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One year follow up of a child with clinico-radiologically diagnosed left Thalomopeduncular Glioma

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Keywords
paediatric thalamic tumours, VP shunt insertion, temozolomide, shunt series, low resource settings

ABSTRACT

Background Absence of or poor facility and equipment have been the bane of management of thalamic tumours in low-resource settings.

Case presentation We present a case of a 3-year-old with clinico-radiologically diagnosed thalamopeduncular-cerebellar glioma, treatments and outcome.

Conclusion In low-resource settings with high reliance on clinico-radiologic data, arriving at a diagnosis requires a high index of suspicion. Early institutions of basic definitive care could give a chance for a good outcome.

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INTRODUCTION

Thalamic tumours make up approximately 5% of paediatric brain tumours [1–5], low-grade glioma (LGG) accounts for the highest percentage of thalamic glioma [6]. Thalamic high-grade glioma is not infrequent [7]. With the advancement in technology, the once dreaded location which was associated with high operative morbidity and mortality can now be accessed with minimal or no morbidity. However, this is not the case in low resource settings, where basic imaging tools such as cranial computed tomography (CT) is located more than 260-560 km away (i.e. approximately 4-8 hours' drive northwest-ward from the location of the facility- Modibbo Adama University Yola, in northeast Nigeria) [8,9]. More so, many patients are financially constrained and

cannot do basic blood workup, purchase the cheapest available chemotherapeutic agent, or afford referral to private facilities in faraway southwestern Nigeria. These facilities have some of the modern imaging equipment (such as tractography) and intraoperative neuronavigation. Hence, the reliance on basic facilities to give the patients optimal care.

Modibbo Adama University Teaching Yola, is a new tertiary health institution in northeast Nigeria, approved by the Federal government of Nigeria 2 years ago, with a nascent stable Neurosurgery Unit which serves both its host and neighbouring states.

Herein, we present a child with clinico-radiologically diagnosed left Thalomopeduncular-cerebellar glioma, who had ventriculoperitoneal shunt and 3 courses of temozolomide with excellent outcome at the time of writing this article.

Case presentation

A 3-year old right-handed Nigerian female child was admitted to our facility with a 4-month history of progressive sequential right hemi-body weakness, ataxic gait, inability to sit, and loss of neck control. There was associated recurrent headache, three episodes of vomiting and aphasia. At presentation, the child was found to have differential spastic quadriparesis, (Medical Research Council (MRC) power grade zero on the right and 3-4 on the left) with a GCS of 10/15 (E-4, V-2, M-4), truncal ataxia, and bilateral papilledema but could fixate and track light.

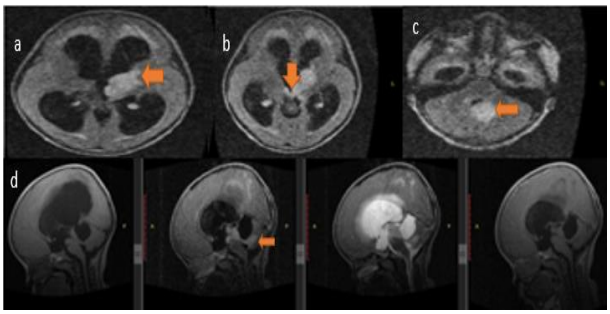

Figure 1. Brain MRI of the 3-year old with clinico-radiologically diagnosed left thalamopeduncular-cerebellar glioma- upper row (a)-(b) shows craniocaudal extension of the tumour highlighted by the brown arrows. (a) tumour epicentred in left thalamus, (b) tumour in the cerebral peduncles (left>>right) and (c) tumour involving the left superior, middle and inferior cerebellar peduncle. The lower row (d) shows extension of the tumour from the cerebral peduncle via the midbrain to the cerebellar peduncles on different intensities.

Brain magnetic resonance image (MRI) at presentation, revealed a non-contrast enhancing, isointense on T1W and hyperintense on T2W left thalamic mass, differentially involving the cerebral peduncle (left>>right), extending via the midbrain tectum to involve the left superior, middle and inferior cerebellar peduncles, with effacement of the fourth ventricle. There is tri ventriculomegaly (with transependymal seepage) and cerebrospinal fluid (CSF) in the suprapineal space displacing the cerebellum posteriorly. We made a clinico-radiological diagnosis of Obstructed Hydrocephalus due to a left Thalamic Peduncle-cerebellar low-grade glioma (Figure 1).

Patient was planned for a right occipito-parietal ventriculoperitoneal (VP) shunt insertion (via Keen's point) with post-op administration of temozolomide 200 mg daily for 5 days every 28-day cycle for 12 courses or when patient has clinical recovery and or radiologic regression of tumour. She was also placed on dexamethasone tablets pre-operatively.

