NARRATIVE REVIEW

Role of neurosurgeons In strengthening paediatric neuro-oncology In low- and middle-income countries: a narrative review with case examples

Ahsan Ali Khan[1], Mohammad Hamza Bajwa[2], Naureen Mushtaq[3], Muhammad Osama[4], Afia Arif[5], Saqib Kamran Bakhshi[6], Michael C. Dewan[7], Kee B Park[8], Eric Bouffet[9], Syed Ather Enam[10]

Abstract

Paediatric neuro-oncology in low- and middle-income countries (LMICs) accounts for a significant proportion of cancer-related mortalities in this age group. The current dearth of structured paediatric neurosurgery training programmes in LMICs requires multidisciplinary coordination; neurosurgeons play certain key roles, as discussed in this article, in ensuring safe and effective care for paediatric neuro-oncology patients. This document intends to elaborate through illustrative cases of the technical and structural nuances required by neurosurgeons in LMICs to provide appropriate surgical care.

Keywords: Neuro-oncology, neurosurgery, Neoplasms

DOI: https://doi.org/10.47391/JPMA.S3.GNO-05

Introduction

Paediatric central nervous system tumours (CNSTs) are 15-20% of all paediatric population tumours and are the second most common neoplasm within children after leukaemia.[1] These are the first cause of mortality in paediatric patients with cancer. Within high-income countries (HICs), advances in neurosurgical interventions, neuro-imaging, and histopathological classifications have guided treatment algorithms and improved 5 year progression free survival rates for children with CNSTs to rates as high as 70 - 80%.[2] Unfortunately, more than 80% of the world's children live in low- and middle-income countries (LMICs) where the 5 year progression-free survival for such patients is often between 0 - 40%.[3,4] Studies have identified causes of this to include lack of multimodal infrastructure in paediatric care, evidence-based treatments, and interdisciplinary collaborations with a focus on neuro-oncology.[5] Training in neuro-oncology is also severely lacking.[6] Ultimately, this demands a multidisciplinary approach with involvement of experienced paediatric neurosurgeons, neuro-radiologists, neuro-oncologists, radiation oncologists, and neuro-pathologists; there is a dearth of such specialists in most LMICs.[7]

In 2014, it was reported that there were only 35 neurosurgical centres in Pakistan, and only one neurosurgeon per 1.37 million people within the country. As the population is expected to grow rapidly, this already insufficient neurosurgical capacity will be further burdened.[8] A similar case can be seen in Africa where an approximately one billion people are covered by an estimated 1200 neurosurgeons. Only 142 are located in sub-Saharan Africa (excluding South Africa) which means for every five million people there is one neurosurgeon catering to their needs.[9] If we look to Southeast Asia, the WHO estimates that there is approximately one neurosurgeon per three million people, and for Eastern Europe and the Western Pacific there is approximately one neurosurgeon per 250,000.[10] We can contrast this with more equitable ratios seen within Europe (1:121,000) and North America (1:81,000); overall the ratio of neurosurgeons to the world population is 1:230,000.[11]

Table-1: Summary of recommendations.

Roles of neurosurgeons in paediatric neuro-oncology in LMICs
Role in appropriate acute management
definitive surgery was indicated with a focus on improving patient outcomes
Developing training programmes
dedicated paediatric neurosurgical experience and training programmes
Twinning programs
collaborations with international centres of excellence in diagnosis and treatment of cases
Paediatric neuro-oncology tumour boards
multi-disciplinary, holistic care and following up patients after surgery
Communication and counselling
considering situations of patients and their families to tailor care
Research and development
research infrastructure for generating evidence for best-practice guidelines in LMICs

LMICs-Low and Middle Income Countries.

[1,2,6,10]Department of Neurosurgery, The Aga Khan University, Karachi, Pakistan. [3,5]Department of Paediatric Oncology, The Aga Khan University, Karachi, Pakistan. [4]Dr Ruth K. M. Pfau, Civil Hospital Karachi, Pakistan. [7]Department of Neurosurgery, Vanderbilt University Medical Centre, Nashville, USA. [8]Department of Global Health and Social Medicine, Harvard Medical School, Boston, USA. [9]Division of Haematology Oncology, The Hospital for Sick Children, Toronto, Canada.

