Vol 46 (2) June , 2022

Print: ISSN 0304 4904
Online: ISSN 2305-820X

PAKISTAN PEDIATRIC JOURNAL

A JOURNAL OF PAKISTAN PEDIATRIC ASSOCIATION

Indexed in EMBASE/Excerpta Medica, Index Medicus WHO,CPSP
IMEMR & Global Health/CAB Abstracts and UDL-EDGE Products and Services

www.pakpedsjournal.org.pk

http://www.pakmedinet.com/PPJ

ORIGINAL ARTICLE

Histopathological Study of Small Round Cell Tumors (SRCTS): 12 Years Study

ARASH DEHGHAN, PARISA MOKHLES, HAMIDREZA GHASEMIBASIR, Nasrin Jeyriaee

Pak Pediatr J 2022; **46(2):** 169-73

Correspondence to:

Parisa Mokhles
Department of Pathology
Laboratory of Hazrat Rasoul Akram Hospital, Iran University of Medical Science, Tehran, Iran

E-mail: Pa.mokhles@gmail.com

Received 7th October 2021;
Accepted for publication
25th March 2022

ABSTRACT

Objective: To study the incidence and comparison of various SRCTs in relation to age, sex and site distribution.

Study Design: Cross-sectional

Place and Duration of Study: The present study was undertaken in histopathology laboratory at Besat Hospital in Hamadan, Iran for period of 12 years from April 2009 to March 2021.

Material and Methods: All specimens admitted with pathology findings as SRCT were included. Tissues were processed and histopathological and immunohistochemical studies were done and recorded.

Results: Out of 176 cases 72 (41%) were female and 104 (59%) were male with the mean age of 33.72 ± 26.96 years. Small cell carcinoma was the most common type of SRCTs (23.9%) followed by Ewing Sarcoma (ES)/Primitive Neuroectodermal Tumor (PNET) (17.6%), non-Hodgkin's lymphomas (14.7%), Wilms tumor (10.2%) and Neuroblastoma (8.5%). IHC staining was performed for 87 cases (49.4%).

Conclusion: The demographic characteristics of SRCTs vary as much as their diversity. Obviously, it is necessary for the pathologist to confirm the final diagnosis by checking the consistency of the diagnosis with the patient's initial clinical information according to the statistics recorded in valid reference books and articles.

Key words: Small round cell tumor, Pathology, Ewing sarcoma, PNET, Small cell carcinoma

INTRODUCTION

Small round cell tumors are undifferentiated neoplasms with little or no evidence of differentiation. Some may link this terminology to morphologically undifferentiated neoplasms that cannot be otherwise classified.[1] The reason for naming this group as SRCT is the characteristic of this group's tumor cells that have poor or no differentiation, with a high N/C ratio and a slight blue cytoplasm in H&E staining.[2] These tumors, despite their morphological similarities, have completely different prognosis and treatments depending on their morphology.[3]

Making a correct diagnosis when dealing with a small round cell tumor (SRCT) of children and adolescents may be relatively straightforward if the tumor arises in the typical clinical setting and the classic pathologic features are all recognizable. However it is widely known that diagnostic difficulties may arise because of the

considerable clinical, pathologic, and immunohistochemical variations and their morphological and/or immunohistochemical overlapping features.[4]

A rapid and accurate diagnosis is essential for proper treatment. However, accurate detection of SRCTs solely based on hematoxylin-eosin staining and light microscopy findings may be difficult.[5] Other auxiliary methods include cytochemistry (specific staining), immunohistochemistry (IHC), electron microscopy, morphometry, tissue culture, DNA ploidy, karyotyping and molecular analysis.[6-9]

Due to the difficulty of precisely identifying these tumors and their completely different therapies, despite their morphological similarities, epidemiological and demographic information can help to identify these tumors more rapidly.

