

Department of Neurology and Psychiatry and Department of Ophthalmology, and †Neurosurgery Unit, Department of Surgery, University College Hospital, Ibadan, Nigeria

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Summary. Three patients who showed primary neuro-ophthalmological presentation of Burkitt's lymphoma are described. A 7-year-old girl presented with unilateral palsy of cranial nerves (second, third, fourth, fifth and sixth). Another 10-year-old girl, presented with unilateral complete internal and external ophthalmoplegia in association with an epidural mass producing a flacid paraplegia. A 20-year-old male showed features of Guillain–Barré syndrome (including bilateral cranial nerve palsies). Examination of CSF by phase contrast microscopy and tissue culture technique was diagnostic in one patient. The cranial nerve palsies responded dramatically to tumour chemotherapy (endoxan and intrathecal methotrexate).

Résumé. Trois malades présentant un aspect neuro-ophtalmologique primaire du lymphome de Burkitt sont décrits. Une fille de 7 ans présentait une paralysie unilatérale des nerfs crâniens (2e, 3e, 4e, 5e et 6e). Une fille de 10 ans présentait une ophtalmoplégie interne et externe unilatérale complète, associée à une masse épidurale suscitant une paraplégie flasque. Un homme de 20 ans montrait des caractères du syndrome de Guillain–Barré (y compris des paralysies bilatérales des nerfs crâniens). L'examen du LCR par microscopie à phase constrastée et la technique des cultures de tissus a été déterminant chez un malade. Les paralysies des nerfs crâniens ont répondu dramatiquement à la chimiothérapie des tumeurs (endoxan et méthotrexate intrathécal).

Burkitt's lymphoma, a poorly differentiated lymphocytic lymphoma, with unique epidemiologic features and characteristic histologic pattern is well known for the multiplicity of its clinical presentation. Proptosis, unilateral or bilateral, usually in association with involvement by tumour mass of maxilla, mandible, testis, spinal cord or abdomen (Burkitt & O'Connor 1961; Templeton, 1967; Wright, Bell & Williams, 1967) constitute a common syndrome due to Burkitt's lymphoma in African children. A correct diagnosis can usually

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Correspondence: Professor B. O. Osuntokun, Department of Neurology and Psychiatry, University College Hospital, Ibadan, Nigeria.

be made confidently on clinical grounds. However, when tumour masses are not clinically discernable, primary neurological presentation of Burkitt's lymphoma is a diagnostic pitfall, unless the clinician is aware of the possibility of Burkitt's lymphoma. Where a child presents with proptosis, even in the absence of other tumour deposits, the diagnosis of Burkitt's lymphoma is usually considered (Templeton, 1970). On the other hand, cranial nerve palsies with or without other neurological deficit as a primary presentation of Burkitt's lymphoma is less well recognized. The purpose of this paper is to report three patients with Burkitt's lymphoma, who presented primarily with cranial nerve palsies with or without other neurological deficit and initially without clinically detectable tumour masses elsewhere.

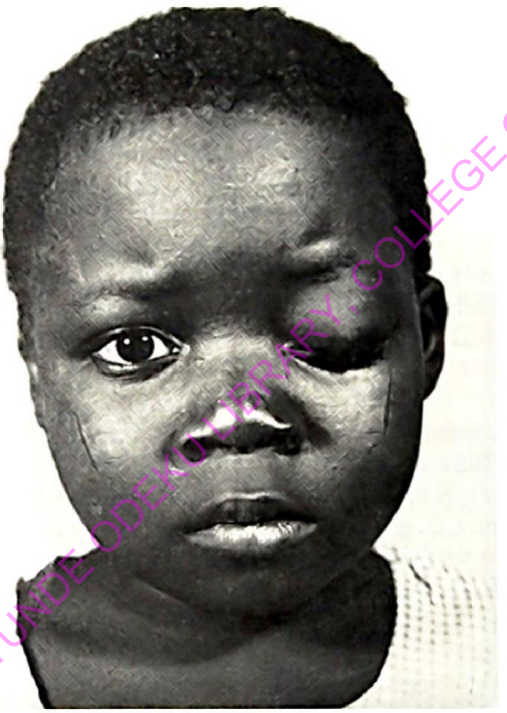

FIG. 1. Case 1: before treatment.

