

UNDERSTANDING LATE DIAGNOSIS IN PEDIATRIC NEURO- ONCOLOGY: AN ANALYSES OF ASPECTS AND IMPACTS

Marcela Yasmin Leroy

Faculdade de Ciências da Saúde de Barretos
Barretos - São Paulo
<http://lattes.cnpq.br/5960204568521849>

Luiz Fernando Lopes

Hospital de Câncer Infantojuvenil de
Barretos
Barretos - São Paulo
<http://lattes.cnpq.br/2276295670840482>

Raniela Ferreira Faria

Hospital de Câncer Infantojuvenil de
Barretos
Barretos - São Paulo
<http://lattes.cnpq.br/6658213096301477>

Thaissa Maria Veiga Faria

Hospital de Câncer Infantojuvenil de
Barretos
Barretos - São Paulo
<http://lattes.cnpq.br/2485522730163998>

Denise Leonardi Queiroz Prado

Centro Universitário Claretiano de Rio Claro
Rio Claro - São Paulo
<http://lattes.cnpq.br/8468111599377735>

Wellington Yoshio Hirai

Fundação Pio XII, Barretos - São Paulo,
<http://lattes.cnpq.br/9381931562832257>

Bruna Minniti Mançano

Hospital de Câncer Infantojuvenil de
Barretos
Barretos - São Paulo
<http://lattes.cnpq.br/2915533388906468>

All content in this magazine is licensed under a Creative Commons Attribution License. Attribution-Non-Commercial-Non-Derivatives 4.0 International (CC BY-NC-ND 4.0).



Abstract: Introduction: Central nervous system (CNS) tumors comprise 20% of all childhood cancers, being the second most frequent group of tumors. Furthermore, they constitute the major cause of morbidity and mortality among childhood cancers, and approximately 60% of surviving patients have sequelae due to both neoplastic growth and treatment. Therefore, late diagnosis negatively influences prognosis, which is evidenced by the inverse relationship between time to diagnosis and survival. Objective: To analyze the pilgrimage of pediatric patients with CNS tumors to the reference center. Method: This is a retrospective-prospective cohort study, with analysis of medical records and application of a questionnaire. Results: The mean age of the patients was 8 years. The mean time to diagnosis was 381.12 days. The most popular medical specialties for the first consultation were pediatrics, internal medicine and ophthalmology. Clinical medicine was the specialty associated with the shortest time to diagnosis. The most frequent first signs and symptoms were neurological symptoms, with a frequency of 72%, which were associated with a long pilgrimage time. Conclusion: CNS tumors in pediatric patients require a high level of suspicion from health professionals. The patients' pilgrimage time to Barretos was mainly due to failures in the health system. The professionals who most perpetuate early diagnosis are specialists in the basic area.

Keywords: Late diagnosis; pediatric oncology; central nervous system; Signs and symptoms; pilgrimage.

INTRODUCTION

Central nervous system (CNS) tumors are, by definition, neoplasms that primarily affect the brain and spinal cord. They are the second most common group of tumors in childhood, being the most frequent group of solid tumors and corresponding to about

20% of neoplasms in this age group. In Brazil, the incidence is 1500 to 2000 new cases/year (INCA, 2016). The most common tumor types are pilocytic astrocytoma, medulloblastoma and ependymoma.

CNS neoplasms are the major cause of morbidity and mortality among childhood cancers ("Version for healthcare professionals", [sd]) and approximately two thirds of surviving patients have significant sequelae. (SHANMUGAVADIVEL et al., 2020). Damage to intelligence, information processing speed and executive function are the main impairments, followed by impairments in memory and attention. (KRULL et al., 2018). These consequences are due both to tumor growth and the aggressiveness of the treatment.

The accumulation of sequelae due to neoplastic growth is directly related to the time to diagnosis. Despite being the main cause of morbidity and mortality among pediatric neoplasms, the diagnosis of CNS tumors in these patients is a challenge, also due to the diversity and irregularity of symptoms.