MATERIAL AND METHODS

The present study was undertaken in histopathology laboratory at Besat Hospital in Hamadan, Iran. All the patients attending Besat Hospital with SRCT features in H&E slides were studied in the duration of April 2009 to March 2021. Tissues were processed and studied. Demographic data (age, sex) of the patients were extracted from the hospital archive electronic file and recorded in a checklist. Of the 176 cases, 87 required IHC staining for definitive diagnosis. For this purpose, according to the possible differential diagnosis, the samples were stained by relevant markers such as Ki67, Vimentin, CK, LCA, CD99, EMA, Desmin, etc and examined with a light microscope and the final diagnosis was recorded. The final diagnosis of patients who were referred to other centers to complete the diagnostic process was followed up and recorded. About 8 patients were excluded from the study due to lack of final information. Data were analyzed with SPSS software version 17 and summarized in table, ratio, percentage and mean.

RESULTS

The present study was conducted from April 2009 to March 2021 in Department of Pathology at Besat hospital in Hamadan, Iran, with following observations in 176 cases of SRCTs on histopathology. The most common site of involvement was lung (18.8%) followed by bone (15.3%) and soft tissue (13.6%). (table 1 to 3 and fig 1 to 3)

TABLE 1: Incidence of SRCTs based on their anatomical location (n=176)

Tumor location	Number (%)
Lung	33 (18.8%)
Soft tissue	24 (13.6%)
Bone	27 (15.3%)
Retroperitoneal	15 (8.5%)
Kidney	20 (11.4%)
Brain/spinal cord	13 (7.4%)
Gastrointestinal tract	10 (5.7%)
Mediastinum	7 (4%)
Sinuses	8 (4.5%)
Lymph nodes	7 (4%)
Skin	4 (2.3%)
Liver	4 (2.3%)
Sum	**176 (100%)**

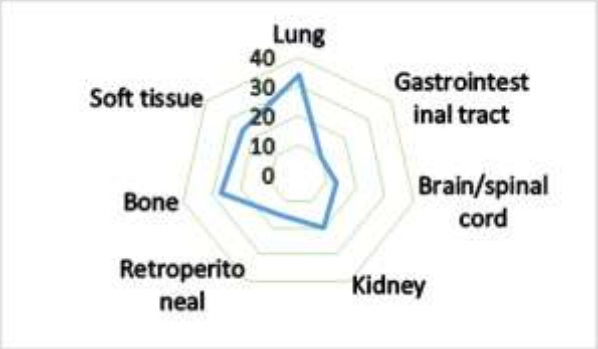

Fig 1: Incidence of SRCTs based on their anatomical location (n=176)

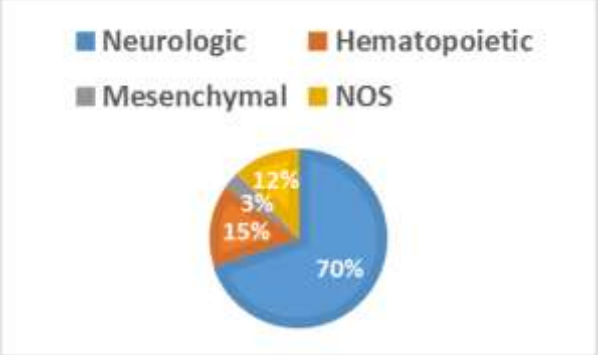

Fig 2: Distribution of the SRCTs by their origin (n=176)

The majority of tumors were of neuroectodermal (69.9%) and hematopoietic (14.8%) origins. In 21 cases (11.9%) the origin of the tumor was unclear. (fig 2) Out of 176 cases, 87 (49.4%) required IHC staining for definitive diagnosis.

