

MATURE B CELL LYMPHOMA AT VIETNAM NATIONAL CHILDREN'S HOSPITAL: CLINICAL CHARACTERISTICS AND INVESTIGATION FINDINGS

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ABSTRACT

Background: Mature B cell lymphoma (B-NHL) is a highly aggressive and fast-growing human disease in children. Clinical symptoms and investigation findings have characteristics of lymphoma in general and B-NHL in particular, which helps in the diagnosis and treatment process. This study aims to review some clinical characteristics and investigation findings of B-NHL patients at the Vietnam National Children's Hospital.

Objective and methods: A descriptive study was carried out in all B-NHL patients under 16 years old that start their treatment in VNCH since 01 January 2015 and end before 30 June 2021, excluding patients can't follow up.

Results: 84 B-NHL patients had a mean age of 5.4 years. Male accounts for 75%, male/female ratio is 3/1. The most common clinical symptoms on admission were gastrointestinal symptoms (58.3%), symptoms in the head and neck area appeared less (26.2%). The group had symptoms of onset in the digestive system, the most common was abdominal pain (77.6%), followed by abdominal distension and palpable abdominal mass (42.9%). In the group with symptoms that started in the head and neck region, the most common was the appearance of head and neck mass and cervical lymphadenopathy. Symptoms B was seen in 26 patients (31%). On imaging, 45.2% of patients had tumors from 2 or more locations, 85.7% of patients had lesions in the abdomen, followed by head and neck (40.5%). In the group of abdominal lesions on imaging, the most common are gastrointestinal infiltrates and renal infiltrates; In the group of lesions in the head, face and neck, sinus and cervical lymph nodes are common. 11.9% of patients had central nervous system (CNS) infiltrates and 29.8% of bone marrow infiltrates. BL histopathology was the most common (75%), followed by DLBCL 11.9% and others 13.1%. The BL type is more common with bone marrow and CNS metastases than other histopathological types. Patients are mainly in stage 3 (51.2%) and stage 4 (33.3%). 57.1% of patients had LDH concentration below 1000 IU/ml and 45.3% of patients had LDH concentration above 1000 UI/ml. The c-MYC gene rearrangement was found in 10 out of 15 patients, of which 8 were BL.

Conclusions: Patients with B-NHL had mean age 5.4 years old and their own clinical and investigation characteristics that help in diagnosis, monitoring of treatment.

Keyword: Mature B cell lymphoma, clinical characteristic of mature B cell lymphoma.

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I. INTRODUCTION

Mature B cell lymphoma (B-NHL) accounts for 50-60% of non-Hodgkin's lymphoma in children and adolescents worldwide [16]. According to the histopathological classification (WHO 2008), B-NHL is divided into many subgroups, but in children, Burkitt's lymphoma (BL) and diffuse large B-cell lymphoma (DLBCL) are commonly encountered. A study by Do Thi Thanh Thuy in 2016 on 125 children with non-Hodgkin's lymphoma found that Burkitt's lymphoma accounted for 56.8% and diffuse large B-cell lymphoma accounted for 3.2% [3].

B-NHL is malignant, prone to spreading and progresses rapidly. Clinical symptoms manifest in various organs, particularly in the abdominal and cervical regions. Specific clinical examinations, notably imaging diagnostics, play a crucial role in guiding the diagnosis and treatment of this condition.

II. RESEARCH SUBJECT AND METHOD

We conducted a cross-sectional descriptive study, longitudinally followed on 84 patients under 16 years old diagnosed with B-NHL based on histopathology, immunohistochemistry and immunophenotype at the Vietnam National Children's Hospital (VNCH) from January 1, 2015, until the treatment endpoint before June 30, 2021. Exclusions comprised individuals unwilling to participate in the study or those lost to follow-up.

Variables under study included: age (year), age group (< 5 years old, 5 - 10 years old, ≥ 10 years old), gender (male, female), rates of clinical symptom groups (digestive, cervical, respiratory, nervous system, B symptoms), and the frequency of occurrence within these groups. Clinical symptom groups in imaging diagnostics included: tumor site rates at diagnosis encompassing abdominal, cervical, respiratory, central nervous system (CNS); number of tumor sites, both singular and multiple; lesion characteristics based on site groups. Individuals with bone marrow involvement (under 25%, ≥ 25%) and those without, CNS-involved and non-CNS-involved cases, LDH blood concentration:

<1000 IU/ml, ≥1000 IU/ml. Histopathological types' rates: BL, DLBCL, and others; categorized by disease stage, bone marrow and CNS infiltration status. Disease stage ratios (stages 1, 2, 3, 4). Identification of individuals with c-MYC translocation, without, and c-MYC translocation based on histopathology.

