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Prevalence and Characteristic of Pediatric Solid Tumor in Sanglah Hospital Bali

I Made Suwananta
Department of Child Health, Medical Faculty of Udayana University, Sanglah Hospital Denpasar, Indonesia
Email: 5uwananta@gmail.com

Ketut Ariawati
Department of Child Health, Medical Faculty of Udayana University, Sanglah Hospital Denpasar, Indonesia
Corresponding author email: ketutari_hemato@yahoo.com

A. A. N. K. P. Widnyana
Department of Child Health, Medical Faculty of Udayana University, Sanglah Hospital Denpasar, Indonesia
Email: gungmanikledo@yahoo.co.id

Kadek Ayu Yani Lastariana
Department of Child Health, Medical Faculty of Udayana University, Sanglah Hospital Denpasar, Indonesia
Email: yanilastariana2@gmail.com

***Abstract*---*Tumor is one of major cause of mortality and morbidity in children and adolescents. Tumor is classified as hematologic and solid tumor. Solid tumors represent approximately 60-70% of all pediatric tumor where are hematologic showed 30-40% cases. Embryonic solid tumor has its peak incidence in childhood, otherwise bone and skeletal tumor in adolescent. There is still limited research about characteristics of solid tumor. To know about prevalence and characteristic of solid tumor in Sanglah Hospital. Retrospective study using secondary data from Pediatric Hematology Oncology division registry from 2016-2020. There were 92 solid tumor subjects with prevalence rate 38.6%. Among all of tumor in children and adolescent, 56.5% was found in ≤5 years group of age with the highest prevalence rate was retinoblastoma. About 60.9% was male and 65.2% domiciled in Bali. Major clinical manifestation was palpable mass 77.2% and lymphadenopathy (29.3%). The most hematology problem was anemia (57.3%). The mortality rate was 32.6%, with brain metastases was major cause of death. The prevalence of solid tumor was 38.6%. Retinoblastoma was the most common case in children with range of age 0-5 years. Major clinical manifestation was palpable mass and lymphadenopathy. Anemia became major hematology problem in tumor patient.*
Keywords*---*hematology, hyper leukocytosis, pediatric, prevalence, retinoblastoma, solid tumor

Introduction

Tumor is one of major cause of death in children and adolescents. The incidence has been slowly increasing since 1975. Worldwide, the annual number of new childhood tumor exceeds 200,000 and more than 80% of these are from the developing country. Tumor affects all nations, become endemic disease with considerable variation in frequency according to the site. In Indonesia, tumor case reach 11,000 every years. Tumor is classified as hematologic and solid. Solid tumors represents approximately 30-40% of all pediatric tumor that was dominated by lymphoma, retinoblastoma and bone tumor. Hematologic tumor incidence especially leukemia from 2005 until 2009 was 14.3%. In Bali, from 2008-2017, the incidence of leukemia and solid tumor were 58.5% and 41.5% respectively (Abba & Khalil,2012; Adinatha & Ariawati, 2020).

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Solid tumors are abnormal mass of tissue that usually does not contain cysts or liquid areas. Solid tumors may be benign (not cancerous), or malignant (cancerous). Solid tumors in children and adolescents are different from those of adults in clinical features and diversity of cellular origins. This tumor has specific characteristic including variation of age and gender. In early childhood, embryonal type solid tumors are more common, such as Retinoblastoma, Neuroblastoma, Hepatoblastoma, Wilms tumor, and Medulloblastoma that have high incidence in first ten years of live. Otherwise, in adolescents solid tumors often arise from bone and soft tissues such as osteosarcoma, Ewing sarcoma, germ cells (germ cell tumor) and epithelial cells (thyroid carcinoma). Retinoblastoma is a malignant tumor that arises from the developing retina in very young children. The incidence of retinoblastoma is not equally distributed around the world with similar distribution in boys and girls and about 75% are diagnosed before reaching age 2 years (Agarwal, 2016; Allen-Rhoades et al., 2018; Arya e al., 2004).