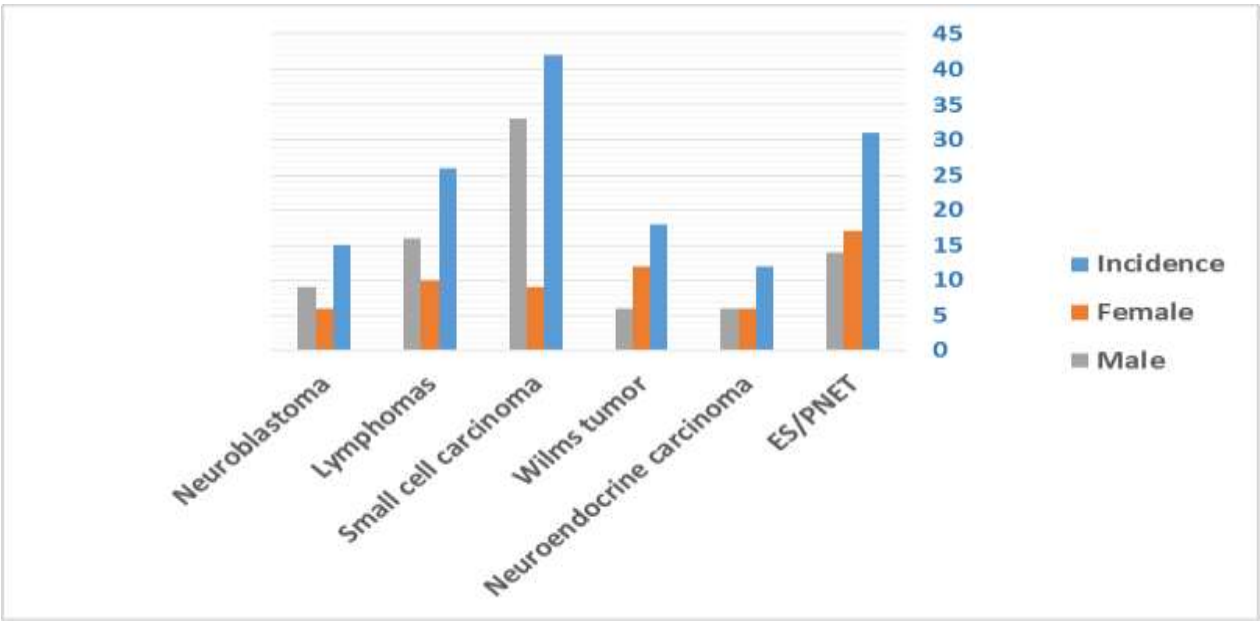

Fig 3: Incidence and distribution of the SRCTs by gender (n=176)

In terms of gender, except for small cell carcinomas with a male to female ratio of 3.6 to 1, no significant gender differences were observed at the rest of the tumor types (fig 3). The most common tumors were small cell carcinoma (23.9%), ES / PNET (17.6%), non-Hodgkin's lymphoma (14.7%), Wilms tumor (10.2%) and Neuroblastoma (8.5%) respectively. (table 2)

TABLE 2: Incidence and distribution of the SRCTs and their origins by gender

Origin	SRCT	Incidence (%)	Female (%)	Male (%)
Neuroectodermal	ES/PNET	31 (17.6)	17 (54.8)	14 (45.2)
	Neuroblastoma	15 (8.5)	6 (40)	9 (60.0)
	Medullary thyroid carcinoma (small cell)	3 (1.7)	0 (0)	3 (100.0)
	Small cell carcinoma	42 (23.9)	9 (21.4)	33 (78.6)
	MPNST	4 (2.3)	1 (25.0)	3 (75.0)
	Melanoma small cell variant	6 (3.4)	2 (33.3)	4 (66.7)
	Medulloblastoma	6 (3.4)	3 (50.0)	3 (50.0)
	Merkel cell tumor	4 (2.3)	3 (75.0)	1 (25.0)
	Neuroendocrine carcinoma	12 (6.8)	6 (50.0)	6 (50.0)
Hematopoietic	Lymphoblastic lymphoma	9 (5.1)	3 (33.3)	6 (66.7)
	Burkitt's lymphoma	9 (5.1)	4 (44.4)	5 (55.6)
	Extra nodal lymphoma	8 (4.5)	3 (37.5)	5 (62.5)
Mesenchymal	Myxoid/round cell liposarcoma	1 (0.6)	1 (100.0)	0 (0.0)
	Rhabdomyosarcoma	3 (1.7)	1 (33.3)	2 (66.7)
	Small cell osteosarcoma	1 (0.6)	0 (0.0)	1 (100.0)
NOS	DSRCT	2 (1.1)	1 (50.0)	1 (50.0)
	Synovial sarcoma	2 (1.1)	0 (0.0)	2 (100.0)
	Wilms tumor	18 (10.2)	12 (66.7)	6 (33.3)
Sum		**176 (100)**	**72 (40.9)**	**104 (59.1)**

The mean age of patients with ES/PNET diagnosis was 21.5 years, Wilms tumor 3.3 years, Neuroblastoma 6 years and small cell carcinoma 60.2 years (table 3).

