

ORIGINAL

Clinical and epidemiological characteristics of pediatric cancer presentation: A retrospective study in an Emergency Department

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Abstract

Introduction: The low incidence of cancer in children and nonspecific symptoms at onset may **delay early diagnosis and lead to a worse prognosis.**

AIM: To determine the **incidence of cancer presentation** in a Pediatric Emergency Department (PED) and to analyze **the frequency of different cancer types**, as well as to describe the clinical and epidemiological characteristics of the patients and to **identify** potential factors leading to diagnostic delay.

Methodology: This descriptive-observational retrospective study included patients younger than 18 years old with a suspected cancer diagnosis in the PED of a tertiary hospital between 2019 and 2020.

Results: Out of 180,124 admissions to the PED during this time frame, 175 cases of cancer presentation were found. The median age at onset was 5.5 years (IQR: 2.5–13.5). Solid tumors were diagnosed in 103 cases (58.9%), including 48 (27.4%) involving the central nervous system (CNS). Hematologic malignancies accounted for the remaining 72 cases (41.1%), of which 48 (27.4%) were leukemia. The median time to diagnosis (TD) was 50.5 days in adolescents, compared to 18.28 days in infants and 20.5 days in toddlers and children. The median TD was 19 days for hematologic malignancies and 39 days for solid tumors. Forty-one patients (23.4%) presented as oncological emergencies.

Conclusions: Cancer presentations accounted for 0.1% of admissions to the PED. CNS tumors and leukemia were the most common types of cancer observed. Onset during adolescence and the presence of solid tumors were associated with a longer time to diagnosis (TD). Additionally, around **a quarter of these cases** presented as oncological emergencies.

CARACTERÍSTICAS CLÍNICO-EPIDEMIOLÓGICAS DE PACIENTES CON DEBUT ONCOLÓGICO. ESTUDIO RETROSPECTIVO EN UN SERVICIO DE URGENCIAS PEDIÁTRICAS

Resumen

Introducción: La baja incidencia de cáncer en la infancia y la sintomatología inespecífica al debut **pueden dificultar un diagnóstico precoz y condicionar un peor pronóstico.**

Objetivos: Conocer la **incidencia de debut oncológico en un Servicio de Urgencias Pediátricas (SUP) y la frecuencia de los distintos tipos de cáncer**, describir las caracte-

ísticas clínico-epidemiológicas de los pacientes y **describir** factores relacionados con el retraso diagnóstico.

Metodología: *Estudio descriptivo-observacional retrospectivo. Se incluyeron pacientes menores de 18 años con sospecha diagnóstica de debut oncológico en el SUP de un hospital de tercer nivel entre los años 2019 y 2020.*

Resultados: *Se incluyeron 175 debuts oncológicos de un total de 180.124 visitas a Urgencias en dicho periodo de tiempo. La mediana de edad al debut fue de 5,5 años (p25-75: 2,5-13,5). Se diagnosticó tumor sólido en 103 (58,9%) casos (48; 27,4% del sistema nervioso central [SNC]) y enfermedad oncohematológica en los 72 (41,1%) restantes (48; 27,4% leucemias). La mediana de tiempo al diagnóstico (TD) fue de 50,5 días en adolescentes vs. 18, 28 y 20,5 en lactantes, preescolares y escolares; de 19 días en enfermedad oncohematológica vs. 39 en tumores sólidos. En 41 (23,4%) pacientes el debut fue en forma de emergencia oncológica.*

Conclusiones: *Los debuts oncológicos representaron el 0,1% de las visitas en el SUP. Los tumores del SNC y las leucemias fueron los tipos de cáncer más frecuentes. El diagnóstico de tumor sólido y el debut en la adolescencia fueron factores relacionados con un mayor TD. Aproximadamente **un cuarto de los debuts** se presentó como emergencia oncológica.*

INTRODUCTION

Survival of pediatric patients with cancer has increased significantly in recent years. According to data from the National Childhood Cancer Registry (NCCR) of the National Cancer Institute of the United States, the relative 5-year survival rate in the population under 20 years of age was 86.5% between 2013 and 2019⁽¹⁾. However, cancer remains the leading cause of mortality from non-traumatic causes and is one of the diseases with the highest morbidity in childhood⁽²⁾.