There is a set of the most common signs and symptoms (headache, vomiting upon awakening, increased intracranial pressure, cranial nerve paralysis, lack of motor coordination, visual deficits, endocrine changes and seizures), however, they tend to vary greatly according to the patient's age, tumor type and location. For example, more central tumors present as symptoms of headache, strabismus and abnormal eye movements, while supratentorial tumors manifest with papilledema, increased intracranial pressure and seizures. (SHANMUGAVADIVEL et al., 2020).

Thus, the clinical diagnosis of the patient becomes more difficult, especially when the physician does not have extensive experience with CNS tumors. Incidentally, the average number of consultations with a health

professional between the onset of symptoms and diagnosis varies between 2.4 and 3.4 visits. Furthermore, a British article showed that the time to diagnosis is also influenced by the patient's age at the time of onset of symptoms, with adolescents (12 to 18 years old) presenting a longer period until diagnosis. (SHANMUGAVADIVEL et al., 2020).

As a good prognosis is related to the patient's age, the extent of the neurological lesions and the tumor location, it is logical to infer that late diagnosis negatively influences the prognosis, which is evidenced by the inverse relationship between the time for diagnosis and the survival. (SHANMUGAVADIVEL et al., 2020).

Therefore, the present study aims to investigate the time taken for the diagnosis of pediatric patients with tumors of the central nervous system at the Hospital Infantojuvenil de Barretos and the factors that influence the delay in diagnosis.

MATERIALS AND METHODS

STUDY DESIGN

This is a retrospective and prospective cohort study. Data were collected at the Children's and Youth Cancer Hospital in Barretos, using a data collection form and analysis of medical records. The variables used were: age; time until the perception of the first sign or symptom; time between the perception of the first sign or symptom and the first assistance; time between the first assistance and arrival at the reference center; first sign or symptom that led to seeking medical attention; specialty of the first doctor; number of professionals consulted after the first consultation. The study is part of a larger scientific project entitled "Late diagnosis in pediatric oncology".

STUDY POPULATION

This study brings together data from 216 patients selected for convenience. Exclusion criteria are: being over eighteen years of age at diagnosis; foreign nationality.

STATISTICAL ANALYSIS

Initially, a descriptive analysis of the data was carried out, with the quantitative variables summarized through the mean, median, standard deviation and quartiles. Qualitative variables were summarized through absolute and/or relative frequency. In order to verify the association between the time (days) between the appearance of the first signs and symptoms until the diagnosis of the neoplasm with the socioeconomic factors, the T tests (or Man-Whitney) were used in order to compare the mean time between the different categories of these factors. If the factor has more than two categories, we use the ANOVA technique in order to carry out the same verification and, when such a difference between some of these categories is identified, we use the Bonferroni technique to make multiple comparisons between them. In order to verify the influence of clinical, sociodemographic factors and the times covered (dichotomized after searching the literature), we will use the Log-rank test. To carry out the aforementioned tests, we used a significance level of 5% and the analyzes were performed using the SPSS v21.0 software.

RESULTS

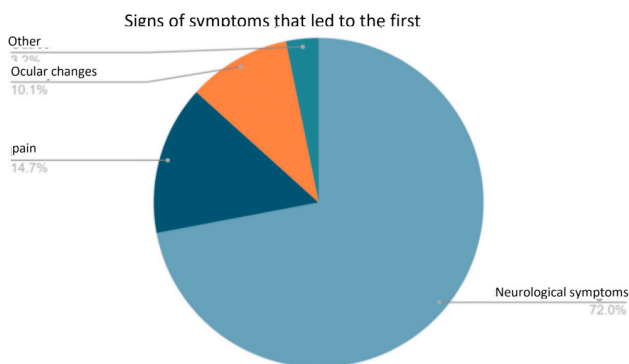
A total of 216 pediatric patients with CNS tumors treated at the Children's Cancer Hospital were included in the study. The mean age of the patients was 8 years old, with a bimodal peak of incidence at 3 and 10 years old.

The time until the diagnosis, or pilgrimage time, was subdivided into three categories: time for the perception of the first sign or symptom, time between the perception of the

first sign or symptom until the first medical assistance and the time between the first medical assistance and arrival at the reference center.