Hepatoblastoma is slightly higher in boys than in girls and mean age at diagnosis is 19 months. Neuroblastoma is another extracranial solid tumor in children, accounting for 7% of all childhood malignancies and at the time of diagnosis, 50% of subject are under 2 years old, 75% under 4 and 90% under age 10 with the peak incidence is 2 years. Renal tumors account for 7% of all childhood malignancies with dominant case is wilms tumor in young children. In adolescent, bone tumor become most common malignant tumor in children. They are osteosarcoma and Ewing sarcoma. The average age at diagnosis of osteosarcoma was 11.9 years. Skeletal Ewing sarcoma is other most common bone tumor in children. The highest incidence is in the second decade of life aged 10-19 years (Badr et al., 2012; Barros et al., 2016; Batista et al., 2015). Data regarding tumor prevalence and characteristic are important to give attention to children with tumor, who have an increasing likelihood of cure with appropriate treatment. These data also provide support for tumor treatment program and facilities in addition to tumor prevention across the nation. Previous study about tumor has been conducted to know about prevalence of solid tumor but data about characteristic, distribution of solid tumor based on gender, age, hematologic manifestation and cause of death in solid tumor still obscure. To know about prevalence and characteristic of solid tumor, we conduct descriptive study in Sanglah Hospital in Bali (Bickley et al., 2020; Brown et al., 2008).

Method

A retrospective observational study was conducted in division of Pediatric Hematology Oncology Sanglah Hospital, from 2016-2020. This retrospective study using secondary data from Pediatric Hematology Oncology division registry. Baseline data include age, gender, domicile of subject, clinical manifestation, diagnosis, hematologic problem, outcome, and cause of death. Target population is all pediatric inward tumor subject diagnosed with solid tumor. Inclusion criteria is children who diagnosed with solid tumor age 0-18 years old. Exclusion criteria was incomplete registry data (Buhtoiarov, 2017; Chae et al., 2019; Chapman et al., 2017). Sample size estimation uses formula for estimation proportion of population with alpha sets at 5% and absolute precision 5%, and prevalence of solid tumor in children base on reference was 41.5%. The study uses total sampling 92 cases. In this study, characteristic data include age, gender, domicile, clinical manifestation, hematologic problem, diagnosis, outcome, and cause of death.

Age is defined as the difference between date of hospitalization and date of birth that presented into categorical data: 0-5 years, >5-14 years and >14 years based on peak prevalence of different kind of tumor diagnosis. Gender defined as phenotypically finding from physical examination. Domicile is legally residen or origin of place of subject base on identity card. Diagnosis was final diagnosis that confirmed from imaging, anatomic pathologic, or immunophenotyping examination. Hematologic manifestation is abnormal parameter find in blood cell count from CBC examination like leukopenia if WBC value less than 4.0 x 109/L, hyperleukocytosis is leukocyte count exceeding 100,000/mm, leukocytosis is leukocyte count exceeding 50,000/mm, neutropenia if value of absolute neutrophil count less than 1.5 109/L, thrombocytosis is platelet count more than 400,000/µL, thrombocytopenia is platelet count less than 150,000/µL and anemia if hemoglobin less than normal value based on age. Outcome is presented as death or live during the study is conducted. Cause of death was direct cause of death based on sertificate of death (Chen et al., 2015; Chintalacheruvu et al., 2018).

Result

Tumor consists of solid and hematologic. In this study we found total solid tumor and leukemia case in five years from January 2016 until December 2020 were 92 and 146 cases respectively with the prevalence rate of solid tumor is 38.6%. Total solid tumor in 2016, 2017, 2018, 2019 and 2020 are 18 (19.6%), 7 (7.6%), 16 (17.4%), 20 (21.7%) and 31 (33.7%) respectively. Solid tumor cases in five years study are showed in figure 1. Table 1 shows about characteristic of all tumor case and table 2 views about the most five tumor cases characteristic. It was 56.5% of

tumor case in 0-5 years of age followed by 31.5% in >5-14 years and 12.0% in >14 years group. Solid tumor case was dominated by male (60.9%) and domiciled in Bali (65.2%). In this study, palpable mass and lymphadenopathy were most clinical manifestation with proportion 77.2% and 29.3% respectively. Majority of palpable mass was complained in retinoblastoma and most of lymphadenopathy found in NHL.

