



Paediatric Pontine Glioma in Southeast Nigeria: A Case Report

Eneh, C. I.

Department of Paediatrics,
Enugu State University of Science and Technology and
Enugu State University Teaching Hospital (ESUT-TH)
Parklane, P.M.B. 1030, Enugu State, Nigeria

Egwuonwu A. C.

Enugu State University Teaching Hospital (ESUT-TH) Parklane,
P.M.B. 1030, Enugu State, Nigeria

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BACKGROUND

A pontine glioma is a diffuse intrinsic brainstem tumour^{1,2}. Histologically it has a high degree of tumour anaplasia with necrosis (high grade III-IV). The prognosis for intrinsic brainstem glioma is extremely poor as the tumour is inoperable, radiotherapy and chemotherapy are not curative and median survival is less than one year.

INTRODUCTION

Gliomas are tumours formed from glial cells-these form supporting tissues carrying oxygen, nutrient, and protect the brain from infections³. Brainstem gliomas are among the four most common types of infratentorial tumours in children. Pontine glioma is a rare tumour that occurs in the most delicate part of the brain stem-the Pons¹ It occurs almost exclusively in children. Anatomically the pons lies antero-superior to the other structures of the brainstem (midbrain and medulla oblongata)². These structures connect the cerebellum to the spinal cord and has control over important functions in the body- respiratory centre, blood pressure, CN III, VIII, X chiefly. The falx cerebri separates the brain into two compartments with the brainstem lying in the infratentorial compartment. Infratentorial tumours form approximately fifty percent of childhood CNS tumours and are most common in children aged one to ten years.

CASE REPORT

Seven-year-old female C.C presented to our unit with history of progressive unsteadiness of gait while walking then while standing for one week. This was followed by child becoming progressively withdrawn. She had fever and dizziness but no visual or speech impairments. There was no history of head-trauma, drug-use or seizures

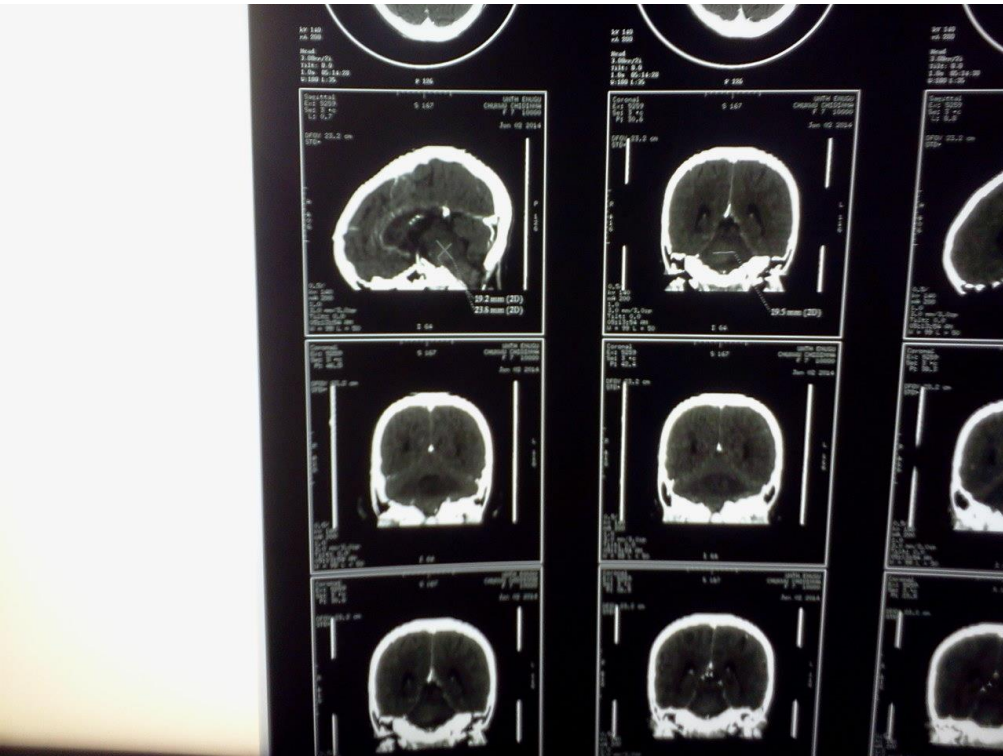
Physical examination showed somnolent, afebrile child with signs of cerebellar dysfunction, otherwise normal CNS findings. Patient later developed features of raised intracranial pressure for which she was managed accordingly. She had normal fundus, cerebrospinal fluid and skull x-ray but computerized tomography of the brain showed a diffuse pontine mass with