CASE REPORTS

Case 1

A 7-year-old girl presented with a 6-week history of persistent frontal headache. A week after onset of headache, she developed drooping of the left eyelid. On examination, she was well nourished, showed a complete left ptosis (Fig. 1) and complete internal and external ophthalmoplegia. She was totally blind in the left eye. There was complete anaesthesia in the face and scalp in the distribution of the trigeminal nerve, with absent direct left and consensual right corneal reflexes: the left consensual and right direct corneal reflexes were present. The muscles of mastication were normal. Fundoscopy showed no abnormality.

There was no other neurological deficit. No masses were palpable in the face, jaw, neck, and abdomen. The initial diagnosis was polyneuritis cranialis, possibly due to a metastatic tumour or nasopharynyeal malignant disease.

Plain radiographs of chest, skull and orbits were normal. The erythrocyte sedimentation rate was 5 mm in the first hour (Westergren). Lumbar puncture showed normal opening pressure, macroscopically normal CSF, with a protein concentration of 30 mg/100 ml and no pleocytosis. Phase contrast microscopy and tissue culture of CSF cells (Dr Osunkoya) yielded no definitive results. Haemoglobin (Hb) was 13 g/100 ml, white cell count was 1400/ml, with normal differential counts. A left carotid percutaneous angiogram done a month after admission was normal, but during the procedure, one lobe of the thyroid gland

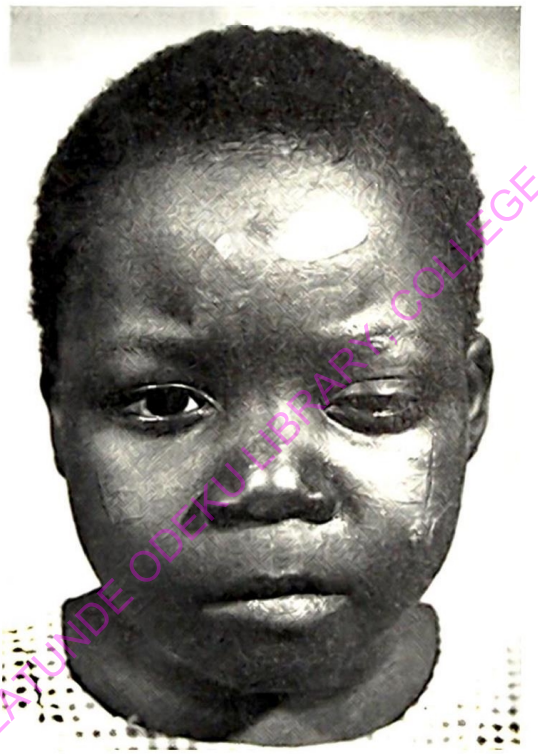

FIG. 2. Case 1: 2 weeks after commencement of tumour chemotherapy.

was observed to be slightly enlarged. Examination of needle aspirate of the enlarged portion of the thyroid gland by phase contrast microscopy and tissue culture technique, showed typical cells of Burkitt's lymphoma. She was treated with intravenous endoxan, 10 mg/kg body weight, for 7 days and intrathecal methotrexate 10 mg weekly for four doses. Within a month, the thyroid swelling disappeared and the ophthalmoplegia and trigeminal neuropathy recovered almost completely (Fig. 2). There was some slight improvement of vision in the left eye. When last seen, 7 months after discharge from UCH, she had remained well, with no recurrence of ophthalmoplegia or trigeminal neuropathy: her visual acuity in both eyes had returned to normal.

Case 2

A 10-year-old girl presented with a 3-week history of weakness of both lower limbs, and drooping of the right eyelid. Examination showed a well nourished girl, with complete right ptosis (Fig. 3) and a complete right external and internal ophthalmoplegia. Visual acuity was normal. The rest of the cranial nerves showed no other abnormality. Fundoscopy was normal. There was no significant proptosis. There was flaccid paraplegia with a sensory level at cord segment T10. The rest of the systems showed no abnormality, and with no palpable masses in the abdomen, jaws and thyroid.