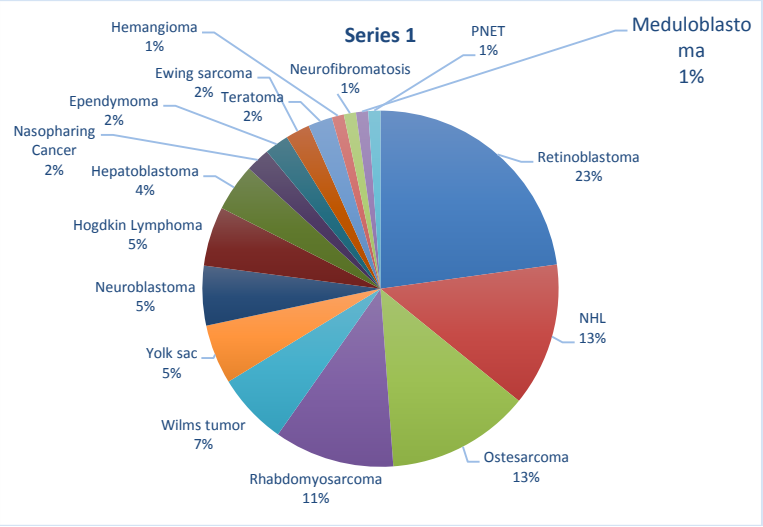

Figure 1. Solid tumor proportion

Median of hemoglobin level in this study was 10.74 (4.57-15.0) mg/dL and median of thrombocyte was 405 (17.14-930) x 103/µL, so most of case had anemia or thrombocytosis. Most case of anemia and thrombocytosis was found in retinoblastoma. Other hematologic parameters were white blood cell level median 10.76 (0.64-975.0) x 103/µL and neutrophil median 5.42 (0.07-43.0) x 103/µL. Hyper leukocytosis case were found in NHL and leukopenia occurs in wilms tumor and rhabdomyosarcoma. Most of neutropenia were in Wilms tumor. Thrombocytopenia was found mostly in rhabdomyosarcoma. The mortality rate in this study was 32.6 % and most of subject still alive until study was conducted. Cause of death was dominated by brain metastases (42.9%) and infection (39.3%). Most of brain metastasis was found in retinoblastoma and infection in NHL (Evers et al., 2017; Fernandez-Pineda et al., 2015).

Table 1
Characteristic of pediatric solid tumor

Characteristic	N (%) Total=92 subjects
Age	
≤5 years	52 (56.5)
>5-14 years	29 (31.5)
>14 years	11 (12.0)
Gender	
Male	56 (60.9)
Female	36 (39.1)
Domicile	
Bali	60 (65.2)
NTB	21 (22.8)
NTT	6 (6.5)
Jawa	2 (2.2)
Kalimantan	1 (1.1)
Sulawesi	2 (2.2)
Clinical manifestation	
Chief complaint	

Palpable mass	71 (77.2)
Bleeding	1 (1.1)
Pain	7 (7.6)
Fever	4 (4.3)
Other	9 (9.8)
Clinical sign	
Hepatomegaly	14 (15.2)
Splenomegaly	7 (7.6)
Lymphadenopathy	27 (29.3)
Hematology manifestation	
Hyper leukocytosis	2 (2.2)
Leukopenia	3 (3.3)
Neutropenia	3 (3.3)
Anemia	53 (57.6)
Thrombocytopenia	8 (8.7)
Thrombocytosis	48 (52.2)
Outcome	
Death	30 (32.6)
Live	62 (67.4)
Cause of Death	
Brain metastases	12 (42.9)
Infection	11 (39.3)
Bleeding	2 (7.1)
Other	3 (10.7)

Table 2
Characteristic of the most five tumor cases

Characteristic	Tumor diagnosis					
	Retinoblastoma	NHL	Osteosarcoma	Rhabdomyosarcoma	Wilm's Tumor	Other
Gender N (%)						
Male	14 (25.0)	8 (14.3)	7 (12.5)	9 (16.1)	4 (7.1)	14 (25.0)
Female	7 (19.4)	4 (11.1)	5 (13.9)	1 (2.8)	2 (5.6)	17 (47.2)
Clinical manifestation						
Chief complaint N (%)						
Palpable mass	18 (25.4)	9 (12.7)	8 (11.3)	10 (14.1)	4 (5.6)	22 (30.9)
Bleeding	0	0	0	0	1 (100.0)	0
Pain	0	1 (14.3)	4 (57.1)	0	0	3 (42.8)
Fever	0	1 (25.0)	0	0	1 (25.0)	2 (50.0)
Other	3 (33.3)	1 (11.1)	0	0	0	5 (55.5)
Clinical sign N (%)						
Hepatomegaly	2 (14.3)	2 (14.3)	0	0	1 (7.1)	9 (64.2)
Splenomegaly	0	2 (28.6)	0	0	1 (14.3)	4 (57.1)
Lymphadenopathy	4 (14.8)	9 (33.3)	0	0	2 (8.0)	12 (44.4)
Hematology manifestation N (%)						
Hyper leukocytosis	0	2 (100.0)	0	0	0	0
Leukopenia	0	0	0	1 (33.3)	2 (66.7)	0
Neutropenia	0	0	0	0	2 (66.7)	1 (33.3)
Anemia	10 (18.9)	9 (17.0)	3 (5.7)	7 (13.2)	4 (7.5)	20 (37.7)
Thrombocytopenia	0	1 (12.5)	1 (12.5)	2 (25.0)	0	4 (50.0)
Thrombocytosis	12 (25.0)	7 (14.6)	5 (10.4)	4 (8.3)	3 (6.3)	17 (35.4)
Outcome N (%)						
Death	9 (30.0)	4 (13.3)	4 (13.3)	2 (6.7)	1 (3.3)	10 (33.3)
Live	12 (19.4)	8 (12.9)	8 (12.9)	8 (12.9)	5 (8.1)	21 (33.8)