The average time that parents or guardians took to notice the child's first sign or symptom was 48 days. The average time between perception and first medical care was 29.8 days, while the mean time between first medical care and arrival at the referral center was 313.87 days. Thus, the average obtained for the peregrination time of pediatric patients with CNS tumors was 381.12 days. The medical specialties most frequently sought for the first consultation were pediatrics, internal medicine and ophthalmology, with a frequency of 45.8%, 27.1% and 13.6%, respectively. The mean age of patients seen by a pediatrician was 4 years, while the mean age of patients who first saw a general practitioner or an ophthalmologist was 10 years. Internal medicine was also the medical specialty associated with the shortest time to diagnosis, with an average of 223.5 days and a median of 109 days.

The most frequently presented signs and symptoms were neurological symptoms, with a frequency of 72%. The average age of patients who presented these symptoms was 8 years, and neurological symptoms were associated with a longer peregrination time, with an average of 436.39 days.



Ocular alterations, more presented by patients with an average of 7 years, were

related to an average of 318.68 days to arrive in Barretos. Consumptive symptoms, such as pain, fever, paleness and weakness, and weight loss, were also associated with a longer time to diagnosis, with an average wandering time ranging from 251.33 days (weight loss) to 360 days (paleness and weakness).

Interestingly, gastrointestinal alterations had a shorter average time, with 143.82 days.

Finally, while some patients were referred to the Children and Adolescent Cancer Hospital of Barretos without having to actively look for any other professional after the first consultation, others had to go through more than 30 consultations to reach the referral center. However, this showed no relationship with the patient's age.

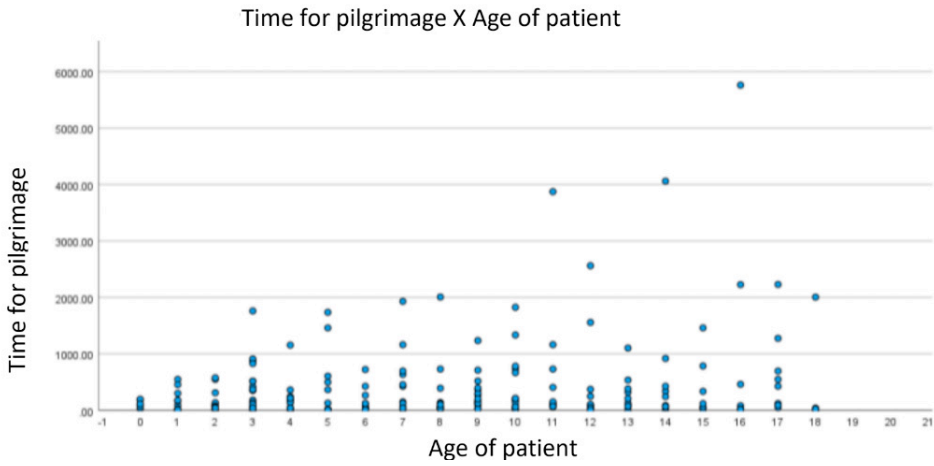
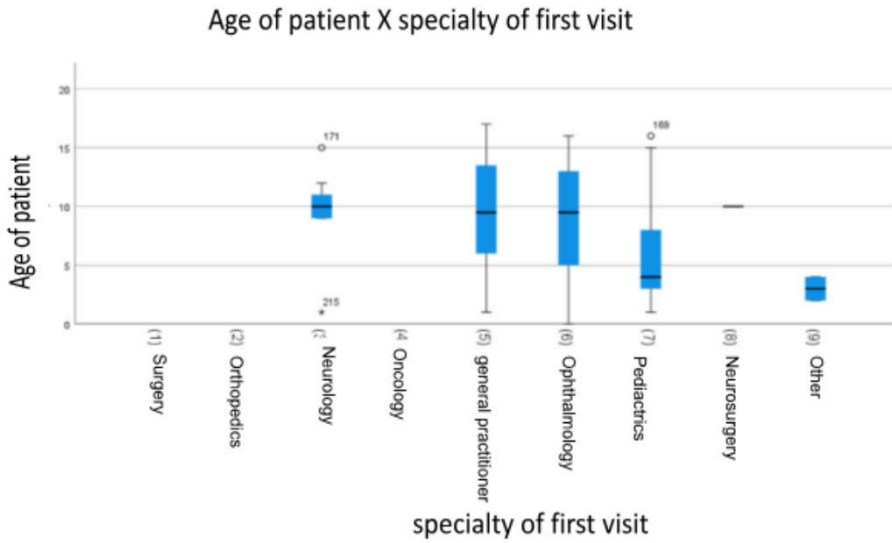
DISCUSSION