Correspondence: Syed Ather Enam **Email:** ather.enam@aku.edu

In this paper, we intend to highlight and address the important roles of a neurosurgeon as a key member of a multidisciplinary approach towards paediatric neuro-oncology and the role of neurosurgeons in strengthening this challenging area in LMICs (Table 1).

Role in appropriate acute management

Decision making by neurosurgeons is crucial in the management of paediatric brain tumours. Hydrocephalus is a common presentation in children with brain tumours and it is common for neurosurgeons without an understanding of paediatric brain tumours´ management to immediately place a Ventriculo-peritoneal shunt (VPS) for symptomatic relief. While a shunt can ameliorate the acute symptoms, it does not address the underlying cause and makes definitive surgery technically challenging. Families of patients with no understanding of the disease and necessary repeat interventions are often lost to follow-up once they see symptomatic improvement. The majority of paediatric tumours causing hydrocephalus reside in the posterior fossa. Only a third of patients who undergo posterior fossa tumour resection ultimately develop persistent hydrocephalus requiring permanent cereberospinal fluid diversion.[12] Thus, shunting up-front unnecessarily exposes most patients not only to an additional, superfluous surgery, but also commits such patients to the life-long morbidity associated with VPS. In other circumstances, neurosurgeons lacking skills and training can deny an intervention when the tumour can be removed safely. Knowing when to operate and when not to operate can change the whole picture. Unnecessary interventions not only lead to increased morbidity rather they also overburden the system which is quite inadequate. Similarly, not being able to operate when it is indicated, results in disastrous outcomes as well.

Case example

A 5 ½ year old boy presented to The Aga Khan University neurosurgery clinic, Karachi with the complaints of drowsiness and progressively worsening vision in his right eye for the past 1 month. He was initially taken to a public-sector hospital, where after being diagnosed with hydrocephalus secondary to a suprasellar mass, his team decided against surgical resection due to the complexity of the case. A VPS was inserted in January 2021. Afterwards, his drowsiness improved and was discharged from the hospital with no intent for further surgical intervention, despite the present tumour. At our clinic, he had difficulty seeing with his right eye with no other focal neurological deficits. An MRI scan of brain showed a large, heterogeneous, partially circumscribed, multilobulated lesion with its epicentre in the suprasellar region (Figure

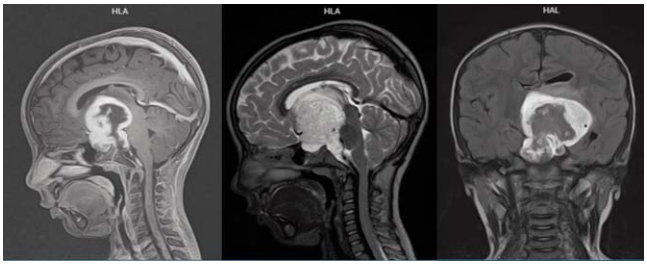

Figure-1: A 5 ½ year-old boy with a large lesion showing extension into the sella with suprasellar expansion, with compression of the midbrain. Histopathology reported this as pilocytic astrocytoma (WHO Grade I).

1). The lesion also showed extension into the sella with suprasellar expansion, with effacement of the pituitary gland, superior extension along the floor of the third ventricle and significant mass effect on the brainstem and left thalamus. The mass was encasing both common carotid arteries and abutting the basilar artery. In comparison to previous scans, there was progression of the disease. He was admitted for surgery for a presumed suprasellar pilocytic astrocytoma. Chemotherapy as an alternative to surgery was discussed, however, the multidisciplinary team decided to opt for surgical resection. Initially, there was a plan for endoscopic resection of the tumour; however due to decompression by the shunt, this was deemed too difficult. He thus underwent neuro-navigation guided supratentorial craniotomy and maximum safe resection of the sellar and parasellar tumour (Figure 2). Postoperatively, he developed right upper and limb weakness of 1/5 and mild right sided facial nerve palsy. However, these gradually improved with physiotherapy and time. After a prolonged hospital stay, he was eventually discharged in a neurologically stable condition. Final histopathology report showed pilocytic astrocytoma WHO grade I. In the follow-up multidisciplinary tumour board, it was decided that he would be continued on surveillance MRI scans.