Table 3: distribution of the SRCTs by age (n=176)

SRCT	Mean age	SD
ES/PNET	21.48	13.7
Neuroblastoma	6.07	4.5
Medullary thyroid carcinoma (small cell)	69.67	8.5
Small cell carcinoma	60.24	13.5
MPNST	43.50	19.0
Melanoma small cell variant	63.17	22.8
Medulloblastoma	11.17	10.3
Merkel cell tumor	75	4.2
Neuroendocrine carcinoma	59.75	17.2
Lymphoblastic lymphoma	8.67	8.2
Burkitt's lymphoma	11.89	7.1
Extra nodal lymphoma	42.38	14.4
Rhabdomyosarcoma	15.67	14.4
Small cell osteosarcoma	18	-
DSRCT	19.5	0.7
Synovial sarcoma	24.5	10.6
Wilms tumor	3.28	1.8
Sum	**33.72**	**26.96**

DISCUSSION

Mean age of the patients in this study was 33.72 years (1-89 years with SD: 26.96), consistent with the results of Ptaszyński et al.'s study of 131 patients with the diagnosis of SRCT in 2009 which had a mean age of 36.74 years.[10]

In the present study, 41% were female and 59% were male. According to a study by Rani G Patel (2017), the ratio of women to men is 2: 1. But Ptaszyński et al. noted that there was no significant gender difference among the patients studied, which may be due to the lack of small cell carcinomas (SmCC) as an SRCT in their studies.[11]

In the present study, small cell carcinomas (23.9%), ES/PNET (17.6%), non-Hodgkin's lymphomas (14.7%), Wilms tumor (10.2%), and Neuroblastoma (8.5%) were the most common SRCT tumors, respectively. It is almost similar to the study findings of Rani et al. (2017). According to their reports, the most common SRCTs were non-Hodgkin's lymphoma, Neuroblastoma, ES/PNET and Rhabdomyosarcoma, respectively, the inclusion of DLBCL in their study population seems to be the reason for their small statistical difference.[11]

According to the study by Ptaszyński et al, the family of Ewing sarcomas with a frequency of 38 cases followed by synovial sarcoma with a frequency of 26 cases were the most common SRCT tumors, whereas in our study, synovial sarcoma with a frequency of 2 (1.1%) was among the rarest tumors have been studied, because of the limitation of Synovial sarcomas to round cell variants in the present study.[10]

Shah et al. (1999) reported the most common tumors, respectively: ES/PNET (28.6%), Rhabdomyosarcoma (23.2%), non-Hodgkin's lymphoma (16.1%), and Neuroblastoma (14.2%). This seems to be the statistical difference due to the limitation of their study to SRCTs that require specific staining.[12]

In a study by Ptaszyński et al., the prevalent age of PNET/ES involvement was reported in the second decade of life. The mean age of patients with this diagnosis was 23.21 years (range: 1-59 years SD: 14.8) with a male to female ratio of 1.6.[10]

According to Dehner's study, Neuroblastoma is the most common solid tumor in children under one year of age and is seen in children less than 5 years of age. In our study, the mean age of Neuroblastoma patients was 6.7 ± 4.5.[13]

According to the Ackerman Reference Book, 90% of Wilms patients were less than 6 years of age[14] while the mean age of the patients in our study was 3.3 years.

Rani et al. cited the prevalent age of non-Hodgkin's lymphomas, including Burkitt's, lymphoblastic, and DLBCL, below 10 years.[11] The mean age of patients in our study for Burkitt's, lymphoblastic and extra nodal primary lymphomas was 11.9, 8.7, and 42.4 years, respectively.

In the present study 89 (50.6%) out of 176 cases were diagnosed without IHC studies and 87 (49.4%) final diagnosis required IHC follow-up, similarly, according to the Shah Sh study, 56 of the 124 cases (45%) required IHC.[12]

CONCLUSIONS

According to the data obtained from the study, the mean age of patients with a specific tumor was similar to the mean age reported in different studies and reference books. The ratio of male to female involvement in the present study was different from that of other studies. The most

common sites of involvement were lung, soft tissue, and bone, the most common tumors involving them were small cell carcinoma, non-Hodgkin's lymphoma, and Ewing's sarcoma, respectively.