Cause of Death n (%)						
Brain metastases	5 (41.7)	1 (8.3)	1 (8.3)	1 (8.3)	0	4 (33.3)
Infection	2 (18.2)	3 (27.3)	2 (18.2)	1 (9.1)	0	3 (27.2)
Bleeding	0	0	0	0	1 (50.0)	1 (50.0)
Other	2 (66.7)	0	0	0	0	1 (33.3)

Prevalence rate of solid tumor was classified based on age because tumor has different distribution according to age.13 It was divided into 0-5 years, >5-14 years and >14 years. The highest case of 0-5 years age group was retinoblastoma. Osteosarcoma had the highest case of >14 and >5-14 years group. Complete data about prevalence rate based on age is presented in figure 2.

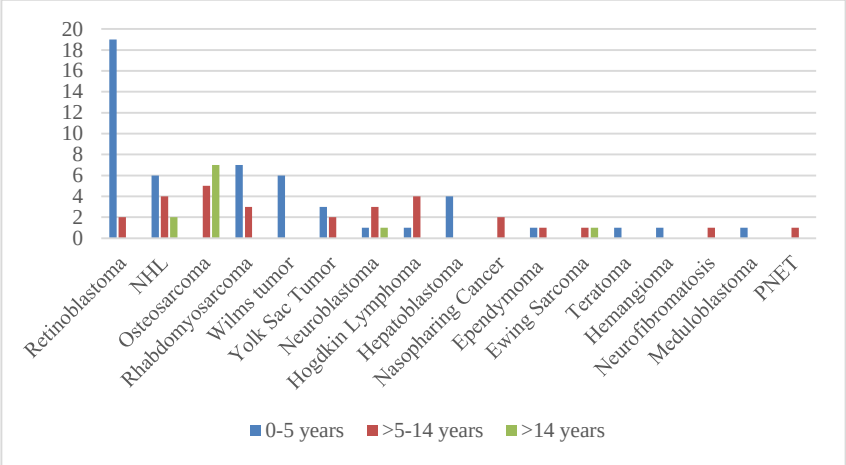

Figure 2. Solid tumor proportion rate based on age

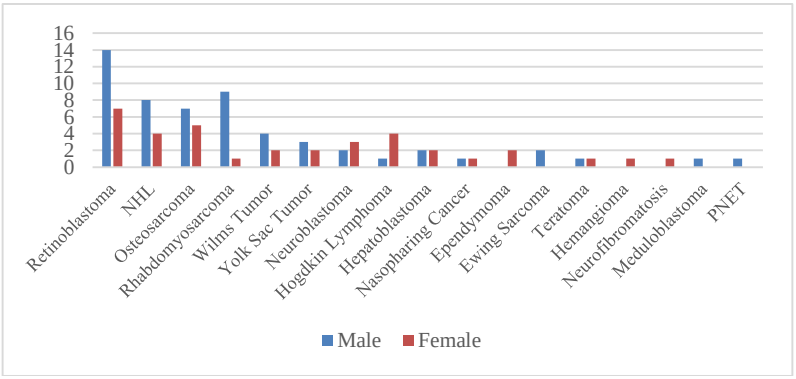

Figure 3. Solid tumor proportion rate based on gender

Prevalence rate of solid tumor was also different according to gender. Retinoblastoma is the tumor with highest case in male and female. Complete data is presented in figure 3 (Friedman, 2013; George et al., 2014; Griscom & Wolf, 2020).