Disease staging according to Murphy's classification (1980).

Data handling: Data entry and processing were performed using SPSS 20.0 software.

Ethical issue: The study received ethical approval from the Medical Ethics Committee of the Vietnam National Children's Hospital.

III. RESULTS

3.1. General characteristics of the 84 patients in the study

The mean age was 5.4 years. The majority of patients were under 5 years old (51.2%), followed by the group aged 5 to 10 years (33.3%) and those over 10 years old (15.5%).

Males accounted for the majority at 75%, while females comprised 25%. The male-to-female ratio was 3:1.

3.2. Clinical symptoms

Table 1. Rates of symptoms presenting by initial location groups

Location	Number of patients	Percentage %
Digestive	49	58.3
Head-neck	22	26.2
Nervous	13	15.5
Respiratory	3	3.6
Genital	1	1.2

Comment: The most prevalent clinical symptoms are related to the digestive system (58.3%), followed by fewer incidences in the cervical region (26.2%), and least frequently, neurological symptoms (15.5%). Some patients exhibit symptoms in multiple locations.

Table 2. Rates of clinical symptoms upon admission

Location	Symptom	Number of patients
Digestive (n=49)	Abdominal pain	38
	Abdominal distension/palpable abdominal mass	21
	Enlarged liver/spleen	9
	Vomiting/vomiting blood	8
	Bloody stool	4
Head - neck (n=22)	Mass in the head-neck area	11
	Neck lymph nodes	11
	Persistent nasal congestion/runny nose	6
Nervous (n=13)	Drooping eyelid	9
	Decreased vision	4
	Weak limbs	3
	Headache	3
	Urinary retention	2
Chest (n=3)	Persistent cough	2
	Pulmonary basilar atelectasis	2
	Chest pain	1
Genital (n=1)	Enlarged testicle	1
Symptom B		26

Comment: Among the digestive symptom group, abdominal pain is the most common (38/49). The most prevalent symptoms in the head-neck group are masses in the neck and cervical lymph nodes (11/22). Neurological symptoms include ptosis (9/13) and decreased visual acuity (4/13). B symptoms appeared in 26 patients (31%).

3.3. Subclinical symptoms

Table 3. Rates of tumor location occurrence by imaging diagnosis location groups

Number of tumor locations	Number of patients	Percentage %
1 location	46	54.8
≥ 2 locations	38	45.2
Total	84	100

Comment: 54.8% of patients showed tumors at only one location; 45.2% exhibited tumors at two or more locations.

Table 4. Rates of tumor location groups on imaging diagnosis (n=84)

Location	Number of patients	Percentage %
Abdomen	72	85.7
Head-neck	34	40.5
Chest	18	21.4
Central nervous system	6	7.1
Bone	23	27.4

Comment: Abdominal lesions were most common (85.7%), followed by facial and head-neck lesions at 40.5% and thoracic lesions at 21.4%, respectively.

Table 5. Rates of lesions by imaging diagnosis location groups

Features on imaging diagnosis	Specific location	Number of patients	Percentage %
Abdomen (n=72)	Stomach - intestine	40	55.6
	Kidney	33	45.8
	Liver/spleen	28	38.9
	Pancreas	16	22.2
	Lymph nodes	15	20.8
	Peritoneum	12	16.7
	Chest mass	9	12.5
	Ovarian/testicular	8	11.1
Head-neck (n=34)	Sinus	16	47.1
	Lymph nodes	15	44.1
	Soft mass	11	32.3
	Extracranial base	7	20.6
	Pharynx pleura	5	14.7
Chest (n=18)	Pleura	9	
	Ventricle	4	
	Lung	2	
	Chest wall mass	2	
	Lymph nodes	2	
	Heart	1	
Central nervous system (n=6)	Spinal marrow	5	
	Brain	1	
Bone (n=23)	Facial bone	21	
	Rib	1	
	Pelvis	1	

Comment: - In abdominal lesions, stomach - intestine infections were most common (55.6%), followed by kidney (45.8%), liver - gallbladder (38.9%), and spleen (22.2%).

For head-neck lesions: sinus masses were predominant (47.1%), followed by cervical lymph nodes (44.1%), soft tissue masses (32.3%), and extracranial base masses (20.6%).