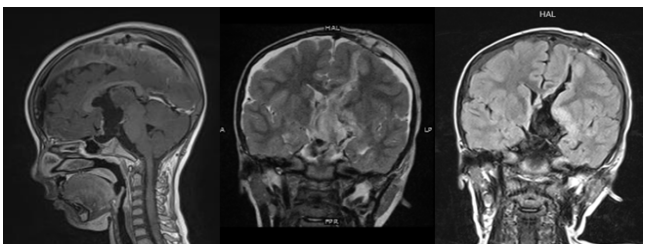

Figure-2: Immediate postoperative MRI scan showing near-total resection of the tumour.

This proved to be an excellent case for highlighting the importance of decision-making by the neurosurgeon in resection of a difficult pathology, with great postoperative outcomes for a young patient, rather than

leaving him with a shunt and waiting for disease progression.

Twinning programmes

Twinning programmes between hospitals in HIC and LMIC have improved outcomes in the paediatric brain tumours management in LMICs.[1] Such collaborations are also helpful in capacity building of the facilities in LMIC. However, there is a need of similar collaborations between the hospitals within the LMICs. Tertiary care hospitals providing care to paediatric brain tumour patients should have collaborations with hospitals lacking such facilities. Paediatric patients are first seen by paediatricians and it is important for paediatric hospitals to have access to consult and refer their patients to more sophisticated hospitals where definitive treatment can be done. A peer-to-peer training can also be part of such collaborations of hospitals in LMICs. In such settings, neurosurgeons working in limited resources and having limited experience of paediatric neuro-oncology can be invited to the centres where they can attend workshops, seminars, observe surgeries, communicate with trained paediatric neurosurgeons and experts of the other areas involved in paediatric neuro-oncology. Such training programmes can also play a part in filling the gaps, capacity building and improving the overall management in limited resource settings. By developing capacity through virtual presence technology, satellite centres across the country can be linked with high-volume, academic centres and conduct remote training modules emphasizing paediatric neurosurgical procedures.

Case example

An 18 year-old male presented with history of right eye visual deterioration and hyposmia for 3 months associated with sneezing and snoring. On examination there was finger counting in left eye only and in right eye there was only light perception. His MRI brain with contrast (Figure 3) showed a solid-cystic lesion with calcification involving right maxillary sinus extending superiorly into anterior cranial fossa up to nasopharynx, sellar and supra sellar region resulting in bony erosion and destruction leading to superior displacement of both

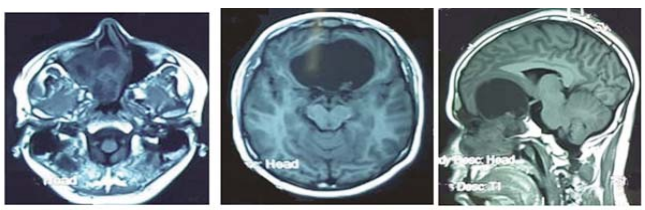

Figure-3: An 18-year-old patient with a large, heterogeneous, solid-cystic lesion. This was an adamantinoma Tous craniopharyngioma (BRAF V600E negative).

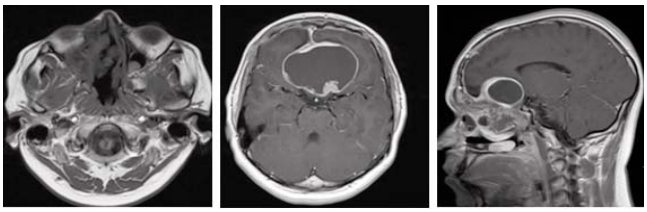

Figure-4: Post-op MRI (6-months post-op) shows debulking of the nasal component of the lesion. There is a large intracranial and paranasal sinus residual disease which appears grossly unchanged.