Discussion

There were 92 cases in five years of pediatric solid tumor in Sanglah Hospital from January 2016 until December 2020 with prevalence rate 38.6%. The data have variation worldwide especially between developing and developed country (Hewitt et al., 2003; Hockenberry et al., 2002). Several study in USA, Bangladesh and Indonesia showed solid tumor prevalence range from 0,8%, 4.4%, 41.5% respectively. The different of prevalence is influenced by many factor, such as radiation, genetic, chromosome disorder, economic factor, education status of parent, and health service facilities. Based on Indonesia Cancer Registration System on 2005-2007, highest case of cancer in children was 0-5 year's group compared with 5-14 years group. Other data also stated that there is a risk of one in 650 to one

in 400 that a child will be affected during the first 15 years following birth (Hu et al., 2018; Jain et al., 2013). The data was appropriate with this study that found most case of pediatric tumor occur in 0-5 years old and case was decreased after 14 years old. Genetic factors, certain prenatal (e.g., radiation, diethylstilbestrol [DES]) and postnatal exposures (radiation, viruses) are known to increase the risk of developing some childhood cancers, but for most cases of childhood cancer, the cause remains unknown (Bhalodia Jignasa & Patel Mandakini, 2011).

In this study we find most of tumor case among children was male with ratio 1.5:1. This result was similar to previous study by Jabeen et al. (2010) that stated frequency of cancer was found to be higher among boys (62%) than girls (38%). Male predominance is a salient feature of the childhood tumors. Genetic difference in immune function may be responsible for the increased incidence of tumors in males. In this study, we found most of case was domiciled in Bali followed by NTB and NTT. This condition due to Sanglah Hospital was referral hospital in East of Indonesia so most of tumor case that needed advanced treatment will be referred (Kline & Sevier, 2003; Krishnamurthy et al., 2013). Clinical manifestation of solid tumor in children was varied based to tumor histology and site. In this study majority of case came with palpable mass as chief complained. The condition is caused by abnormal mass in the body brought the great attention to parent or guardian send children to the primary care provider. Other clinical manifestation in this study was lymphadenopathy (Lanzkowsky, 2005). Lymphadenopathy is defined as lymph nodes that are abnormal in size, consistency or number. This condition can be localized or generalized. It can cause by infiltration of neoplastic cells carried to the node by lymphatic or blood circulation. Alternatively, primary neoplastic proliferation of lymphocytes may be the underlying pathology of lymphadenopathy (Lee, 2018; Li et al., 2018; Lin et al., 2014). In this study, lymphadenopathy was found in 32.1% case and most of them in NHL. This result was appropriate to previous study that find lymphadenopathy mostly found in metastasis cancer (61.2%) and lymphoma (38.7%).

Hepatomegaly is the condition of having an enlarged liver. It is a non-specific medical sign that have many causes such as infection, hepatic tumor, or metabolic disorder. Normal liver size is based on normative values of liver span by percussion, degree of extension below the right costal margin, or length of the vertical axis estimated from imaging techniques. In general, a liver edge greater than 3.5 cm in newborns and greater than 2 cm in children below the right costal margin suggests enlargement (Liu et al., 2014; Manipadam et al., 2011). In tumor case, this condition can cause by primary tumor or metastasis process. The spreading of tumor can occur via direct spreading intraabdominally or from hematogenous. Because liver have dual vascular supply from systemic and portal vein, so chance for spreading was increased. Liver was metastasis destination of solid tumor such neuroblastoma and Wilms tumor (Mantadakis et al., 2008; Michon, 2002). Other solid malignant tumors which may give liver metastases are germ cell tumor, gastrointestinal stromal tumors, osteosarcoma, desmoplastic small round cell tumors and neuroendocrine tumors. In this study, we found 15.2% case with hepatomegaly and 28.6% found in hepatoblastoma (Mottl et al., 1993; Orraca et al., 2014).

Splenomegaly is defined as enlargement of the spleen measured by weight or size. A normally sized spleen measures up to 12 cm in craniocaudal length. A length of 12 cm to 20 cm indicates splenomegaly, and a length greater than 20 cm is definitive of massive splenomegaly (Poniewierska-Baran et al., 2016; Sharma et al., 2017). Splenomegaly is also described based on a shuffler scale. This method divides spleen into 8. Enlargement from left arcos costa to umbilical is Shuffler I-IV and from umbilical to SIAS Shuffler V-VIII. The normal-sized spleen is usually not palpable. Splenomegaly may be diagnosed clinically or radiographically. One of potential causes of splenomegaly is hematologic malignancies such as lymphomas, leukemia, myeloproliferative disorders. Neoplastic cells cause infiltration of the spleen leading to splenomegaly. In study conducted by Arya et al. 2004, found splenic involvement was seen in 22 children (15.6%) with lymphoma. Most of tumor relapse occurs significantly in children with splenic involvement and in those with splenomegaly. Presence of splenic deposits of neoplastic cell was an adverse prognostic factor for 5-year event-free survival. In this study, we found splenomegaly was one of clinical manifestation in tumor case and was found in lymphoma. It because spleen become the most common intraabdominal site of lymphoma metastasis through bloodstream and lymph circulation (Gavhane et al., 2011; Ueno et al., 2004; Wolf & Lavine, 2000).