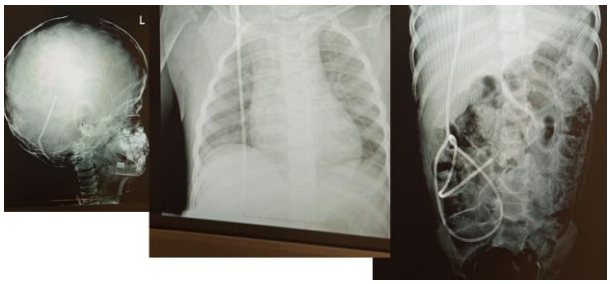

Figure 2. Shunt series of the 3-year old with left thalamopeduncular-cerebellar glioma.

Right occipito-parietal VP shunt was successfully done 2 days after presentation (Figure 2) and patient was placed on IV Ceftazidime and IV Paracetamol post-op. She started chemotherapy treatment on 14th postoperative day, based on Temozolomide 200 mg daily, alongside 0.5 mg of tabs Dexamethasone and IV Ondansetron 2 mg over 15 minutes, 30 minutes before temozolomide, then at 4 hours and 8 hours after first dose of Ondansetron daily for 5 days, to avoid chemotherapy induced vomiting. The CSF cytology returned negative; however, we continued the chemotherapy based on the clinico-radiologic diagnosis of left thalamopeduncular-cerebellar glioma.

Patient was later discharged on 19th postoperative day after completing the first course of temozolomide chemotherapy. She showed

satisfactory improvement with a GCS of 15/15, modified Rankin score (mRS) of 4 (achieved neck control, sits unsupported and walked with "*clumsy and drunken*" ataxic gait with maximum support) and Glasgow coma scale extended (GOSE) lower moderate.

She had only 3 of the 12 planned courses of chemotherapy due to financial constraints, following which the mother could not present her for follow-up. We however, contacted the mother via mobile phone who revealed that they could not afford the transport fare from the state where they reside (about 185 km, i.e. 3 hours 30 minutes' drive), more so the chemotherapy and the first post chemotherapy MRI. She however responded that the child had greatly improved and played around with steady gait (which was confirmed on WhatsApp video call). The child also answered every question intelligently over the phone conversation. She is currently doing well with mRS of 1 and GOSE upper normal and is doing well in school 6 months post-operation. Mother has, however, declined physical follow up and further postoperative radio imaging due to financial constraints.

During the course of chemotherapy, she had clinico-haematological evidence of anaemia and had to be transfused with whole blood on three occasions. She also had left otitis externa that warranted otorhinolaryngology consultation after the first course of chemotherapy. Furthermore, she was admitted for severe diarrhoeal disease after the third course of chemotherapy. Throughout the period, her white cell and platelet count were within normal limits.

Discussion

Functional anatomy of the thalamus

The thalamus is a paired ovoid deep brain structure composed mainly of grey matter, each measuring 3.5 cm long and connected by grey matter "massa intermedia". Medially, it forms the upper two-third of the lateral wall of the third ventricle (with the hypothalamus forming the inferior third); laterally it is delineated by the internal capsule, cranially it shapes the floor of part of the lateral ventricle, inferiorly it is separated by the subthalamus from the midbrain and anteriorly it forms the posterior border of the foramen of Munro. The pulvinar, is the posterior part of the thalamus, which communicates with the superior and inferior colliculi via its metathalamic (geniculate) bodies. The pulvinar is grooved superiorly by the fornixes [10].

The thalamus is divided into several nuclei. Most anteriorly, is the anterior nucleus whose affectation could lead to diencephalic amnesia. Medially, are the large dorsal and small ventral nuclei. Laterally, are the dorsal and ventral tier of nuclei. The dorsal tier is divided into the lateral and posterior (which includes the pulvinar and its geniculate bodies) nuclei. The ventral tier is divided into ventral posteromedial (VPM) and ventral posterolateral (VPL) nuclei. Furthermore, additional nuclei include intrathalamic, midline and reticular nuclei [10].

Functionally, only the lateral ventral tier nuclei (VPM and VPL) and geniculate bodies are assigned specific functions [10]. The medial geniculate forms part of the auditory pathway between the inferior colliculus and the auditory cortex, whilst the lateral geniculate body plays a role in the visual pathway and its affectation will cause homonymous hemianopsia or quadrantanopia. The VPM receives sensory information from the head and face through the trigeminal lemniscus and tastes information through the solitary tract. The VPL receives exteroceptive sensory information (pain, touch, temperature) from the contralateral side of the body by the ascending spinothalamic tract (spinal lemniscus) and proprioceptive information (sense of the relative position of body parts and of muscle strength) through the medial lemniscus (cuneate and gracile nuclei). Motor information is also received from the cerebellum (via the superior cerebellar peduncle to the ventral lateral nucleus) and the corpora striata. Affectation of the pulvinar could lead to varying sensory deficits, weakness, memory impairment, aphasia, hand tremor, and dystonia.

