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Soft tissue sarcomas in the first year of life

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ABSTRACT

Background: Soft tissue sarcomas (STS) occurring in the first year of life represent a rare entity. Challenges in delivering optimal therapy may affect the outcome in this very young population.

Methods: We searched the SEER database for records of infants less than 1 year of age, with a reported diagnosis of STS who were diagnosed from 1973 to 2006. We analysed their clinical features and survival. These patients were also compared to older patients (1–18 years old) in order to understand the differences between the two groups.

Results: The incidence rate of STS in the first year of life was 16.0 per million. As an entity, they represented 7.3% of malignancies reported in the first year of life. One fifth of these tumours (20.9%) were reported to be metastatic at diagnosis. The most common histologies were rhabdomyosarcoma ($n = 99$, 32.8%), fibrosarcoma ($n = 74$, 24.5%), malignant rhabdoid tumours ($n = 43$, 14.2%) and haemangiopericytoma ($n = 12$, 4.0%); except for rhabdomyosarcoma, the other 3 entities were very rare in older children. The 5-year survival of STS in children less than 1 year of age (62 ± 3.0%) was significantly worse than that of older children (71 ± 0.9%, $P = 0.0002$). In a multivariate model, histologic types other than fibrosarcoma and haemangiopericytoma (HR, 5.7; 95% CI, 2.28–14.20) as well as advanced stage (HR, 5.15; 95% CI, 3.28–8.10) were found to be significant adverse prognostic factors. Significantly less use of radiation was reported in infants when compared to older children ($P < 0.0001$).

Conclusion: As a group, infantile STS are associated with worse survival than STS in older children. Outcome, however, is significantly associated with histologic subtype, with infantile fibrosarcoma and infantile haemangiopericytoma having better outcomes. Avoidance of radiotherapy in this young age may contribute to worse outcomes.

1. Introduction

Paediatric soft tissue sarcomas (STS) represent about 8% of all childhood malignancies; rhabdomyosarcoma (RMS) represents approximately half of the cases, while the remainder is the heterogeneous group of the so-called "non-rhabdomyosarcoma" STS (NRSTS).[1,2]

STS may occur at any age. In the paediatric group, STS are widely distributed from newborns to adolescents. The epidemiological pattern of the different STS subtypes varies with

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age; likewise, the clinical behaviour of a given subtype is not always uniform across age groups. In particular, infants seem to represent a peculiar subset; specific entities such as infantile fibrosarcoma (IFS) and malignant rhabdoid tumours (MRT) have their incidence peak in the first year of life,[3,4] an age group in which RMS also has unique clinical findings and outcome.[5] The natural history of STS in infants may be different from that in older children due to differences in tumour biology,[6] but also due to differences related to the host. Infants are particularly vulnerable to the acute and late effects of therapy,[7] and developmental differences in drug metabolism represent a major challenge in the appropriate use of chemotherapeutic agents.[8,9] In comparison to older children, the management of patients during the first year of life is therefore particularly difficult; tailored treatments and careful monitoring are necessary, and chemotherapy dose reduction and restricted use of radiotherapy are common practices.

To better characterise the clinical characteristics and outcome of STS occurring in patients under one year of life and their distinctive features from older children, we performed an analysis of all STS cases (occurring in 0–18 year-olds) registered in the Surveillance, Epidemiology, and End Results (SEER) public-access database collected from various geographic areas in the United States.

2. Patients and methods

2.1. Data source and study population

The clinical and outcome data of infants (<1 year old) with a reported diagnosis of STS were obtained from the SEER 17 registries (http://seer.cancer.gov/data/).[10] We used the "case listing session" of the SEER*Stat 6.5.2 program to generate a matrix of all individuals diagnosed with STS in the database. A selection query was designed to retrieve data on tumours based on the International Classification of Childhood Cancer, version 3 (ICCC-3)[11] with a selection criteria of "IX: soft tissue and other extraosseous sarcomas" and "VI (a2): rhabdoid renal tumours". The inclusion of rhabdoid renal tumours was based on the assumption that these tumours have similar behaviour, age distribution and outcome to rhabdoid tumours arising from other sites.[3] The query was restricted to patients who were actively followed and who had microscopic confirmation of their tumours. The "frequency session" of the SEER*Stat software was used to calculate the frequency in older children (1–18 years old) and their clinical features. Using this session, the total number of patients registered in the SEER database can be retrieved. The "rate session" of the SEER9 database was used to calculate the incidence of STS in infants and older patients. This session calculates the number of cancer (STS in this study) per 100,000 persons (modifiable) per year. The denominator is represented by the general population census in the areas covered by the SEER registries.

2.2. Data analysis

The resulting matrix from SEER*Stat was transferred to MedCalc for Windows version 10.4.0.0 (MedCalc Software, Mariakerke, Belgium) for statistical calculations. Tumour primary sites were grouped into head and neck, extremities, trunk (including thorax, abdomen and pelvis), genito-urinary tract (including the kidneys) and others and not otherwise specified locations (others/NOS). In the SEER staging system, localised stage refers to an invasive neoplasm confined entirely to the organ of origin; regional stage refers to a neoplasm that has extended beyond the limits of the organ of origin directly into surrounding organs or tissues, has spread to regional lymph nodes by way of the lymphatic system or both and distant stage refers to a neoplasm that has spread to parts of the body remote from the primary tumour either by direct extension or by discontinuous metastasis to distant organs and tissues or via the lymphatic system to distant lymph nodes.

Death from any cause was chosen as an end-point in survival analyses. Overall survival (OS) estimates were calculated using the Kaplan–Meier method; the log-rank test was used to compare survival curves. Survival estimates were presented followed by standard errors (SE). Cox-proportional hazards regression was used to conduct the multivariate analysis. The chi-square test was used to compare categorical variables in the study.

3. Results

3.1. Clinical characteristics of STS in infants

We identified 302 infants with STS who were diagnosed from 1973 to 2006. As a group, STS ranked as the fifth most common malignancy in infants, representing 7.3% of all tumours diagnosed below the age of 1 year and registered in the open-access SEER database. In older children (1–18 years old), STS was the fourth most common malignancy, representing 7.5% of tumours (Table 1). The annual incidence rate of STS in the first year of life was 16.0 per million. The incidence was lower in older children (1–4 years, 9.4 per million; 5–9 years, 8.0 per million and 10–14 years, 10.6 per million).

Table 2 summarises the clinical characteristics of the 302 infants with STS, compared with those of 3316 older children (1–18 years old) with STS. In patients under 1 year of age, the trunk (25.5%) and the head and neck region (23.5%) were the

Table 1 – Paediatric cases registered in the SEER database (1973–2006).

	Less than 1 year old		1–18 year old	
	N	(%)	N	(%)
Neuroblastoma	979	(23.8)	1774	(4.0)
Leukaemia	639	(15.6)	12,721	(28.6)
CNS tumours	531	(12.9)	8004	(18.0)
Retinoblastoma	378	(9.2)	644	(1.4)
Soft tissue sarcomas	302	(7.3)	3316	(7.5)
Nephroblastoma	291	(7.1)	1780	(4.0)
Extracranial GCT	293	(7.1)	1740	(3.9)
Hepatic tumours	188	(4.6)	440	(1.0)
Lymphoma	124	(3.0)	6390	(14.4)
Bone tumours	9	(0.2)	2643	(5.9)
Others	375	(9.1)	5026	(11.3)
Total	4109		44,478	