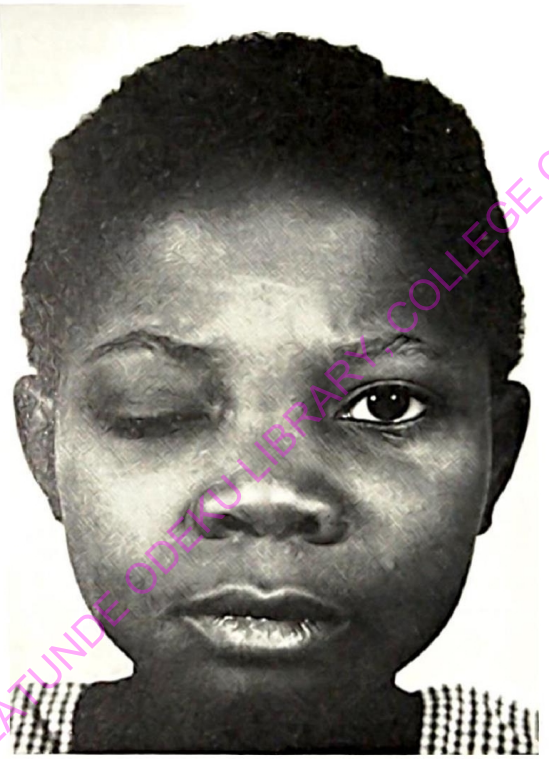

FIG. 3. Case 2: before treatment.

Plain radiographs of the chest, skull, orbit and mandibles were normal, and of the dorso-lumbar spine showed a paravertebral swelling at the level of thoracic vertebra T7. Myelography confirmed a block at T7, and CSF protein obtained at myelography was 180 mg/100 ml. CSF examined by phase contrast microscopy and tissue culture technique showed cells diagnostic of Burkitt's lymphoma. Histology of tissue obtained by dorsal decompressive laminectomy confirmed Burkitt's lymphoma. She was treated by intravenous endoxan 10 mg/kg body weight for 7 days, and intrathecal methotrexate (10 mg) weekly for four doses. The ophthalmoplegia recovered partially (Fig. 4) but there was no improvement in her paraplegia.

Case 3

A 20-year-old male, from Ibadan, was referred from a local hospital and volunteered a 5-month history of headache, pain in the shoulders of 1 month duration, bilateral deep retrobulbar pain for 3 weeks, accompanied by progressive impairment of vision, diarrhoea, vomiting and dysphagia.

FIG. 4. Case 2: 4 weeks after commencement of chemotherapy.

Examination showed an ill-looking emaciated man, with bilateral ptosis (complete on the right, and partial on the left) and bilateral external and internal ophthalmoplegia. Visual acuity in each eye was less than 6/60, and he could just barely count figures. Fundoscopy showed bilateral optic atrophy. The temporalis and masseter muscles were weak and wasted on both sides, being more marked on the right and there was loss of sensations in the face and scalp on both sides in the distribution of the trigeminal nerve. A complete left infranuclear facial palsy was present. Taste sensation was lost in the left half of the tongue in its anterior two-thirds. The rest of the cranial nerves were normal. The limbs were symmetrically hypotonic, with weakness (grade 3–4, MRC scale) and wasting of the periscapular muscles, the deltoid, triceps, pectoralis majora, the intrinsic muscles of the hand and the proximal and distal muscles of the lower limbs. Perception of all the sensory modalities in the limbs, and in the trunk was normal. All the tendon reflexes, as well as the plantar and abdominal reflexes were absent. The chest, abdomen and cardiovascular system were normal. The differential diagnosis on clinical grounds included Guillain–Barré syndrome, sarcoidosis and a malignant syndrome. Burkitt's lymphoma was considered unlikely as the cause of the malig-

