

Review Article

DIAGNOSTIC DELAY AND REDUCING THE DIAGNOSTIC INTERVAL IN CHILDREN WITH BRAIN TUMOR

Mossad Abdelhak Shaban*¹, Abdelbaset Taher Abdelhalim^{2,3}

¹Paediatric Department, International Islamic University of Malaysia (IIUM), Kuantan, Pahang, Malaysia.

²Pharmacology Department, Faculty of Medicine, Alazhar University, Cairo, Egypt.

³Pharmacology Department, Kulliyyah of Medicine & Health Sciences, Universiti Islam Antarabangsa Sultan Abdul Halim Mu'adzam Shah, 09300 Kuala Ketil, Kedah, Malaysia.

ARTICLE INFO

Corresponding author:
Dr. Mossad Abdelhak Shaban

Email address:
mossadshaban@iium.edu.my

Received:
May 2018
Accepted for publication:
June 2018

Keywords:

Diagnostic delay
Brain tumor in children
Post symptomatic diagnostic
interval

ABSTRACT

Brain tumor account for a quarter of all childhood cancers, affecting about 1 in 2400 United Kingdom (UK) children under the age of 16 annually, while brain and other nervous system cancer incidence per 100,000 population in Peninsular Malaysia for age 0-19 years was 84/100000. Death occurs either as a result of catastrophic presentations with raised intracranial pressure or as a result of tumor recurrence and resistance to further treatment. Five-year survival rates became over 70%, and the majority of these patients go on to be long-term survivors. Despite this, 60% of long-term survivors of childhood brain tumors are moderately or severely neurologically disabled. Delayed diagnosis of brain tumor among children is a concern around the globe and has been reported by parents, in the media, and in the courts. These reports can disturb public confidence in healthcare systems. This literature searches studied diagnostic delay and reducing the diagnostic interval in children with brain tumor, using online databases and a manual search. Main keywords used were diagnostic delay, brain tumor in children and post symptomatic diagnostic interval. In some studies post symptomatic diagnostic interval (PDI) was 28 weeks with a parental delay of 11.1 weeks and a doctor's delay of 16.9 weeks. We concluded many recommendations as programmes to raise public and professional awareness of the symptomatology of brain tumor, early referral, CT scan fast track. Along with many other recommendations were discussed in this article.

INTRODUCTION

Mortality and morbidity from cancer is worse in many countries, the reasons for this are multi-factorial, but diagnostic delays and consequent later stage diagnoses are likely to be major contributory factors [1]. Brain tumor account for a quarter of all childhood cancers, affecting about 1 in 2400 UK children under the age of 16 annually [2]. The incidence of brain and other nervous system cancer in Malaysia per 100,000 population in Peninsular Malaysia for age 0-19 years was 84/100000 in 2006 [3]. Primary malignant central nervous system tumors (CNS) are the second most common childhood malignancies, after leukaemia [4]. They are the most common paediatric solid organ tumor [5]. It is the leading cause of death from childhood cancer, surpassing the mortality rate of acute lymphoblastic leukaemia [6]. CT is used for initial workup, but MRI is superior and essential if CT finds abnormalities or inconclusive, MRI spectroscopy can be useful as elevated choline [7]. Although advances in surgical intervention, radiation therapy, and chemotherapy have improved the survival rates in children with central nervous system tumors, mortality

and morbidity associated with these disorders persists [8].

Survival

Five- and 10-year survival rates for children with central nervous system tumors are 73% and 70%, respectively. The likelihood of survival depends upon the type of tumor. Survival has improved, in part due to advances in diagnostic techniques and histological classification of tumours, improvement in neurosurgical and radiation oncology techniques, and the utilization of new single and combination chemotherapeutic agents. Despite advances in the care of children with CNS tumors, improvement in survival and durable remissions has been slower in patients with CNS tumors compared with other cancers, particularly leukemias and lymphomas [9].

Long term morbidity

Paediatric survivors with CNS tumors often have neurologic, cognitive, psychological, and endocrine complications that are due to damage from the tumor itself, its treatment (surgery, radiation, and/or chemotherapy), or subsequent secondary

malignancy. In the Childhood Cancer Survivor Study, 82 percent of the 2821 five-year survivors reported having at least one chronic medical condition. Compared with their siblings, survivors had an increased risk of developing a new endocrine condition, sensory deficit as hearing loss, and neurologic problem. Cranial radiation therapy was associated with an increased risk of subsequent malignancy and neurocognitive impairment [10].