Cancer-related anemia is mainly associated with direct tumor infiltration into the bone marrow, where the bone marrow is replaced by cancer cells. This condition cause hemoglobin values to decrease by 0.8 to 1.0 g/dL each week. Another condition that cause anemia related to tumor subject are treatment effects like chemotherapy on blood cell production that inhibiting the maturation of elytroid lineage cells or synthesis and secretion of erythropoietin suppression of erythropoiesis or anemia of chronic disease. In this study we found proportion of anemia was 57.6% with median of hemoglobin level is 10.74 (4.57-15.0) mg/dL that was considered mild anemia. Previous study in Europe also found more than half (80%) cancer patient have anemia. Hyper leukocytosis is defined as peripheral leukocyte count exceeding 100,000/mm. This condition can occur in lymphoma. Hyper leukocytosis is a medical emergency condition. The increased blood viscosity, secondary to high white cell count and leukocyte aggregates,

results in stasis in the smaller blood vessels. In this study we found hyper leukocytosis in tumor setting and all of case was in lymphoma. Similar study by Inaba et al. (2007), found hyper leukocytosis was found in lymphoma (10-35%).27 Lymphoma are more common to present with a leukemic phase and the presence of circulating lymphoma cells in peripheral blood giving rise to hyper leukocytosis. Leukopenia is low total white blood cell (WBC) count in the peripheral blood with value less than 4.0 x 109/L and neutropenia is value of absolute neutrophil count less than 1.5 109/L. In this study we found leukopenia in Wilms tumor (66.7%) and rhabdomyosarcoma (33.3%). All of neutropenia case was found in Wilms tumor (100%). Both of condition cause by bone marrow spreading of cancer and suppress blood cell production.

Thrombocytosis is elevation in the peripheral blood platelet count to values more than 400,000/µL. It is common in infancy and childhood, occurring in 3 to 13% of children. It can occur in underlying hematological disease, acute infection, chronic inflammation, chronic clonal diseases, Langerhans cell histiocytosis, and myeloproliferative disease. In this study thrombocytosis was found almost in all cases of tumor, mostly occur in retinoblastoma. Tumor cells activate platelets, and the metastatic potential of tumor cells correlates with their efficacy in inducing platelet aggregation. Tumor cells generate thrombin, a potent platelet activator agonist, either by direct contact with platelets or indirectly by stimulating tissue factor-mediated activation of the coagulation system that generates thrombin within the tumor microenvironment. This result is appropriate with previous study by Lastariana et al. (2018), which found mean thrombocyte in retinoblastoma was 448 103/µl considered as thrombocytosis and 36% of retinoblastoma was with thrombocytosis. Thrombocytopenia is platelet count less than 150,000/µL. Thrombocytopenia in cancer patients is induced by several mechanisms such as decrease in platelet production caused by bone marrow infiltration or by bone marrow suppression due to cytotoxic drugs, radiotherapy, or infections. Other cause is increasing in platelet destruction due to immune pathologies or disseminated intravascular coagulopathy (DIC) and platelet sequestration as a result of splenic metastasis. In our study, we found thrombocytopenia proportion was 8.7% and most of cases was in neuroblastoma. This result was appropriate with previous study by Ikizoglu et al. (2017), which stated neuroblastoma infiltration in bone marrow cause thrombocytopenia.

The immediate causes of death related to tumor or cancer were infections (39.6%), bone marrow suppression (29.2%), treatment-related mortality (27.1%), organ failure (22.9%), bleeding (16.7%) and other metabolic causes (8.3%). We found brain metastases and infection was dominated cause of death in our study because retinoblastoma was the most case of tumor and has higher risk of metastasis to central nervous system. This result was consistent with previous study that stated 56.6% retinoblastoma presented with meningeal involvement and 38.7% presented with intracranial mass. The metastasis occurrence was mainly due to direct invasion of the optic chiasma, intracranial optical nerve, supra sella cistern, meninges, even locally brain parenchyma. Meningeal involvement combined with spinal cord membrane involvement might be due to the meninges invasion and/or the spreading of CSF.