Table 6. Patients with bone marrow and central nervous system infiltration

CNS infiltration	Bone marrow infiltration	Number of patients
With CNS (10)	Bone marrow < 25%	1
	Bone marrow ≥ 25%	6
	No marrow metastasis	3
Without CNS (74)	Bone marrow < 25%	1
	Bone marrow ≥ 25%	17
	No marrow metastasis	56

Comment: 10 patients had CNS infiltration (11.9%), and 25 patients had bone marrow CNS infiltration (29.8%).

Table 7. Proportion of patients by histopathology

Histopathology	Number of patients	Percentage %
BL	63	75
DLBCL	10	11.9
Other	11	13.1
Toal	84	100

Comment: Burkitt’s Lymphoma (BL) accounted for the highest percentage at 75%, followed by Diffuse Large B cell Lymphoma (DLBCL) at 11.9%, and other types at 13.1% (B cell non-Hodgkin lymphoma, intermediate between BL and DLBCL).

Table 8. Proportion of patients by disease stage

Stage	Number of patients	Percentage %
1	4	4.8
2	9	10.7
3	43	51.2
4	28	33.3
Total	84	100

Comment: Predominantly, stage 3 (51.2%) and stage 4 (33.3%) were observed.

Table 9. Distribution of histopathology by bone marrow and CNS infiltration status

Histopathology	Infiltration		
	Bone marrow <25% (n=2)	Bone marrow ≥25% (n=23)	CNS (n=10)
BL	2	21	9
DLBCL	0	1	0
Other	0	1	1

Comment: Most patients with bone marrow and CNS infiltration had BL.

Table 10. Proportion of patients by LDH concentration

LDH concentration	Number of patients	Percentage %
< 1000	48	57.1
≥ 1000	36	42.9
Total	84	100

Comment: 57.1% of patients have LDH < 1000, 45.3% of patients have LDH ≥ 1000

Table 11. Distribution of c-MYC gene rearrangement by histopathology

	BL	DLBCL	Other	Total
With rearrangement	8	1	1	10
Without rearrangement	1	1	2	4
No result	0	0	1	1
Total	84	100		

Comment: Among 84 patients, 15 were tested for gene rearrangement. c-MYC gene rearrangement was mainly observed in BL.

IV. DISCUSSION

4.1. General characteristics

The average age of onset at 5.4 years is lower than that in studies worldwide. A multicenter study in Israel on 88 cases of mature B cell lymphoma conducted by Eldar showed a male predominance (72%), with a median age of 8.9 years [4]. Our study predominantly involves patients under 5 years old (51.2%), differing from previous studies that often involve older patients. Mario's study in Mexico showed the over-5 age group constituted 68.3%, with the under-5 age group at 31.7% [5]. Male prevalence over females, with a male-to-female ratio of 3:1, aligns with most other studies. Differences in average age might relate to the trend of cancer affecting younger individuals or the Vietnam National Children's Hospital possibly admitting younger patients compared to cancer treatment centers catering to both children and adults.

4.2. Clinical and subclinical symptoms

4.2.1. Clinical symptoms

Our study indicates that the most prevalent symptoms upon admission are related to the digestive system (58.3%). Symptoms in the cervical region were less frequent (26.2%), followed by neurological symptoms (15.5%). Among those presenting digestive symptoms, abdominal pain was the most common (38/49), followed by abdominal distension and palpable abdominal masses (21/49). In cases with symptoms originating from the head and neck, the most common presentations were masses in these regions and cervical lymph node enlargement. Ptosis and decreased visual acuity were common neurological symptoms. B symptoms were observed in 26 patients (31%). Some patients exhibited symptoms in multiple organs.

The clinical symptoms observed at onset are largely similar to studies in American and European countries but differ from some African countries. Mario's study in Mexico showed that tumors primarily appeared first in the abdomen, followed by the cervical and thoracic

regions, with B symptoms in 34% of patients [5]. Biko's study in the US found that common gastrointestinal symptoms included palpable masses, abdominal pain, and abdominal distension [2]. However, McGoldrick's study in Uganda (Africa) revealed that 44% of patients presented clinically in the cervical region, 42% in the abdomen, and 22% with neurological symptoms [10]. In North and South American countries, isolated BL predominates and often presents with initial symptoms in the abdomen. Conversely, in African countries, endemic BL is predominant, and initial symptoms often present in the head - neck region.

4.2.2. Subclinical symptoms

On imaging diagnosis, 54.8% of patients showed tumors at a single location, while 45.2% exhibited tumors at two or more locations, indicating the disease's disseminating nature. When suspecting B-NHL, it's crucial to assess all body locations using computed tomography scans, magnetic resonance imaging, and PET-CT scans. In our study, 85.7% of patients had abdominal involvement, followed by the head and neck region (40.5%). Among those with abdominal lesions, stomach-intestine infections and kidney involvement were most prevalent. Within the head - neck lesion group, sinus masses and cervical lymph node enlargement were commonly observed.