Diagnosis can be complex and delayed due to nonspecific or seemingly insignificant symptoms at the time of diagnosis^(2,3). The literature identifies various factors associated with diagnostic delay, including the type and aggressiveness of the cancer, the age of the patient, and access to health services (related to the sociocultural environment). A late diagnosis of cancer can negatively impact the patient's prognosis, leading to increased tumor burden, advanced staging, or greater complexity in the therapeutic process⁽³⁾.

It is therefore crucial to establish early diagnostic suspicion and perform appropriate complementary examinations. This requires adequate training for general pediatricians to recognize the main signs and symptoms indicative of an oncological process and to refer patients to a specialized center⁽²⁻⁶⁾. Improving knowledge of the clinical profiles of the most common tumor types and their presentations in the Pediatric Emergency Department (PED), in coordination with the Department of Pediatric Hematology and Oncology, will facilitate earlier diagnosis and improve morbidity and mortality outcomes⁽²⁾.

While extensive research exists in adult medicine due to the increasing incidence of the disease, studies focused on newly diagnosed pediatric cancer are less common. The objectives of this study were: first, to determine the incidence of cancer presentation in the PED of a tertiary hospital, as well as the frequency of different cancer types diagnosed; second, to describe the clinical and epidemiological characteristics of patients with cancer presentation in the PED studied; and finally, to identify factors related to the time to diagnosis (TD) of cancer.

MATERIAL AND METHODS

A retrospective, descriptive-observational study was conducted, following a previous study that assessed the impact of the SARS-CoV-2 pandemic on the detection of cancer cases in a PED⁽⁷⁾. The study took place in the PED of a tertiary maternal and children's hospital with a mean of 120,000 visits per year. This hospital is a referral center for pediatric hematologic and oncologic disorders, with an annual mean of 135 new cancer diagnoses in recent years.

Using the tumor database of the Department of Pediatric Hematology and Oncology at the hospital, cases from January 1, 2019, to December 31, 2020, were selected. The study included patients under 18 years of age who had a diagnostic suspicion of cancer established in the PED. Patients with an initial suspicion of cancer that was ultimately ruled out, those with a history of cancer who were diagnosed with relapse or disease progression, and those referred from another center with a confirmed diagnosis of cancer were excluded.

Patient data were collected from computerized clinical records and the emergency department reports. The data collected included: sociodemographic variables; symptoms at onset (retrospectively categorized); duration of symptoms and previous medical care; information from the emergency department (complementary tests and patient disposition at discharge); characteristics of the diagnosed or suspected cancer (type, location, and whether it presented as an oncological emergency); and the time lag from symptom onset to final diagnosis.

In this study, an 'oncologic emergency' was defined as any acute event in a cancer patient that, directly or indirectly related to the tumor, poses a life-threatening risk⁽⁸⁻¹²⁾. 'Time to diagnosis' (TD) was defined as the total time from the onset of clinical symptoms to the establishment of suspicion in the PED, plus the time from suspicion in the PED to diagnostic confirmation^(2,13,14).

The collected data were stored and processed using a Microsoft Access® relational database. Quantitative and categorical variables were tabulated and analyzed with SPSS® 27.0 statistical software. The Kolmogorov-Smirnov test was used

TABLE 1. Symptoms at debut in the PED (n= 170)