nancy. ESR was 150 mm in the first hour. Haematological indices were normal. CSF examination (on three occasions) showed, persistently elevated protein concentration of 100 mg/100 ml, but without pleocytosis, normal sugar content, and no Burkitt's tumour or malignant cells demonstrable by phase contract microscopy or tissue culture techniques. The Heaf test was negative. Kveim's antigen was not available at the time. Electromyography confirmed neurogenic atrophy. Motor nerve conduction velocity in the limbs was normal. Plain radiographs of chest, sinuses, spine, hands, wrists (skeletal survey), intravenous pyelography, serum urea, electrolytes, calcium, phosphates, liver function tests, glucose tolerance test and histology of percutaneous needle liver biopsy (de Menghini), and bone marrow aspiration revealed no abnormality. Within a month of admission he deteriorated rapidly and developed almost complete bulbar palsy and quadriplegia. As the CSF showed cyto-albuminological dissociation compatible with the Guillain–Barré syndrome, he was treated with prednisolone 20 mg t.d.s. He died 3 weeks after therapy was commenced. Post-mortem examination showed Burkitt's lymphoma involving the retro-orbital tissues, the meninges, myocardium, liver, kidneys, adrenals, the pituitary and the spinal nerve roots.

DISCUSSION

The clinical neurology of Burkitt's lymphoma as found in Nigerian patients has been documented elsewhere (Odeku & Osuntokun, 1968). However, the account of Odeku & Osuntokun (1968) deals mainly with patients who showed clinical multicentric evidence of Burkitt's lymphoma, or presented predominantly with epidural mass. It was also noted that a syndrome of anterior polyradiculopathy mimicking Guillain–Barré syndrome could be a complication of Burkitt's lymphoma.

The three cases described here illustrates unusual presentations of Burkitt's lymphoma. These presented as unilateral or bilateral cranial nerve palsies, with or without other neurological deficit and unassociated with other clinically detectable extraneural presence of Burkitt's lymphoma. The ages of the patients in Case 1 and Case 2 suggested Burkitt's lymphoma, although in Case 1, this diagnosis was not initially entertained, and led to investigation of her left complete external and internal ophthalmoplegia by carotid angiography. In Case 3, an adult aged 20 years, with a picture of polyneuritis cranials, combined with spinal anterior polyradiculopathy, Burkitt's lymphoma was a surprise finding at autopsy. In view of our experience, we believe it would be justifiable to institute a therapeutic trial of endoxan and intrathecal methotrexate in young African patients, who come from areas 'endemic' for Burkitt's lymphoma, are under the age of 25, and present as the Guillain–Barré syndrome and who fail to respond to corticosteroid therapy and whether or not there are other indications to suspect Burkitt's lymphoma. In fact, Odeku & Osuntokun (1968), reported a patient with Burkitt's lymphoma, complicated by Guillain–Barré syndrome, whose flaccid paraplegia responded to chemotherapy.

Only in one of the three patients with apparent primary neuro-ophthalmological presentation was examination of cerebrospinal fluid by phase contrast microscopy and tissue culture technique diagnostic. The tissue culture behaviour of cells of Burkitt's lymphoma is well defined (Pulvertaft, 1964), and a smear preparation of Burkitt's lymphoma cells has a diagnostic appearance (Wright, 1963). Case 1 who did not show malignant pleocytosis showed good response to chemotherapy. Case 2 on the other hand who showed malignant pleocytosis, did not show as good a response to chemotherapy as Case 1. Case 3 was not

treated with endoxan and methotrexate. Ziegler & Bluming (1971) suggest that the prognosis is poor in patients with Burkitt's lymphoma and malignant pleocytosis even after chemotherapy, but reported initial good response to intrathecal methotrexate and cytosine arabinoside given daily for 4 days.

Presumably all our three patients had meningeal infiltration, confirmed in Case 3 at autopsy. It is possible that in a few patients the lymphoma may arise primarily within the neuraxis and spread by meningeal infiltration or through CSF pathways. On the other hand foci of lymphoma in one or more of the visceral organs may not be clinically discernable, and may seed into the neuraxis. In case 3 for example, tumour deposits were found at autopsy in the liver, myocardium, kidneys and adrenals, although a liver biopsy showed no evidence of Burkitt's lymphoma.

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