Diagnostic delay and, diagnostic interval

Diagnosis of brain tumors in children is often delayed in relation to the presenting symptoms. In

some studies, Post symptomatic diagnostic interval was 28 weeks with a parental delay of 11.1 weeks and a doctor's delay of 16.9 weeks. Main clinical symptoms were headache (66.7%), vomiting (57.7%), vision (46.2%) and gait (41.6) disorders and fatigue (41.0%) followed by other neurological signs [11] (Figure 1). Another cohort study and meta-analysis of symptomatology and referral practice for childhood brain tumors, total diagnostic interval (TDI, time between first symptom onset and diagnosis) ranged widely from a day to 6.9 years, with a median of 3.3 months (14 wk) [12] (Figure 2).

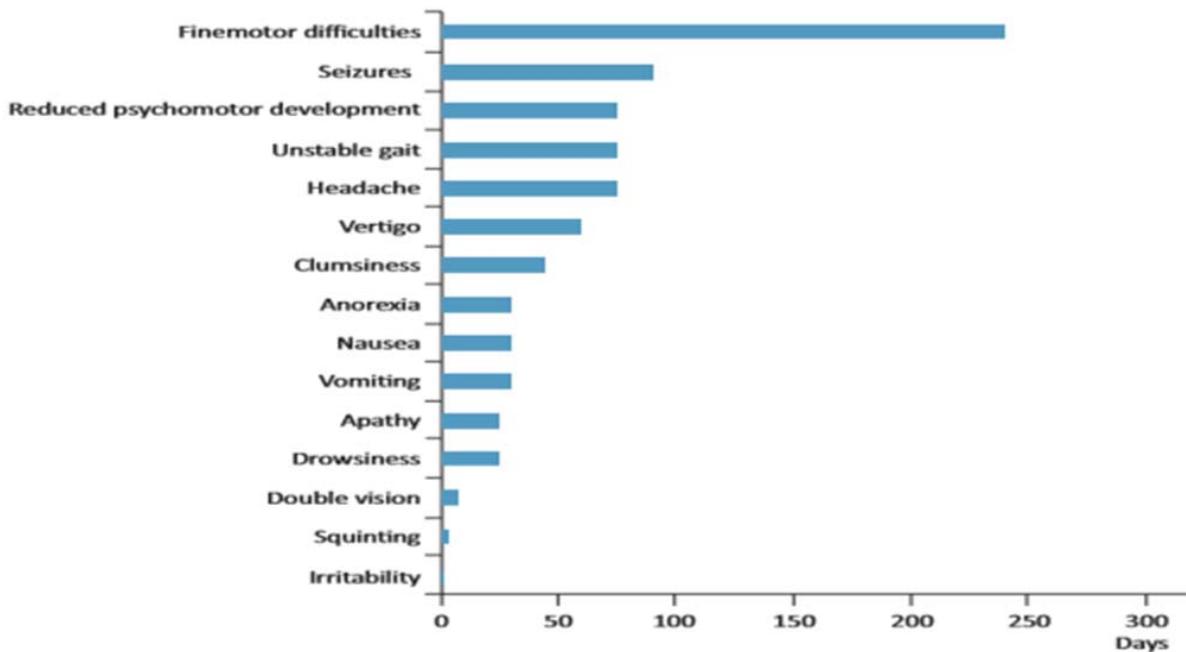


Figure 1: Key milestones and time intervals in the pathways from first symptom until start of treatment.