Tumor proportion have different distribution in child and adult. In our study, the five highest order of tumors case are Retinoblastoma, NHL, Osteosarcoma, Rhabdomyosarcoma, and Wilms Tumor. Retinoblastoma is as dominant case in this study due to age group 0-5 years as the highest distribution age of retinoblastoma case. Retinoblastomas are among the most common tumors in infants and are rarely diagnosed after 5 years of age. Retinal progenitor cell proliferation occurs during the first two trimesters, and there are reports of premature infants diagnosed with retinoblastoma. These observations, combined with studies on genetically engineered mouse models, suggest that retinoblastomas likely initiate from a retinal progenitor cell in utero and the time from tumor initiation to diagnosis ranges from a few months to a few years.

Malignant bone tumor consists of some tumor variant. Osteosarcoma and Ewing sarcoma are two most common malignant bone tumor in children. The average age at diagnosis of osteosarcoma was 11.9 years. All tumors were located in long bones and 96% of them in the lower limbs. In this study, we found osteosarcoma was the most common solid tumor in >5-14 and >14 years group of age. This condition was appropriate with some study that stated most common malignant solid tumors in adolescents are extra cranial germ cell tumors, bone and soft tissue sarcomas, melanoma, and thyroid cancer. The peak prevalence of osteosarcoma coincides with rapid growth of the skeletal system during puberty. Females under 15 years of age have a higher prevalence of osteosarcoma and the prevalence of the disease has an earlier peak in females when compared with males (12 versus 16 years), correlating with an earlier age of onset of puberty. Osteoblasts likely undergo rapid expansion during this period of development, making them more susceptible to malignant transformation. Furthermore, changes in hormone levels, cytokines or chemokine in adolescents may contribute to the initiation and progression of osteosarcoma.

Skeletal Ewing sarcoma is other common bone tumor in children. It is thought to represent a clinic pathologic spectrum of the same neoplastic entity to primitive neuroectodermal tumor (PNET). The highest incidence is in the second decade of life, with approximately 9-10 cases per million per year seen in patients aged 10-19 years compared to an overall incidence of three cases per million per year in the United. It is uncommon in patients

younger than 5 years or older than 30 years. A slight male predominance exists with ratio 1.5:1. Primitive neuroectodermal tumors are in the Ewing's sarcoma family of tumors and are composed of small round cells. The prognosis in general is poor because of overt metastasis at the time of diagnosis. Most of patient were less than 20 years of age.38 In this study, we found prevalence Ewing sarcoma and PNET 2.0% and 1.0% respectively, with prevalence in >5 years old. Ewing sarcoma found predominantly in male. This result was appropriate with previous study in United States that stated Ewing sarcoma predominantly in males with peak prevalence 10-19 years.

Lymphoma is a neoplasm caused by malignant transformation of lymphoid cells. Lymphoma is one of the most frequent childhood malignancies (prevalence rate of 12%–15%), closely following acute leukemia. There are 2 clinic pathologic lymphoma types: Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL), with distinct clinical subtypes within each of those types. Variations in lymphoma prevalence, age, and sex distribution occur in different pediatric populations according to geographic location and socioeconomic environment. In this study we found higher case of NHL than HL. This result was appropriate with previous data that found most lymphoma case occur before 20 years old and HL case was increasing with age but HL dominated in adult (Harvey et al.,2012; Harvey, 2001).

Neuroblastoma is an embryonic malignant tumor originating from the neural crest. Each year, approximately 1,500 cases occur in Europe and 700 in the United States and Canada, accounting for about 28% of all cancers diagnosed in European and United States infants. Its incidence peaks in infancy and then drops by half in the second year of life. In this study, we found prevalence of neuroblastoma was 5% and case was decreased after 14 years old. This result was appropriate with previous study by Sutaryo & Kristian (2019), that found incidence was decreased after 14 years old because its embryonic tumor (Hosain et al., 2005; Barreirinho et al., 2003). Primary liver malignancies are uncommon in children with annual incidence rate of 1.5 per million and account for only 0.5% to 2% of all pediatric neoplasms (100-150 new cases/year in United States). The two main histology are hepatoblastoma and hepatocellular carcinoma. Hepatoblastoma is the most common malignant tumor of the liver in children with a higher incidence during the first year of life. Hepatocellular carcinoma is the second most common hepatic malignancy and occur primarily in adolescents. In this study we find hepatoblastoma was 4.0% of solid tumor with prevalence rate before 0-5 years. This condition is appropriate with other study that stated patients with hepatoblastoma were younger than those with hepatocellular carcinoma with mean age 9 month (2-36 months) and HCC with mean age 10 years (0.7-15 years). Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children. It represents 5-8% of childhood malignancies. Most case was found in 0-14 years old and young adult 15-19 years. There is a slight predilection for disease in males, with a male to female ratio of 1.3:1. In this study we found prevalence rhabdomyosarcoma was 11.0% of all pediatric solid tumor, with predominant case in male (Solberg et al., 1979; MacLennan et al., 2002).