Clinico-radiologic findings

The thalamus is a location for several pathologies. The pathological entities includes glioma [11] (viz LGG are hypointense, non-contrast enhancing and HGG are contrast enhancing with necrotic core [12]), lymphoma [13] (especially the primary CNS type is hyperattenuating contrast enhancing on CT and isointense with restricted diffusion, however homogeneously contrast enhancing in the immunocompetent, but ring-enhancing with necrotic core in the immunocompromised occurring more in the cerebral hemisphere, but could occur in the periventricular white matter, corpus callosum,

basal ganglia and thalamus), metabolic disease (namely Wilson's disease presents with dysarthria, dystonia and tremor and copper deposit seen lentiform nucleus and thalamus as hypointense on T1W and gradient echo, but hyperintense in the outer rim of putamen on T2W and FLAIR; Fahr's disease- calcium deposit involving the basal ganglia symmetrically, seen as hyperdense on CT, but variable intensity on MRI; and Wernicke's encephalopathy seen in thiamine deficiency, commonly in alcoholics), congenital anomalies such as Neurofibromatosis type 1 (seen as focal areas of signal intensity, non-contrast enhancing with no mass effect), vascular lesions (such as arteriovenous malformation presenting with flow voids, described as "bag of worms" on MRI. Other vascular abnormalities are haemorrhage, hypoxia or ischemia from arterial or venous pathology), infections (namely thalamic abscess, which could be confused with subacute haematoma and Creutzfeldt-Jakob disease presenting with hyperintensity involving the pulvinar and dorsomedial nuclei bilaterally known as "hockey stick sign" or "pulvinar sign") and metastasis which should be suspected in a patient with confirmed primary and multiple intracranial lesions [10].

The index patient presented with clinico-radiologic features of an LGG epicentre in the left thalamus and progressively involved the cerebral peduncles (worse on the left), the midbrain and the ipsilateral superior, middle and inferior cerebellar peduncles with tri ventriculomegaly, which to the best of our knowledge is the first account of thalamic peduncle-cerebellar glioma in the literature. Hence the child presented with speech impairment, differential quadriparesis (dense on the right), truncal ataxia resulting in loss of neck control, and depressed consciousness. Similarly, in the study of 60 children with thalamic tumours by Bernstein et al [14], 75% had hemiplegia, 68% had headache, 47% had vomiting, 22% had altered sensorium and 7% had speech dysfunction; however, none had truncal ataxia, since they had no cerebellar involvement. However, in another study by Kim et al [15], only 22% had hemiparesis and 2.7% had gait imbalance, dizziness and rigidity. 19.4% had thalamic-peduncle-midbrain involvement. Furthermore, in a study of 8 children by D'Amico et al [3], 75% had hemiparetic and 12.5% had ataxia. In a study of 27 children by Cinalli et al, 77.8% had thalamopeduncular tumours of various histologic types, though majorly glioma and 7.4% of the bilateral thalamopeduncular tumour being high grade tumours [6]. In a study of 33 children by Nayel et al, 36.4% had hemiparesis, of which 6.1% were bilateral [1]. Unilateral thalamic tumours like in this patient have the propensity to grow inferiorly [18,19].

Management and outcome

In the past, the diagnosis and treatment of thalamic gliomas relied solely on imaging due to the deep location of the thalamus. However, with the advancement in both technology and surgical techniques, various approaches to the thalamus have been developed with reduced morbidity and mortality. In the area of technology, 3-Tesla MRI have made the study of the lesion and its relation to white matter (diffusion tensor image (DTI) or tractography) very clear for preoperative planning as regards the approach to be made [3,15]. Furthermore, intraoperative neuronavigation also contributes to the precise localization of the lesion [3,15]. More so, if biopsy is the sole goal of surgery, except in the situation where the tissue may be considered inadequate, stereotactic biopsy could be deployed with utmost precision. Also, for tumours that meet the criteria of radiosurgery, stereotactic radiosurgery without the benefit of tissue biopsy is available. These are not easily available in low resource settings like ours where the highest form of MRI is 1.5T in the whole country, and the closest from our facility is 260 km away, coupled with the dilapidated road network to access the service. Although it is cheaper (approximately 32 United States dollars-price is halved for paediatric age group-, when compared to 95 US dollars elsewhere in southwest Nigeria), most patients and relatives are unable to afford it. However, for those under the National Health Insurance Scheme (NHIS), 2/3 of the payment is covered by the scheme. Unfortunately, most patients are not under the scheme.