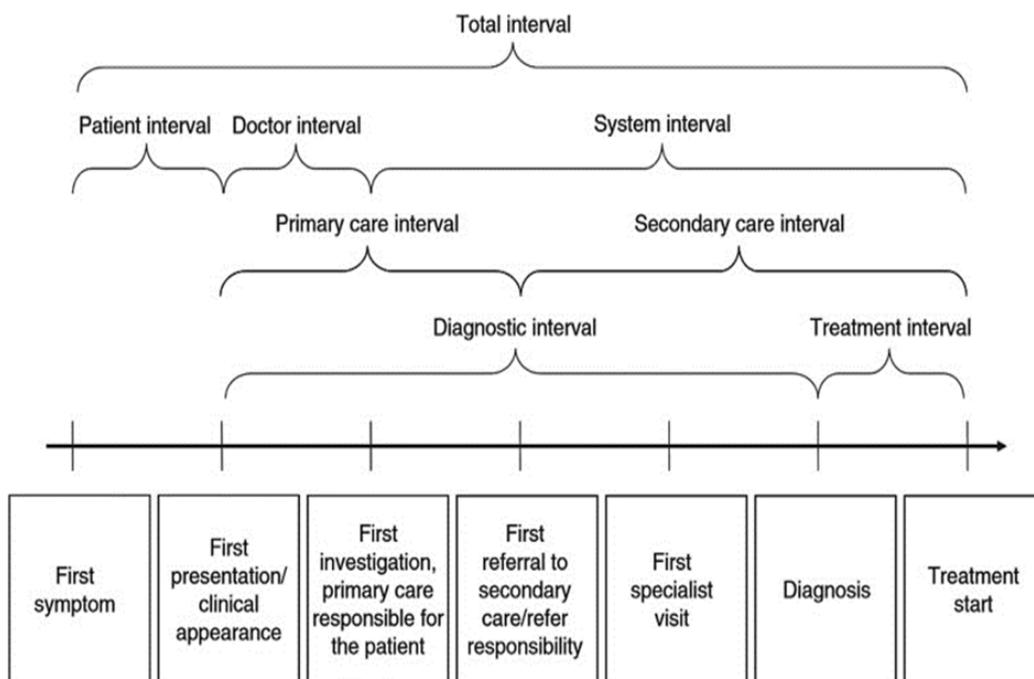


Figure 2: Relationship in median days between symptoms and pre-diagnostic symptomatic interval

Recommendations [7, 11-15]

- Community education (without making them panic).
- Identify that the red flag symptoms have been explored. However, they do not yield significant positive predictive values for individual symptoms that can be used for stratifying childhood patients in primary care.
- Be Cancer Alert Campaign. One of the example is a collaborative project between the University of Malaya, Queen's University Belfast and the National Cancer Society Malaysia.
- Using an awareness intervention (Designed awareness age-stratified symptom) as this offered the opportunity to change practice. The symptoms of brain tumor include persistent or recurrent headache, persistent or recurrent vomiting, balance or coordination problem, abnormal eye movement, or blurred or double vision, behavioural problems, fits or seizures, abnormal head position as wringing head or stiff neck. If a child has one of these symptoms consultation from a doctor is a must, but if two or more symptoms occurred, urgent referral is needed. The risk of excessive public alarm and the potential for swamping imaging facilities at the top of our risk assessment and designed our materials to prioritize reassurance. Materials to be distributed to health care professionals via conferences and seminars and to general practitioner surgeries, health organizations, and professional bodies by direct mail. Materials also distributed to the public through community champions (directly to local schools, nurseries, hospital waiting rooms, etc.), as well as via local authorities and other charities and commercial networks.
- Design an open access decision support website as Head Smart Website.
- Conferences and Education Outreach Events.
- Professional education and system track by reinforcing an on-going need for population-based surveillance and further etiologic studies. Guideline to Examinations and procedure to follow in children with suspected brain tumor and, linking the revised guideline to policies of childhood and cancer practice raised awareness about features of childhood cancers among paediatricians and were associated with reduction in total diagnostic interval. Conferences and specialised continuous medical education Outreach Events.
- Change in referral practice with early referral was most pronounced in the time from first medical contact to CNS imaging. Computed tomographic fast track. MRI protocols for imaging paediatric brain tumours: Further awareness of the revised protocol, improved access to the guidelines, and strict adherence to the protocols. Computed tomographic study of epilepsy in children as the primary diagnosis of a brain tumor, There were also formulated the practical recommendations

concerning carrying out of CT investigations in children with prolonged resistant epileptic syndromes.