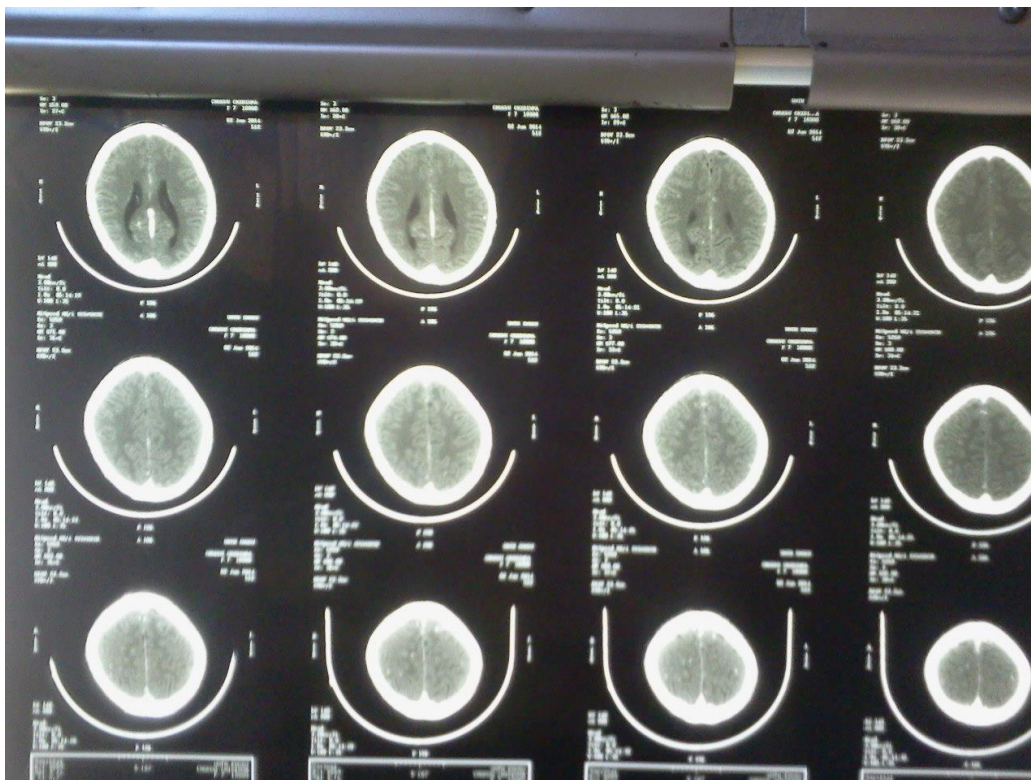
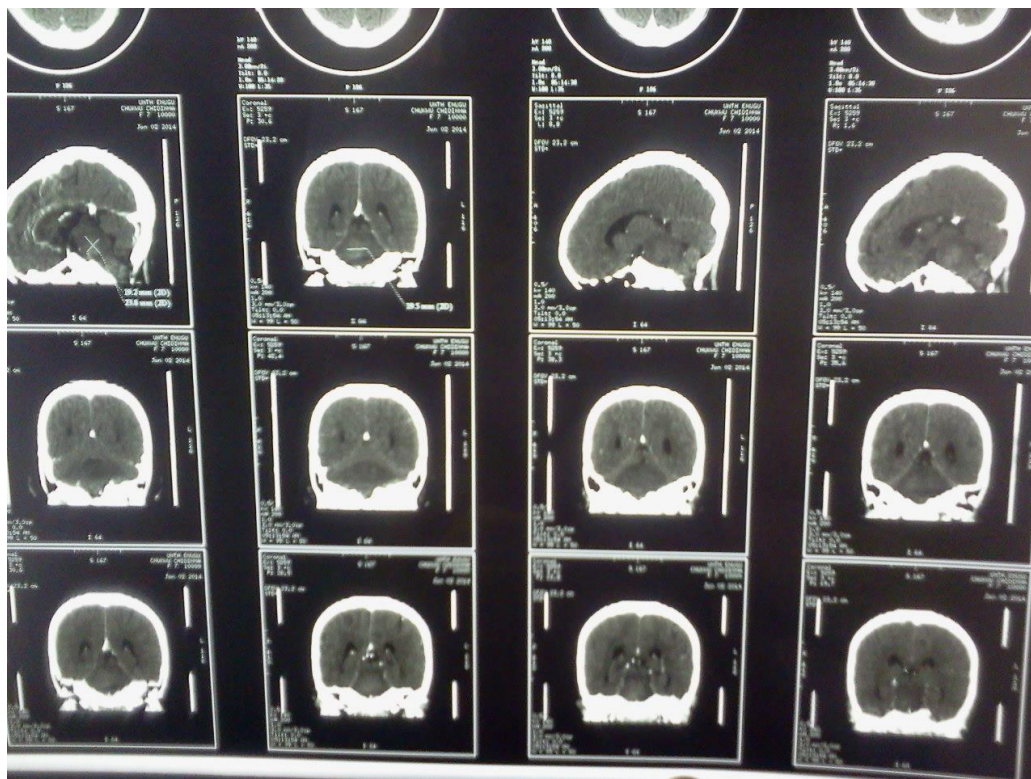
obstructive hydrocephalus of the fourth ventricle (see images). MRI was requested for. However, the patient died before either MRI and subsequent radiotherapy could be commenced.