anterior cerebral arteries and bilateral thalamic arteries. He underwent bi-frontal craniotomy and excision of extra-axial skull base lesion and right lateral rhinotomy plus excision of nasal lesion. Vision improved post-operatively in both eyes. Histopathology demonstrated adamantinoma Tous craniopharyngioma WHO grade I. His first post-operative scan (Figure 4) was done after 6 months due to the COVID-19 pandemic and showed significant progression of the disease. There was interval increase in size of infiltrative solid-cystic neoplastic lesion at the floor of anterior cranial fossa that increased from 68 x 53 mm to 76 x 60 mm in maximum trans-axial dimensions. There was interval development of haemorrhage/accumulation of proteinaceous material within the cystic component of the lesion (Figure 5). Clinically, there was weight gain and visual deterioration in this time span. The case was discussed in our monthly Paediatric Neuro-oncology tumour board with international faculty of SickKids hospital, Toronto, Canada. Tumour board recommended careful safe surgical resection and histopathology review with BRAF V600E. Intracystic treatment may have been discussed as an alternative therapy, however, was not discussed further. In our centre, immunohistochemical staining of BRAF V600E is not available. Therefore, the sample was sent to SickKids hospital and it turned out to be negative. Re-resection of the lesion was done. Neuro-navigation guided bi-frontal craniotomy and extradural resection of anterior skull base lesion was done via lateral rhinotomy approach along with ethmoidectomy and resection and reconstruction of sphenoid. Post-operatively patient

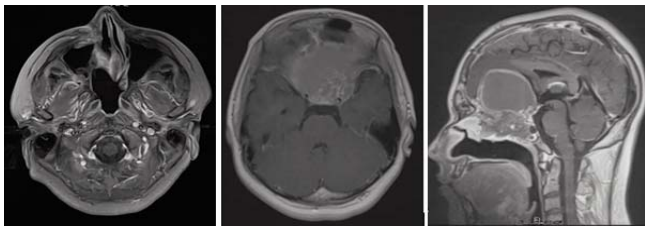

Figure-5: Follow-up post-op MRI showing interval increase in size of infiltrative solid cum cystic neoplastic lesion at the floor of anterior cranial fossa.

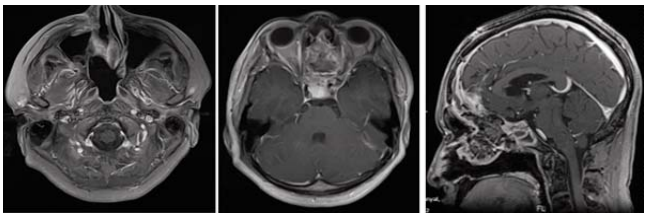

Figure-6: After the second surgery, the patient was followed for residual disease (abnormal cystic area) in left parasellar region with an abnormal enhancing lesion along the antero-inferior aspect of the sella.

remained stable and there were no complications related to surgery. Follow-up MRI scans after second surgery showed some residual disease (Figure 6) and this patient is on regular follow up, doing well with a normal endocrine profile. His vision has also improved.

This case is an example of how international twinning programmes between two hospitals can help in tailoring the management plan with favourable outcomes. Such collaborations can be done within LMICs as well for capacity building.

Paediatric neuro-oncology multidisciplinary tumour boards (PNTBs)

The management of paediatric brain tumours is a highly demanding task in LMICs as it requires a multi-disciplinary approach. A team of well-trained neurosurgeons, neuropathologists, medical and radiation oncologists, well-trained nursing staff, psychiatrists, rehabilitants, and physiotherapists are needed for a comprehensive management of the malignancy.[5] Despite the recent developments of various tumour programmes in LMICs, the mortality of children has failed to improve significantly because of the non-implementation of this multi-disciplinary approach, primarily because of lack of trained doctors and staff, infrastructural short-comings, and management inefficiency at public sector hospitals in LMICs. Lack of experts in paediatric cancer is a modifiable factor in the establishment of a multi-disciplinary system for paediatrics tumour management.