CLINICAL FEATURES*	n (%)	Solid tumors n= 98	Hematologic malignancy n= 72	p
Fever	45 (26.5)	14 (14.3)	31 (43.1)	< 0.001
Neurological symptoms	53 (31.2)	49 (50)	4 (5.6)	< 0.001
Headache	33 (62.3)	29 (59.2)	4 (100)	0.285
Neurological focus	30 (56.6)	29 (59.2)	1 (25)	0.305
Gait disturbances	12 (22.6)	11 (22.4)	1 (25)	1.000
Consciousness impairment	2 (3.8)	2 (4.1)	0 (0)	1.000
Gastrointestinal symptoms	67 (39.4)	49 (50)	18 (25)	< 0.001
Dysphagia	3 (4.5)	1 (2)	2 (11.1)	0.174
Vomiting	40 (59.7)	30 (61.2)	10 (55.6)	0.675
Abdominal pain	25 (37.3)	16 (32.7)	9 (50)	0.193
Abdominal distension	10 (14.9)	8 (16.3)	2 (11.1)	0.717
Altered bowel movement	8 (11.9)	7 (14.3)	1 (5.6)	0.433
Respiratory symptoms	14 (8.2)	2 (2.8)	12 (16.7)	< 0.001
Dyspnea	7 (50)	0 (0)	7 (58.3)	0.462
Cough	10 (71.4)	2 (100)	8 (66.7)	1.000
Cardiovascular symptoms	1 (0.6)	0 (0)	1 (1.4)	0.424
Bone-joint symptoms	32 (18.8)	16 (16.3)	16 (22.2)	0.331
Nephrological symptoms	6 (3.5)	5 (5.1)	1 (1.4)	0.244
Skin symptoms	18 (10.6)	4 (4.1)	14 (19.4)	0.001
Ophthalmological symptoms	18 (10.6)	18 (18.4)	0 (0)	< 0.001
Cachexia	58 (34.1)	13 (13.3)	45 (62.5)	< 0.001
Hemorrhagic symptoms	20 (11.8)	2 (2)	18 (25)	< 0.001
Lymphadenopathy	29 (17.1)	1 (1)	28 (38.9)	< 0.001
Other symptoms	24 (14.1)	16 (16.3)	8 (11.1)	0.335

*Of 170 patients with symptoms, 118 (69.4%) presented with more than one type of symptom.

to assess data distribution. To compare quantitative data, the Student's t-test, Mann-Whitney U test, and Kruskal-Wallis test were applied. For qualitative data, the Chi-square test, contingency tables, and Fisher's exact test were used. A p-value of less than 0.05 was considered statistically significant.

The study was approved by the Ethics Committee of the study center (PIC-83-21). Due to the retrospective observational design, informed consent from patients was not required. Data obtained were pseudonymized.

There were no conflicts of interest.

RESULTS

During the study period, there were 180,124 visits to the PED, of which 175 were cases of newly diagnosed cancer: 103 (58.9%) were solid tumors, and 72 (41.1%) were hematologic malignancies. The median age at diagnosis was 5.5 years (IQR: 2.5–13.5 years), and 92 patients (52.6%) were male. Of the 175 patients, 170 (97.1%) presented with clinical symptoms in the PED, while the remaining 5 patients (2.9%)

were asymptomatic, with cancer suspicion occurring incidentally during routine check-ups by their regular pediatrician. Among those with symptoms, 58 patients (34.1%) had cachexia, 45 (26.5%) fever, and 40 (23.5%) vomiting. Table 1 shows symptoms at presentation for the included patients, categorized by tumor type.

Among the 175 patients, 41 (23.4%) presented with oncologic emergencies at presentation, including 20 (11.4%) with metabolic emergencies (hyperleukocytosis in 8 and tumor lysis syndrome in 12), 20 (11.4%) with mechanical emergencies (spinal cord compression in 1, intussusception in 1, superior vena cava syndrome in 3, and increased intracranial pressure in 15), and one (0.6%) with an infectious emergency (febrile neutropenia).

Overall, 134 patients (76.6%) had previously visited the PED and/or primary care for the same condition, with a median of one visit (range: 0–8 visits). The median time from the onset of clinical symptoms to the initial suspicion of cancer in the PED was 19 days (IQR: 7–60 days).

Table 2 shows the distribution of cancer cases by their physical location, and Table 3 lists the specific diagnoses. A

TABLE 2. Tumor location at debut (n= 175)

Location	n (%)
Blood	69 (39.4)
Central nervous system	48 (27.4)
Abdominal	28 (16)
Musculoskeletal	18 (10.3)
Genitourinary	8 (4.6)
Ear, nose, and throat	3 (1.7)
Eye	1 (0.6)

total of 150 patients (85.7%) were admitted to the hospital, with 32 of them (21.3%) being admitted to the Pediatric Intensive Care Unit (PICU). The remaining 25 patients (14.3%) were referred to oncology outpatient clinics for further diagnosis and treatment.