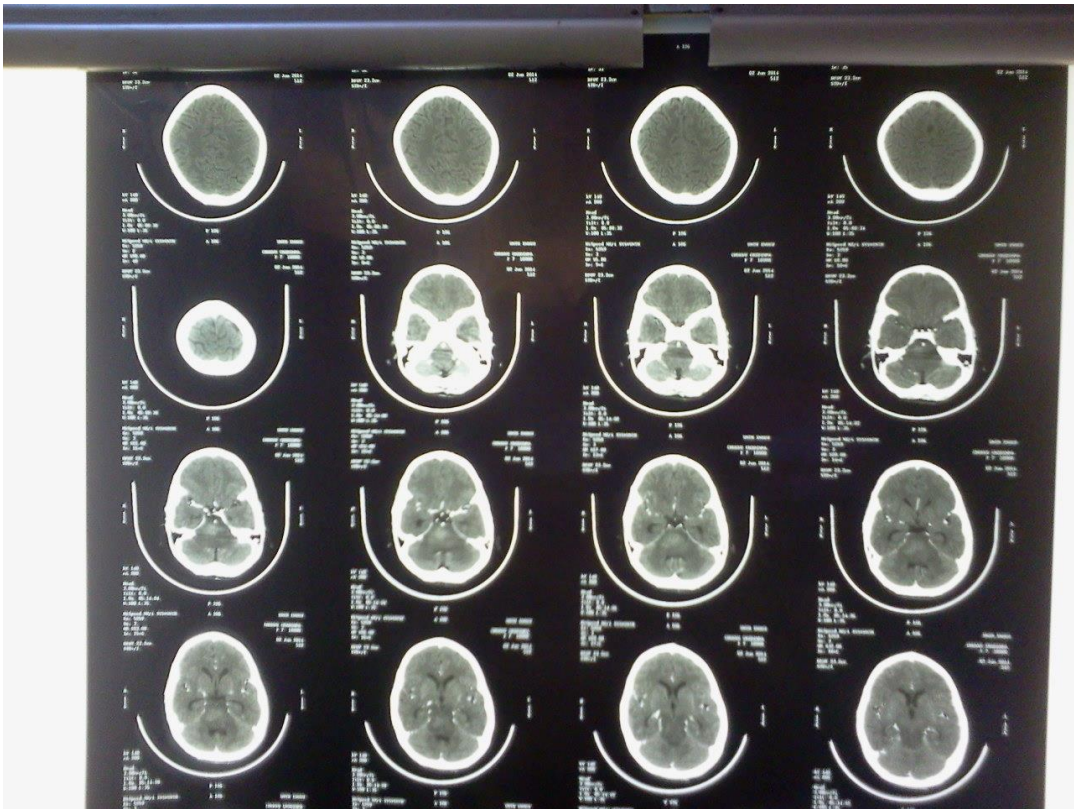
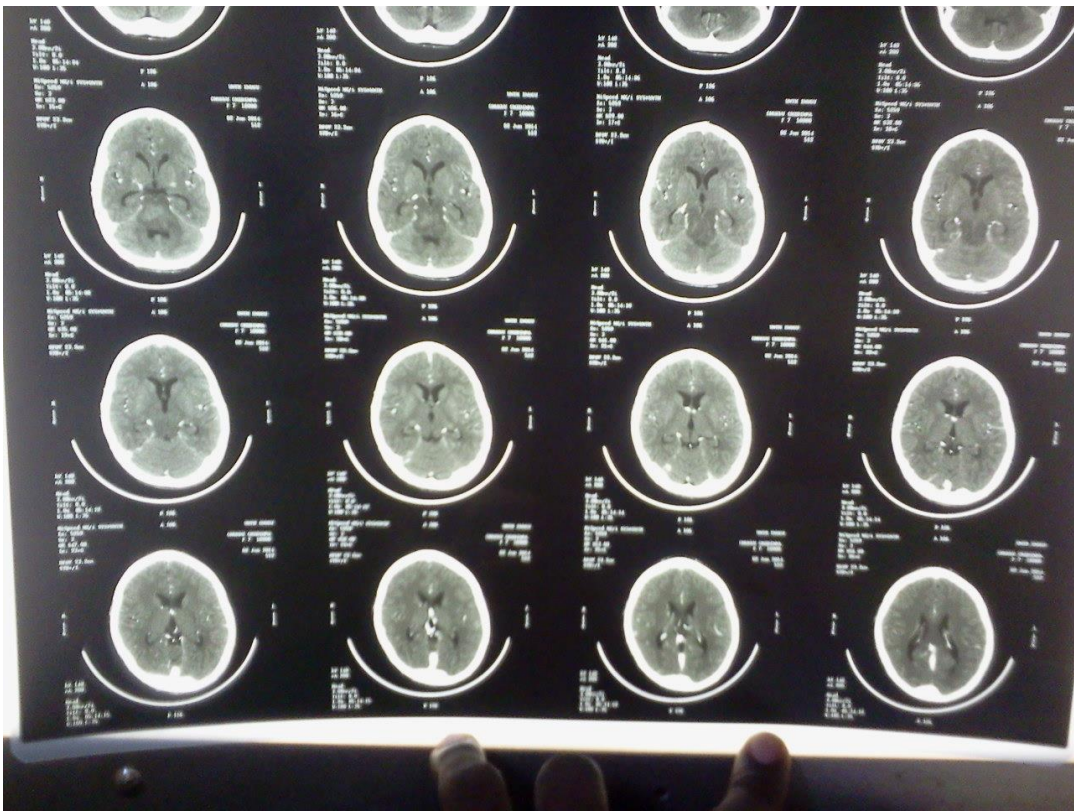
Brain tumours are the second most common childhood tumours in Caucasians but the true prevalence in sub-Saharan Africa is unknown. This case report is mainly to create awareness of the existence and prognostic feature of pontine gliomas in Southeast Nigeria of Sub-Saharan Africa.