Initially, despite having a mean patient age of eight years, the bimodal peak of incidence actually shows the most frequently encountered patient profiles, which agrees with the incidence distribution observed in the most common CNS malignancy in childhood, medulloblastoma. (MILLARD; DE BRAGANCA, 2016).

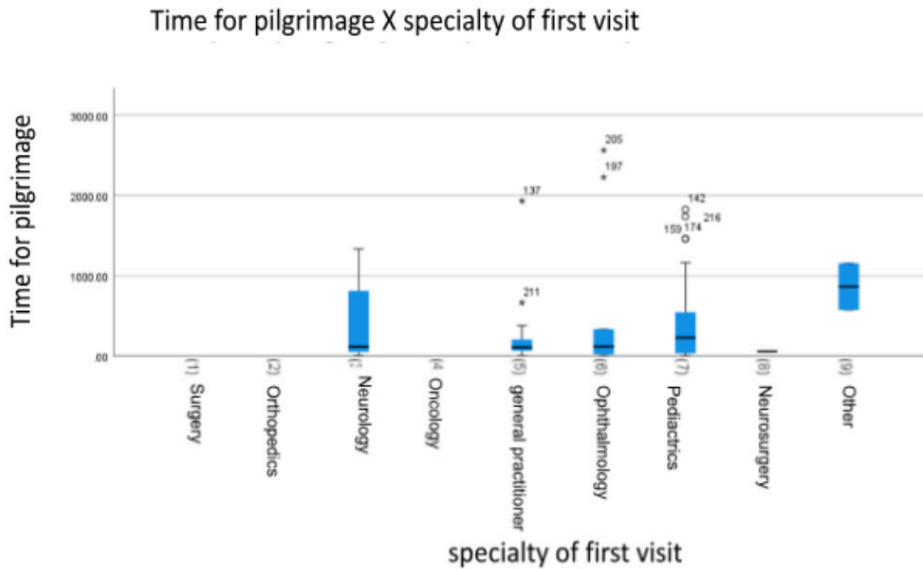
With regard to the first sign or symptom presented by the patient, the fact that the consumption symptoms are related to a longer journey time can be justified by the non-specificity of these symptoms, which does not lead to a high level of suspicion for the health professional. on CNS tumours.

However, patients can and often will experience only nonspecific symptoms. Accordingly, 28% of patients in an analysis cited in a literature review article had neither headaches nor projectile vomiting. (GOLDMAN; CHENG; COCHRANE, 2017).

Worryingly, neurological symptoms, which are more associated with CNS tumors and among which the most common were headache and projectile vomiting, were also



Graph 1: graph shows that there is no correlation between the time of pilgrimage and the age of the patient.



associated with a longer peregrination time. This highlights how, sometimes, even in the face of classic signs and symptoms, the professional's lack of suspicion and knowledge affects the patient's diagnosis.

It is essential that the rarity of a pathology does not preclude its consideration as a differential diagnosis.

The average peregrination time was higher than that found in developed countries, as exemplified by the article "Accelerating diagnosis for childhood brain tumors: an analysis of the HeadSmart UK population data", which shows that the tumor type that presented the longest total time for diagnosis had an average of 15.1 weeks. (SHANMUGAVADIVEL et al., 2020). Even, in disagreement with this article, the present study did not show a correlation between the patient's age and the time spent on the pilgrimage, while the British article shows a clear relationship between the patient's age and the total time for diagnosis, with a time average of six weeks for patients aged less than 5 years and an average time of 12.3 weeks for patients aged between 12 and 18 years.