This result is appropriate with previous study in Egypt.43 It because gonadal steroid-based sex hormones play an important role in normal development and tumor genesis especially in RMS pathogenesis. RMS also share several common markers with the germ line-derived cells like express several cancer testis antigens (CTAs). Germ cell tumors are neoplasms that develop from primordial germ cells of the human embryo, which are normally destined to produce sperm or ovarium. Based on pathologic and histologic examination, it consists of seminoma, embryonic carcinoma, yolk sac tumor, choriocarcinoma, and teratoma (immature, mature, with malignant transformation). In this study we found germ cell tumor prevalence was 7.0% that consist of teratoma 2.0% and yolk sac tumor 5.0%. This result was similar to previous study in Japan that found germ cell tumors are rare in childhood and high incidence younger than 15 years. We also found case dominant in female. The high incidence of germ tumor in female may be due to earlier development of ovarian tumors than testicular tumors (Maeda et al., 2003; Blach et al., 1994).

Nasopharyngeal carcinoma is the most commonly diagnosed head and neck malignancy in China and Southeast Asian countries, but children and adolescent nasopharyngeal carcinoma is very rare worldwide. The incidence among children and adolescents varies greatly among different regions and races, accounts for 0.1-2.3% of all nasopharyngeal carcinoma in China and 2%-18% in other countries. In this study we found prevalence of Nasopharyngeal carcinoma was 2.0% with age >5-14 years old. This result was appropriate to result other study that found median age of 5.2 years. Hemangiomas are true neoplasms of endothelial cells and should be differentiated from vascular malformations which are localized defects of vascular morphogenesis. Hemangiomas are common benign soft tissue tumor of infancy and childhood, occurring in 12% of all infants and are found in greater frequency in girls, whites, premature infants, twins and are usually born to mothers of higher maternal age. In this study, all of hemangioma was found in 0-5 year's group. This result is appropriate to previous study in India that found most case in infant. Neurofibromatosis commonly occurs in the skin and may be cutaneous or subcutaneous (Ribatti et al., 1999; Whyte, 1995). They often arise in later childhood, especially in early puberty, and increase in size and number during adolescence and adulthood. Some type like subcutaneous neurofibromas present some risk of malignant

transformation and may cause pain when pressured. Some kind like Plexiform neurofibromas (PNF) is congenital, as they arise from embryonic Schwann cells, and require monitoring because of their nearly 10-50% lifetime chance of malignant transformation. In this study, we found that prevalence of neurofibroma was 1.0% and case was in >5-14 years group age that appropriate with previous data in Cuba that found prevalence of fibromatosis was high in children aged 9–11 years old (Chekol et al., 2012; Grzych et al., 2019).

Medulloblastoma is a highly malignant neuroectodermal tumors that belongs to high-grade glioma (HGG). It commonly occurs among children, counting for approximately 30% of pediatric CNS neoplasms, however, it is a rare disease among adults, with an annual incidence rate of 0.05 per 100,000 per year. In this study, we found prevalence of medulloblastoma was 1.0%. This result was appropriate to study in China that state medulloblastoma is fewer than 3% of all the primary neoplasms of the CNS. Ependymomas are the third most common pediatric tumor of the CNS accounting for 6% to 12% of brain tumors in children. Almost 90% of pediatric ependymomas are intracranial in origin, with two thirds arising in the posterior fossa. Nevertheless, pediatric ependymomas are capable of occurring anywhere within the CNS, including the parenchyma of the cerebral hemispheres and, rarely, the spinal cord. In this study we found prevalence of ependymoma is 2%. This result was appropriate to Kilday et al. (2009), which stated ependymoma was almost 2% tumor in children with more case under 5 years.

Conclusion

Total solid tumor in Sanglah Hospital on January 2016 until December 2020 was 92 cases with prevalence rate 38.6%. Retinoblastoma was the most case with range of age 0-5 years. Most of case was male and domiciled in Bali. Palpable mass and lymphadenopathy were major clinical manifestation in child with solid tumor. Hematologic manifestation in tumor case were anemia and thrombocytosis. Mortality rate was 32.6% with majority cause of death was brain metastases (Haswadi et al., 2018; Archana et al., 2016).

Limitation of study

The weakness of this study was the uses of secondary data from registry, therefor some variable can't be evaluated because of incomplete data. It is needed further study about association between characteristic and survival rate in pediatric solid tumor patient.

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