Regular multidisciplinary tumour board meetings play an important and crucial role in deciding the best management plan. A majority of the hospitals in LMICs lack such board meetings and there is extremely limited communication between neurosurgeons and other experts. An aggressive approach to include maximum number of centres lacking tumour boards can be taken. In this way, different centres in LMICs providing care to the paediatric brain tumour patients can be part of virtual multidisciplinary meetings of more sophisticated hospitals where tumour board is being done regularly and experts from these well-established centres can provide consultancy to the other less developed facilities

Case example

A 3 ½ years-old boy presented initially at the age of 18 months with history of excessive cry, neck stiffness for 3 months and difficulty in walking, and vomiting for 15 days. There was no history of seizures or drowsiness. On examination, he was conscious, irritable, and vitally stable

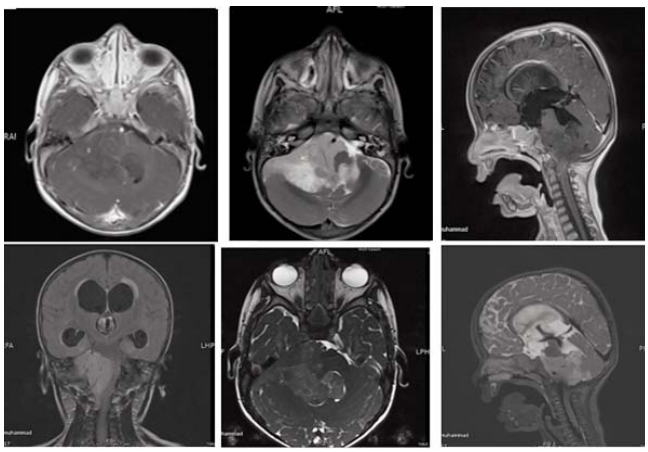

Figure-7: A 3.4-year-old boy with a large abnormal signal lesion in the posterior fossa likely arising from the floor of fourth ventricle, encasing basilar artery and extending up to pre-pontine cistern. Histopathology reported this as an Anaplastic Ependymoma, with loss of H2K27me3 molecular subgroup PF A subtype.

with no neurologic deficit. MRI brain (Figure 7) revealed a large posterior fossa lesion extending to pre-pontine cistern and up to C-2 level of spine. Rest of the spine was normal. He underwent a suboccipital craniotomy for tumour resection and insertion of VPS in December 2018. Post-op MRI brain and whole spine showed significant residual disease (Figure 8). Histopathology was consistent with Anaplastic Ependymoma with loss of H2K27me3 molecular subgroup PFA subtype. He underwent another surgical resection (right retro sigmoid craniotomy and tumour resection) in January 2019. Post-operative scan after second surgery (Figure 9) showed some residual

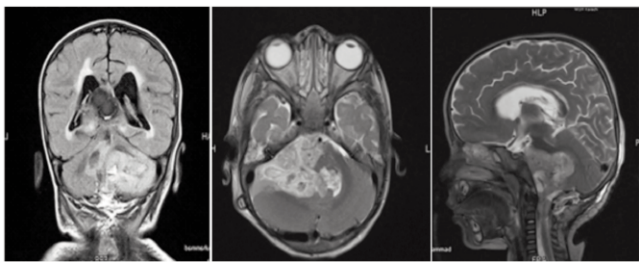

Figure-8: Post-operative MRI brain shows large posterior fossa mass extending into the cervical spinal canal up to the C2 vertebral body level.

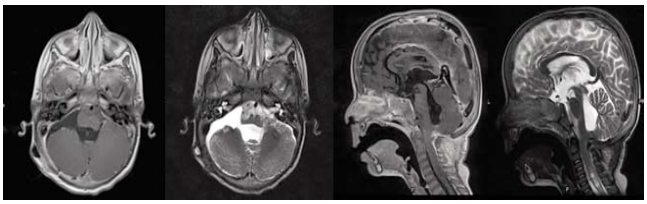

Figure-9: Post-op MRI brain after second surgery. Residual tumour can be seen in front of medulla oblongata and upper cervical cord starting from dens and to level of clivus suggestive of residual tumour.

disease and after discussing this case in the neuro-oncology tumour board with AKUH, Karachi and Sickkids Hospital, Toronto, Canada, it was decided to proceed with focal radiation. He received focal radiation, under general anaesthesia, in a dose of 59.4Gy in 33 fractions @1.8 Gy per fraction. Since then, he is on regular follow ups for the last 2.5 years and recent MRI showed no disease progression (Figure 10).