In the patient who had hydrocephalus and met the criteria for CSF diversion, endoscopic third ventriculostomy with or without choroid plexus cauterization and biopsy of the lesion if possible is done. If the option of VP shunt is preferred, it is done under endoscopic guidance to insert both the ventricular and abdominal catheters [6]. While endoscopic guided VP shunt placement is not currently available in Nigeria, only about five centres

spread across the northwest, southeast, southwest and north central of Nigeria have facilities for endoscopic third ventriculostomy [8,9]. This patient however, had occipito-parietal VP shunt insertion via the Keen's point which is approximately 3 cm above and behind the highest point of the pinna. Other commonly used points include Dandy's point which is 3 cm above the inion and 3 cm away from the midline; Frazier's point which is 6 cm above the inion and 3 cm away from the midline and Kocher's point which 1 cm anterior to the coronal suture and 2-3 cm away from the midline [21]. Post-operatively, the tip of the ventricular catheter above the location of the sphenoid sinus (approximate location of the foramen of Munro) and the intraperitoneal location of the abdominal catheter in a "shunt series" was adjudged by the first author to be adequately placed catheter.

The strategy of management of thalamic gliomas include radiologic diagnosis, biopsy (open or stereotactic), tumour excision (subtotal or gross), radiosurgery (with or without biopsy), radiotherapy and or chemotherapy [1,17]. Different combinations of chemotherapeutic agents have been used and still in use [16], however with the advent of temozolomide an alkylating agent, a single chemotherapeutic agent can be used with good outcome. Temozolomide, although proven to be effective for both LGG and HGG in the thalamus, is not without adverse effects which include aplastic anaemia from myelosuppression, severe infection and death. However, our patient only had severe anaemia necessitating transfusion, otitis externa and severe diarrhoea that was promptly managed. The cost of the 5-day course was 43 US dollars and this was pretty difficult for the relatives to afford during the course of therapy, since chemotherapeutic drugs are not covered by the NHIS and this patient is not registered in the NHIS.

Fortunately, the patient had clinical recovery after the third course of chemotherapy. Khaw et al, in their study of 13 children with LGG, 6 of which had only radiologic diagnosis found out that temozolomide is effective as a second line agent in the treatment of paediatric LGG [16]. However, Badejo et al in their case report of bithalamic LGG (diffuse astrocytoma), who had several courses of chemotherapeutic agents with poor quality of life until demise one-year post biopsy [18]. Bithalamic tumours because of their mostly diffuse histologic nature are usually of poorer prognosis [19]. In the Canadian study, duration of symptoms greater than 3 months and tumour grade rather than extent of resection are the important prognostic factors in unilateral thalamic tumours [19], although Puget et al previously found that duration of symptoms, size of tumour, extent of resection and tumour grade are the factors impacting overall survival [20]. In the study of 20 patients by Eissa et al in which tumour grade was evenly distributed, and 15 (including 5 with LGG) had chemotherapy, while 11 (including one with LGG) had radiotherapy, patients with biopsy alone had better overall survival than their counterparts who had tumour debulking; and tumour size was the determinant for overall survival [17].

This patient with thalamopeduncular-cerebellar tumour (to the best of our knowledge is the first case of thalamopeduncular tumour with cerebellar extension in the literature) is a candidate for stereotactic biopsy and CSF diversion, if the equipment were available. However, in the absence of the necessary equipment, we relied on the radiologic features, which was suggestive of LGG and has been previously shown to respond to chemotherapeutic agent like temozolomide and opted for the safest available care, which was CSF diversion with anatomic landmark-guided, ventriculoperitoneal shunt placement, confirmed post-operatively with "shunt series" and single chemotherapeutic agent- temozolomide.

Conclusion

In a low resource setting, high index of suspicion is required to make radiologic diagnosis of thalamopeduncular glioma and early institution of chemotherapeutic agent could be the only chance to good outcome in children under 3-years of age, despite the general poor prognosis of thalamic gliomas irrespective of their grade. In the absence of endoscopic guidance for catheter insertion, anatomic landmarks and shunt series are respectively greatly relied upon for intra-operative catheter insertion and post-operative confirmation of adequate placement of VP shunt in low resource settings. Once radiologic diagnosis of glioma can be made, chemotherapy can be commenced with an expectant favourable outcome.

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