Our study demonstrates the highest incidence of tumors in the abdominal region, aligning with findings from studies in the Americas and Europe. Morale's study highlighted the most frequent initial location as the abdomen, accounting for 48%, followed by the head and neck at 20% [6]. According to Molyneux and Thomas, particularly in computed tomography scans, the most common location for lesion is the abdomen [12]. In the abdominal and pelvic areas, lesions often occur in the stomach-intestine, mesenteric lymph nodes, renal, hepatic, and splenic regions. Eldar's study of 88 patients indicated that 43% initially presented with abdominal symptoms, and 45% had head and neck manifestations [4]. Similarly, Kamona's study exhibited similar lesions to ours,

albeit with varying ratios. Lesions to the stomach-intestine were found in 19 children (57.5%), kidneys in 27.2%, mesenteric regions in 24.2%, liver in 12.1%, spleen in 9%, and pancreas in 3%. Head and neck masses accounted for 24.2%, with cervical lymph node enlargement at 24.2% [9]. In another study by Hong, focusing on head and neck primary tumors, imaging identified tumor locations, including the nasopharynx (most common, 40%), followed by the upper jawbone and maxillary sinus [8]. Although the proportions of head and neck characteristics differ, the overall appearance and distribution of locations align closely with our study. Therefore, B-NHL lesions tend to disseminate, primarily appearing in the abdominal and head and neck regions.

4.2.3. Bone marrow and central nervous system infiltration

Our study observed 11.9% of patients with CNS infiltration and 29.8% with bone marrow infiltration, aligning with findings from several authors. According to Worch, approximately a quarter of children with B-NHL have bone marrow infiltration and 5-10% exhibit CNS infiltration [16]. In Morale's study, the bone marrow infiltration rate was 24%, and CNS infiltration was at 10% [6].

4.2.4. Pathological anatomy

In our study, BL was the most prevalent (75%), followed by DLBCL at 11.9%, and other types at 13.1%. BL tended to metastasize more to the bone marrow and CNS compared to the other two histological groups. This outcome resonates with global studies. According to Sandlund, the most common B cell lymphomas in children are BL and DLBCL [14]. Morale's study indicated that 76% of patients were BL, 23% were DLBCL, and 1% were other types [6]. Miles stated that BL frequently correlates with CNS and bone marrow infiltration [11]. This propensity is due to BL's highly aggressive nature in children, leading to a higher risk of infiltration.

4.2.5. Disease stage

In our study, patients predominantly fell within stage 3 (51.2%) and stage 4 (33.3%),

mirroring proportions found in various centers. Morale's study reported 52% of patients in stage 3 and 30% in stage 4 [6]. Afungchwi's study in Cameroon in 2019, comprising 225 BL patients, showed the majority were in stage 3 (81.4%) [1]. In children, due to the high incidence of BL often presenting in the abdomen and the higher rates of bone marrow and CNS infiltration, stages 3 and 4 are more prevalent.

4.2.6. LDH concentration

This study indicated that 57.1% of patients had LDH levels below 1000 IU/mL, while 45.3% had LDH levels above 1000 IU/mL. This aligns with Morale's study (50% of patients had elevated LDH over 1000 IU/mL) but differs from Goldman's study (78% of patients had LDH elevation over 1000 IU/mL) [7]. This disparity could stem from variations in the number of patients among the studies.

4.2.7. c-MYC gene rearrangement

Out of 15 patients, 10 showed a c-MYC gene rearrangement, with 8 of them being BL cases. Although the number of patients tested for this rearrangement was limited, the prevalence of this rearrangement was relatively high, particularly in BL cases, while DLBCL cases showed very few instances of this rearrangement. This outcome aligns with observations worldwide. Previous studies suggested that only 5 to 10% of BL cases lacked the c-MYC rearrangement [15]. Reiter's study indicated that 5-10% of DLBCL cases exhibited this rearrangement [13].

V. CONCLUSION

Patients diagnosed with mature B cell lymphoma had an average age of 5.4 years, with predominant symptoms manifesting in the abdominal and cervical regions, often metastasizing to the bone marrow and central nervous system. The histopathological type, primarily Burkitt lymphoma, was most prevalent, and cells frequently exhibited the c-MYC gene rearrangement. These distinctive characteristics aid in the diagnosis, monitoring, and treatment of the disease.

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