CT SCAN OF PATIENT









LITERATURE REVIEW

Classification: Histologically, brainstem gliomas are classified into: Diffused infiltrative pontine glioma (DIPG), Focal glioma, exophytic glioma and cervicomedullary glioma⁴.

Eighty percent of DIPG are high grade and anaplastic, while the other 20% are low grade⁵. **Aetiology:** This is unknown. There is paucity of data on the cause of pontine gliomas. Some recent evidence points to platelet derived growth factor (PDGF) and its receptors (PDGFR) as among the major driving forces of tumourigenesis in majority of cases⁷. Another study implicated epidermal growth factor receptor (EGFR)- implicated in a majority of high grade DIPG and about 20% low grade DIPG by immune-histo-chemistry staining techniques⁸. Approximately 50% DIPG had p53 gene mutation. Three groups reported loss of a region of 17p containing the p53 gene in 31%, 57%, and 64% respectively⁹. Possible risk factors for brainstem glioma include Neurofibromatosis type1.

Epidemiology: Incidence in Africa is not known. Very little has been published or is known about Paediatric brain tumours in Nigeria especially the South-Eastern part¹⁰ previous reports being from the southwest zone¹¹⁻¹³. According to Central brain tumour registry in US, there were about 400-500 cases of brainstem glioma per year. DIPG represents 10.7% of primary central nervous system tumour¹⁴. The common age at diagnosis for DIPG is 5-9yrs, median age of 6.5yrs. There are no sex predilection¹⁵.

Clinical features: Recognised symptoms of pontine glioma include loss of balance and gait anomalies, aggressiveness or somnolence, excessive sleepiness, behavioural changes, headache (initially early morning and gets relieved by vomiting), vision and hearing problems as well as difficulty in learning¹⁵.