- EEG, brain magnetic resonance imaging and tumor markers (CSF/EEG) for early detection of an evolving occult hypothalamic-stalk lesion in idiopathic central diabetes insipidus as Determination of CSF hCG at the first presentation may be useful, because an increased CSF level of hCG precedes MRI abnormalities.
- The development of paediatric neurosurgery subspecialty, How to create as Correlation of neurosurgical subspecialisations with good outcomes in children with malignant brain tumors.

CONCLUSION

Diagnosis of paediatric brain tumor is often delayed in relation to the presenting symptoms. The duration between first symptom and a cancer diagnosis is important because, if shortened, may lead to earlier stage diagnosis and improved cancer mortality and morbidity. Recent programs have sought to improve survival while decreasing neurologic sequels, design community awareness without making them panic as age-stratified symptom checklist, with instructions that one symptom required medical assessment and two required an urgent referral. So if parents report a combination of headache with other neurological abnormalities, a brain tumor should always be considered. Another pathway for professional and system track with revise of guidelines and policies, continuous medical education, CT fast track, MRI updated protocols, and other special recommendation as EEG and CSF analysis and their role in early diagnosis.

REFERENCES

1. McPhail S, Johnson S, Greenberg D, et al. Stage at diagnosis and early mortality from cancer in England. *Br J Cancer*.2015 Mar 31;112 Suppl 1:S108-15.
2. Cancer Research UK. Childhood cancer incidence statistics; 2012. cancerresearchuk.org/cancerinfo/cancerstats/childhoodcancer/incidence/. Accessed September2015.
3. Omar ZA, Ali ZM, Taming NS, .Malaysian cancer association , Brain and Other Nervous System Age specific Cancer Incidence per 100,000 population (CR) by sex, Peninsular Malaysia 2006.p 92.National Cancer , Ministry of Health Malaysia.
4. Kraft P. National integrated cancer pathways for children. National Board of Health, Denmark: Publ 2009/SUPL (1 May 2011)

5. Linabery AM, Ross JA. Trends in childhood cancer incidence in the U.S. (1992-2004). *Cancer*. 2008; 112(2):416.
6. Ostrom QT, de Blank PM, Kruchko C, et al. Alex's Lemonade Stand Foundation Infant and Childhood Primary Brain and Central Nervous System Tumors Diagnosed in the United States in 2007-2011. *Neuro Oncol* 2015; 16 Suppl 10:x1
7. Craig E¹, Connolly DJ, Griffiths PD, et al. MRI protocols for imaging paediatric brain tumours. *Clin Radiol*. 2012 Sep;67(9):829-32.
8. Ostrom QT, Gittleman H, Liao P, Rouse C, et al. Overview of the management of central nervous system tumors in children's statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2007-2011. *Neuro Oncol*. 2014;16 Suppl 4.
9. Alikhanov AA, Petrukhin AS, Mukhin Klu, et al. A computed tomographic study of epilepsy. *Russian*. PMID.1997;97(8):13-7.
10. Pollack L, Stewart S, Thompson T. Trends in childhood cancer mortality--United States. Centers for Disease Control and Prevention (CDC) 1990-2004. *MMWR Morb Mortal Wkly Rep* 2007; 56:1257.
11. Klitbo D, Nielsen R, Illum NO, et al. Symptoms and time to diagnosis in children with brain tumours *Dan Med Bul* 2011 Jul;58(7):A4285.
12. Trusler J, Evans A, J, A new clinical guideline from the Royal College of Paediatrics and Child Health with a national awareness campaign accelerates brain tumor diagnosis in UK children. *Neuro Oncol*. 2016 Mar 18(3):445-54.
13. Tao Y, Lian D, Hui-juan Z, et al. Value of brain magnetic resonance imaging and tumor markers (CSF/EEG) in the diagnosis and treatment of intracranial germinoma in children. 2011 Apr;33(2):111-5. doi: 10.3881.
14. Hirsch JF. The development of pediatric neurosurgery in Paris. How to create something out of nothing: reflexions on the methodology. *Childs Nerv Syst*. 1997 Aug-Sep;13(8-9):465-7
15. Albright AL, Sposto R, Holmes E, et al. Correlation of neurosurgical subspecialisations with outcomes in children with malignant brain tumors. *Neurosurgery* 2000; 47:879.