The most common tumors of the SRCT category were small cell carcinoma, ES/PNET, non-Hodgkin's lymphoma (including Burkitt's lymphoma, lymphoblastic lymphoma, and extranodal primary lymphoma), Wilms tumor, and Neuroblastoma. Of the total 176 samples, 87 (49.4%) required IHC studies.

Acknowledgments: This article is approved by the Vice-Chancellor for Research and Technology of the University of Medical Sciences (9708154784).

We would like to thank everyone who participated in and assisted in the design and collection of the data. The results of this study are not in conflict with the interests of the authors.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest: Nil

Authors' affiliation

Arash Dehghan, Hamidreza Ghasemibasir, Nasrin Jeyriaee
School of Medicine, Hamadan University of Medical Science, Hamadan, Iran

Parisa Mokhles,
School of Medicine, Iran University of Medical Science, Tehran, Iran

REFERENCES

1. Bahrami A, Truong LD, Ro JY. Undifferentiated tumor: true identity by immunohistochemistry. Archives of pathology & laboratory medicine. 2008;132(3):326-48.
2. Kim NR, Ha SY, Cho HY. Utility of transmission electron microscopy in small round cell tumors. Journal of pathology and translational medicine. 2015;49(2):93.
3. Lewis TB, Coffin CM, Bernard PS. Differentiating Ewing's sarcoma from other round blue cell tumors using a RT-PCR translocation panel on formalin-fixed paraffin-embedded tissues. Modern pathology. 2007;20(3):397-404.
4. Magro G, Longo FR, Angelico G, Spadola S, Amore FF, Salvatorelli L. Immunohistochemistry as potential diagnostic pitfall in the most common solid tumors of children and adolescents. Acta histochemica. 2015;117(4-5):397-4.
5. Ashraf MJ, Beigomi L, Azarpira N, Geramizadeh B, Khademi B, Hakimzadeh A, et al. The small round blue cell tumors of the sinonasal area: Histological and immunohistochemical findings. Iranian Red Crescent Medical Journal. 2013;15(6):455.
6. Bansal C, Gupta A, Kumar A, Srivastava A. Morphometric evaluation and clinical correlations in pediatric malignant small round cell tumors. Indian journal of medical and paediatric oncology: official journal of Indian Society of Medical & Paediatric Oncology. 2014;35(4):267-70.
7. Bayani J, Thorner P, Zielenska M, Pandita A, Beatty B, Squire JA. Application of a simplified comparative genomic hybridization technique to screen for gene amplification in pediatric solid tumors. Pediatric Pathology & Laboratory Medicine. 1995;15(6):831-44.
8. Peter M, Gilbert E, Delattre O. A multiplex real-time PCR assay for the detection of gene fusions observed in solid tumors. Laboratory investigation. 2001;81(6):905-12.
9. Thorner PS, Squire JA. Molecular genetics in the diagnosis and prognosis of solid pediatric tumors. Pediatric and Developmental Pathology. 1998;1(5):337-65.
10. Ptaszyński K, Szumera-Ciećkiewicz A, Pękul M, Nowecki Z. Differential diagnosis of small round cell tumours (SRCT), fluorescence in situ hybridization (FISH) and immunohistochemical (IHC) study. Polish Journal of Pathology. 2009;60(4):151-62.
11. Patel RG, Shah PY, Prajapati SG, Amin NS, Khant VS. Histopathological study of round cell tumors--a retrospective study. International Journal of Medical Science and Public Health. 2017;6(2):388-94.
12. Shah SH, Soomro IN, Siddiqui MS, Pervez S, Hassan SH. Immunohistochemical evaluation of small round cell tumors of childhood. Journal of Pakistan Medical Association. 1999;49(4):87.
13. Dehner L. Peripheral and central primitive neuroectodermal tumors. A nosologic concept seeking a consensus. Archives of pathology & laboratory medicine. 1986;110(11):997-1005.
14. Yaoun R .Rosai and Ackerman's Surgical Pathology. 11th ed. Edinburg: Elsevier Saunders. Vol 3; 2018. P 1014-19.