The median time from suspicion in the PED to diagnostic confirmation was 6 days (IQR: 2–14 days), and the median TD was 31 days (IQR: 14–66 days). A longer TD was observed in adolescent patients and in patients diagnosed with solid tumors, particularly those located in the central nervous system (CNS). In Table 4 the potential factors related to TD are analyzed.

TABLE 3. Specific diagnoses according to the International Classification of Childhood Cancer Third edition (ICCC-3) (n= 175).

Diagnostic group and tumor type	n (%)
I. Leukemias, myeloproliferative and myelodysplastic diseases	55 (31.4)
Leukemias	48 (87.3)
<i>Lymphoid leukemias</i>	40 (83.3)
<i>Myeloid leukemias</i>	8 (16.7)
Histiocytosis	6 (10.9)
Myelodysplastic syndrome	1 (1.8)
II. Lymphomas and reticuloendothelial neoplasms	23 (13.1)
Hodgkin lymphoma	10 (43.5)
Non-Hodgkin lymphoma (except Burkitt lymphoma)	5 (21.7)
Burkitt lymphoma	7 (30.4)
Juvenile nasopharyngeal angiofibroma	1 (4.3)
III. Central nervous system (CNS) tumors and intracranial and intraspinal neoplasms	45 (25.7)
Ependymomas and choroid plexus tumors	5 (11.1)
Astrocytomas	14 (31.1)
Intracranial and intraspinal embryonal tumors	10 (22.2)
<i>Medulloblastoma</i>	6 (60)
Other gliomas*	13 (28.9)
Other intracranial and intraspinal neoplasms**	3 (6.7)
IV. Neuroblastoma and other peripheral nervous system (PNS) tumors	7 (4)
V. Retinoblastoma	1 (0.6)
VI. Renal tumors	6 (3.4)
VII. Hepatic tumors	5 (2.9)
VIII. Malignant bone tumors	8 (4.6)
IX. Soft tissue and other extrasosseous sarcomas	10 (5.7)
X. Germ cell tumors, trophoblastic tumors and neoplasms of gonads	10 (5.7)
Intracranial and intraspinal germ cell tumors	2 (20)
Extracranial and extraspinal germ cell tumors	2 (20)
Gonadal germ cell tumors	6 (60)
XI. Other malignant epithelial neoplasms and malignant melanomas	3 (1.7)
XII. Other and unspecified malignant neoplasms	2 (1.1)

*Other gliomas: diffuse intrinsic pontine glioma (7), gliomatosis cerebri (1), desmoplastic ganglioglioma (1), tectal glioma (1), thalamic glioma (1), low-grade glial tumor (2). **Other intracranial and intraspinal neoplasms: cerebellar hemangioblastoma (1), craniopharyngioma (1), meningioma (1).

TABLE 4. Factors related to time to diagnosis (n= 175).

FACTOR	n (%)	Median TD* (IQR)	p
Age			0.002
Infant (0-2 years)	22 (12.6)	18 (8-39)	
Preschool (2-6 years)	66 (37.7)	28 (15-61)	
School-age (6-12 years)	37 (21.1)	20.5 (11-63)	
Adolescent (12-18 years)	50 (28.6)	50.5 (22-85)	
Sex			0.972
Male	92 (52.6)	31 (16-61)	
Female	83 (47.4)	31 (13-70)	
Tumor type			< 0.001
Hematologic malignancies	72 (41.2)	19 (11-47)	
Solid tumor	103 (58.8)	39 (19-72)	
Location			< 0.001
Blood	69 (39.4)	19 (11-46)	
CNS	48 (27.4)	57 (24-124)	
Abdominal	28 (16)	18 (12-31)	
Musculoskeletal	18 (10.3)	48 (38-83)	
Other**	12 (6.9)	44 (23-66)	
Previous consultations			0.078
Yes	134 (76.6)	31 (16-63)	
No	39 (22.4)	22 (11-41)	

TD: time to diagnosis; CNS: central nervous system. *TD values are expressed in days. **Genitourinary location and location in the ear, nose, and throat and eye are included.