Still on the peregrination time, it is interesting to note that, in its subdivisions, the biggest contributor to the delay in diagnosis was the time between the first medical care and arrival at the reference center. This reinforces that late diagnosis is due more to medical unpreparedness (difficulties in recognizing signs and symptoms, delay in referring to more complex health services, reluctance to request imaging tests, among other reasons) than to the delay of the patient and his family to seek a health professional.

Regarding the first medical consultation, it is interesting to note that the oncologist is not among the professionals sought for a first consultation. Normally, this specialist receives patients when they arrive at the reference center, but they are unlikely to be the ones to

make the first suspicion of a neoplasm.

Especially because, mainly in smaller cities and socioeconomically less favored regions, there is a shortage of highly complex medical professionals, since these, in general in Brazil, tend to accumulate in the South and Southeast regions, where health care programs also accumulate. residence (PÓVOA; ANDRADE, 2006).

In fact, the specialty that most quickly led the patient to the diagnosis was internal medicine, a specialty typically found in primary care units and emergency rooms. Except for neurosurgery, which, despite the short journey time, was the first specialty sought by only 1 of the 216 patients.

This demonstrates how important it is that all medical specialties, especially those that are part of the basic area of medicine, composed of internal medicine, pediatrics, gynecology and obstetrics and general surgery (LIMA et al., 2021), have the ability to recognize signs and symptoms suggestive of a central nervous system tumor in children.

CONCLUSION

As much as the symptomatological presentation of CNS tumors in pediatric patients has some recurrent characteristics, such as headache and jet vomiting, in most cases, it requires a high level of suspicion from the health professional in the face of nonspecific symptoms and a more comprehensive knowledge about the possible symptoms according to tumor location, which often delays diagnosis.

It is possible to observe that the patients' long pilgrimage to Barretos was mainly due to failures in the health system. It is also concluded that the professionals who most perpetuate early diagnosis are specialists in the basic area.

Therefore, it is extremely important that all medical specialties have knowledge about and

remember central nervous system neoplasms when treating their patients.

CONSIDERATIONS

The present study was largely developed during the Covid-19 pandemic, which may have moderately altered its results.

CONFLICTS OF INTEREST

There are no conflicts of interest present in the study.

REFERENCES

- GOLDMAN, R. D.; CHENG, S.; COCHRANE, D. D. **Improving diagnosis of pediatric central nervous system tumours: aiming for early detection.** CMAJ : Canadian Medical Association Journal, v. 189, n. 12, p. E459–E463, 27 mar. 2017.
- KRULL, K. R. et al. **Neurocognitive Outcomes and Interventions in Long-Term Survivors of Childhood Cancer.** Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology, v. 36, n. 21, p. 2181–2189, 20 jul. 2018.
- LIMA, E. J. DA F. et al. **Perfil e trajetória dos egressos de programas de residência das áreas básicas: um corte transversal.** Revista Brasileira de Educação Médica, v. 45, p. e039, 15 fev. 2021.
- MILLARD, N. E.; DE BRAGANCA, K. C. **Medulloblastoma.** Journal of child neurology, v. 31, n. 12, p. 1341–1353, out. 2016.
- PATEL, V.; MCNINCH, N. L.; RUSH, S. **Diagnostic delay and morbidity of central nervous system tumors in children and young adults: a pediatric hospital experience.** Journal of Neuro-Oncology, v. 143, n. 2, p. 297–304, jun. 2019.
- SHANMUGAVADIVEL, D. et al. **Accelerating diagnosis for childhood brain tumours: an analysis of the HeadSmart UK population data.** Archives of Disease in Childhood, v. 105, n. 4, p. 355–362, 1 abr. 2020.
- Versão para profissionais de saúde.** Disponível em: <<https://www.gov.br/inca/pt-br/assuntos/cancer/tipos/infantojuvenil/especificos/tumores-do-sistema-nervoso-central/versao-para-profissionais-de-saude>>. Acesso em: 11 ago. 2023.