This case is an example of how complex cases can be handled efficiently with multidisciplinary approach.

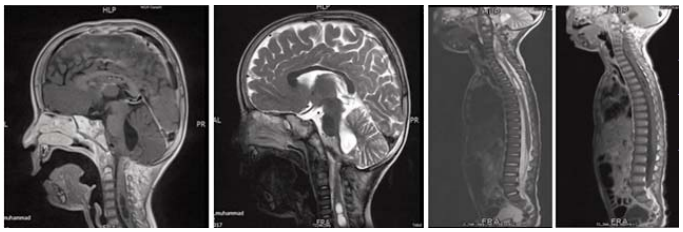

Figure-10: Post-radiation follow-up MRI.

Communication and counselling

Clear communication between neurosurgeons, experts of other disciplines and the families of patients is extremely important in paediatric neuro-oncology. This is due to two reasons: the exorbitant cost of care, and a need for families to understand risks, options, and prognosis of patients in order to make informed decisions.[13] The treatment of paediatric brain tumours is a financially draining process particularly in countries lacking universal health insurance and full coverage for childhood cancer services[3]. A study reported that 50% of the families having a patient of paediatric brain tumours had such a drastic decrease in the total house-hold income that it resulted in the family's socioeconomic status falling into the poverty line.[13] Furthermore, almost 1/3rd of the parents and family members reported that they felt they were not fully involved in their child's care during the treatment process,[14] and many were reluctant to discuss end-of-life and palliative care topics with their health care provider due to a conservative family background.[15] Neurosurgeons have the advantage of experience with such patients and their outcomes and spending considerable time with patients' families with clear outlines and expectations can improve the overall experience they have with the healthcare system. Especially with palliative care, it helps for families to be able to question and hear reliable data from the neurosurgeon handling their child, and thus help come to terms with such realities.

Research and development

There a large disparity between HICs and LMICs in the number of clinical trials and clinical guidelines developed, especially with regards to paediatric neuro-oncology.[13] Making decisions within LMICs settings requires a different understanding of the various socioeconomic and infrastructural differences present as well as a different evidence base. Ultimately, it is researchers and institutions based within LMICs that would have the best vantage point for investigating and researching LMICs paediatric neuro-oncology patients.

Most paediatric neuro-oncology guidelines are developed in HICs and practitioners in LMICs struggle to format these recommendations to their contexts. Neurosurgeons should take charge and develop research protocols that will investigate patient populations within LMICs.[15] With consensus from other specialists in the multidisciplinary team, we can develop guidelines that are geared towards the context and infrastructural capabilities of LMICs. Data from LMICs will provide a new perspective to the concept of global neurosurgery and neuro-oncology and provide us with the best-practice guidelines for paediatric neuro-oncology patients.

Grants for the development of paediatric neuro-oncology capacity within LMICs, such as the My Child Matters initiative taken by the Sanofi Espoir Foundation, help to reduce disparities in access to care and lack of clinical guidelines. Through regional collaborations, this initiative has been able to create networks for helping paediatric patients' access quality care and develop clinical guidelines for resource-constrained settings. Training programmes in the paediatric neuro-oncology can then further help establish the next generation of paediatric neurosurgeons in LMICs, poised to expertly handle paediatric brain tumours and deliver the care our patients ultimately deserve.

Conclusion

These guidelines have been designed to assist physicians operating in settings with limited resources. They offer a practical framework drawn from extensive experience

and have the potential to bring about notable improvements in specific outcomes. The objective is to foster a greater emphasis on multidisciplinary care within low- and middle-income countries (LMICs), such as Pakistan, by providing a valuable roadmap for implementation

Disclaimer: None.

Conflict of Interest: None.

Funding Disclosure: None.

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