DISCUSSION

In the PED of the study center, a mean of one case of cancer presentation was detected every four days. This prevalence, approximately 0.1% of all PED visits, is similar to that reported by Jawaid et al.⁽¹²⁾, but higher than in other PEDs⁽¹⁵⁻¹⁷⁾. These differences may be related to the sociodemographic characteristics of the populations studied and the specific characteristics of the centers where the studies were conducted. The high number of cases with newly diagnosed cancer in our study may be explained by the fact that ours is a referral center for pediatric oncology. In fact, two-thirds of the patients were referred with a suspected diagnosis of cancer by other pediatricians.

In this study, two-thirds of the patients were diagnosed with leukemia, CNS tumors, or lymphomas, which is consistent with findings reported in the literature⁽¹⁵⁾. Statistically significant differences in symptoms were observed based on tumor type. Patients with solid tumors most frequently had neurological, gastrointestinal, or ophthalmological symptoms at the time of PED consultation. In contrast, those with hematologic malignancies most commonly presented with fever, cachexia, skin symptoms, hemorrhagic symptoms, and lymphadenopathies. The symptoms described should alert pediatricians to the possibility of onset of cancer, especially when patients present with repeated consultations for the

same symptoms^(2,3,18,19). Early suspicion of cancer is crucial to request appropriate complementary examinations and refer the patient to specialized services to expedite the diagnostic process.

Our study shows that diagnosing most childhood cancers is often neither rapid nor straightforward, and in some cases, it takes several months from the onset of clinical symptoms to reach a diagnosis. Some authors argue that a certain degree of delay in the TD is inevitable, as more common and prevalent conditions must first be ruled out⁽²⁰⁾. However, the present study indicates that other factors are also associated with a longer TD. It was observed that in younger children, the diagnostic suspicion tended to be established earlier, while adolescents experienced a delay of up to a median of one month compared to infants. This difference may be explained by the fact that as children grow older, they receive less parental supervision, but still have limited knowledge of their own health status and encounter obstacles in accessing the healthcare system^(13,19). On the other hand, statistically significant differences were observed in the TD based on tumor type. Hematologic malignancies were diagnosed in nearly half the time compared to solid tumors. This may be partly because a complete blood count is a basic and first-line complementary examination in the PED for the initial assessment of many conditions and is crucial for diagnosing most hematologic malignancies⁽²⁰⁾. Finally, differences in TD were found based on tumor location, with shorter TD observed in hematologic malignancies and abdominal tumors compared to those in the CNS or musculoskeletal regions. This variation in TD can be attributed not only to the clinical features associated with each organ or system but also to the biological characteristics of the tumors. Bone and brain tumors typically have slower growth rates than other tumor types, which may contribute to their later diagnosis^(14,19). Hematologic malignancies, on the other hand, usually present with acute and evident symptoms, which allows for faster detection.

The main limitation of this study is its retrospective design, which may have resulted in the loss of information and potential biases during data collection and interpretation. However, these losses are assumed to be minimal, as due to type of disease, the information collected at disease onset is usually very complete. In addition, the study was conducted at a tertiary-level hospital and pediatric oncology referral center, which, as previously mentioned, may have led to a bias due to the higher prevalence of new cancer diagnoses occurring in a higher-level PED compared to other centers.

CONCLUSIONS

Oncologic presentations are relatively common in the studied PED, as it is a referral center. Approximately half of the cases occurred in patients under 5 years of age, and leukemia and CNS tumors were the most commonly diagnosed types of cancer, consistent with reports in the classic pediatric literature. Cachexia is more common in hematologic malignancies, while gastrointestinal and neurological symptoms are more frequently associated with solid tumors. The diagnosis of CNS and musculoskeletal tumors, as well

as onset in adolescence, are factors that may contribute to a longer TD. Repeated consultations for the same clinical symptoms, as seen in other disease groups, should also be considered an alarm sign when cancer is suspected.

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