Diagnosis: is suggested by a good history and physical exam with emphasis on a thorough neurological exam eliciting some or all the clinical features. Definitive diagnosis is by MRI scan which shows infiltrative expansion of the pons, typically hypointense on T₂ weighted and hyperintense on T₁ weighted. MR spectroscopy helps rule out other differential diagnosis. CT scan can be used in the absence of MRI. Albright and co-workers¹⁶ reported that two CT scan features including a hypo-dense tumour prior to contrast administration and a tumour involving the entire brainstem correlated with a significantly reduced survival time.⁵ In addition, Stronk and co-workers¹⁷ identified four distinct groups of brain stem gliomas based on CT scan characteristics including group I- iso-dense contrast enhancing with dorsal exophytic component, group IIa- hypo-dense non-enhancing intrinsic tumours, group IIb- intrinsic tumours with hyper-dense exophytic components and group III- intrinsic cystic contrast enhancing and group IV-focally intrinsic iso-dense contrast enhancing. Group IV was reported to have the best prognosis with best response to surgical intervention followed by group I with group II having the worst prognosis. DIPG shows increased choline /N-acetyl aspartate and choline /creatinine ratios differentiating it from brainstem encephalitis, demyelination and other inflammatory processes when MRI and clinical features are inconclusive¹⁸.

Treatment: DIPG lesions are said to be inoperable and not so sensitive to chemotherapy. Radiotherapy remains treatment of choice and must be instituted as soon as diagnosis is made.

The dose is between 5400-6000cGy and it is given in daily fractions of 150-200cGy over six weeks¹⁹.

Prognosis: DIPG has a poor prognosis – 0% 5-year survival rate with median overall survival time of children diagnosed with DIPG being approximately nine months. The 1 and 2-year survival rates are approximately 30% and less than 10% respectively ²⁰. About 75-80% of patients show some improvement after radiotherapy. However, DIPG almost always begins to sprout in form of progression, relapse or recrudescence. Clinical trials report the time between radiotherapy and progression is 5-8.8 months¹⁹. Children under age 3 years and young adults over 18years and those with Neurofibromatosis type1 may have better prognosis.

DISCUSSION

Our study environment as in most developing countries are fraught with such environmental hazards as unregulated gas flaring, crude oil and other petroleum product spillage on human, aquatic and agricultural lives²¹. These pose risks to development of cancers and affect their characteristics, presentation and management outcomes. In addition, paucity of personnel and technology in resource limited settings such as ours did not permit immuno-histochemical or genetic studies by which our index patient could have been classified^{4,5,7-9}. The patient had no feature of Neurofibromatosis as a risk factor.

An earlier review of Paediatric brain tumours in another center in the same setting ¹⁰ reported Paediatric gliomas the most common paediatric brain tumors (37%) and the most common supratentorial tumour. However, brain stem glioma was second to medulloblastoma among the infratentorial tumours¹⁰. Thus, brain stem gliomas as seen in our index patient may be said to be relatively common compared to other Paediatric brain tumours in our setting. The index patient's age of 7 years is consistent with the reported common age at diagnosis (5-9yrs, median age of 6.5yrs) for DIPG¹⁵. These findings support the literature that infratentorial tumours form approximately fifty percent of childhood CNS tumours with brainstem gliomas among the four most common types of infratentorial tumours in children and being most common in children aged one to ten years. Pontine glioma may be reported in a female as in this case and equally in a male child within the age range¹⁰ since there is no sex predilection¹⁵. Several other investigators collaborate this finding¹⁶⁻¹⁸.

Regarding the commonly recognised symptoms of pontine glioma¹⁵, it is noteworthy that our patient presented mainly with dizziness as well as gait anomalies (as did most of the patients with infratentorial tumours (82%) in the earlier review, followed by vomiting (72%) and altered consciousness (48%) in their series¹⁹. In contrast, our index patient though often somnolent remained fully conscious and had neither complaints of headache nor vomiting episodes except for a period of time during admission when she developed raised intracranial pressure.

For the index patient the diagnosis was via history, physical examination and by CT scan. No biopsy was performed in our patient. In the absence of the highly specific and diagnostic MRI, the alternative and acceptable CT scan was carried out and shown in the case report images. The sudden demise of the child has implications for the bad prognostic type; DIPG²⁰.

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