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A Case of Childhood Burkitt's Lymphoma with Gingival Swelling as The First Symptom

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Keywords:

Burkitt's lymphoma; Gingival swelling; Diagnose

Abbreviations:

BL: Burkitt's Lymphoma**;** PET-CT: Positron Emission Tomography-Computed Tomography; CNCL: China Net-Childhood Lymphoma: KFX: Kangfuxin Liquid: BL/B.AL: BL/Leukemia; EFS: Event-free Survival: PFS: Progression-free Survival; LDH: Lactate Dehydrogenase

1. Abstract

Burkitt's lymphoma (BL) is a highly infiltrative malignant lymphoma caused by germinal B-cell differentiation. There are several oral symptoms of BL, including tooth mobility, pain, gingival swelling, maxillofacial swelling and pain, and facial sensory disturbances. In this paper, we report a case of BL in a 4-year-old child who initially presented with gingival swelling. The diagnosis of BL/leukemia (stage IV) was confirmed by the bone marrow examination, bone marrow flow cytometry, and B lymphocytoma mutation gene screening test. After chemotherapy, the general condition improved, and then there was swelling and pain in the right cheek. Considering the recurrence of the disease, the patient died half a year later. This case is characterized by BL with oral symptoms as the first symptom, emphasizing the important role of physicians in early detection of systemic disease.

2. Introduction

In 1958, Burkitt's lymphoma (BL) was initially discovered and named by British surgeon Dennis Burkitt [1]. BL is a highly infiltrative malignant lymphoma caused by germinal B-cell differentiation. Its development is associated with MYC gene dysregulation, Epstein-Barr virus infection and falciparum malaria [2]. The clinical manifestations of BL are endemic, sporadic, and immunodeficiency-associated [3]. Endemic BL is more universal in equatorial Central Africa. More than 95% of endemic BL are associated with Epstein-Barr virus and falciparum malaria infections. Sporadic BL, the most common type, accounts for 30% of childhood lymphomas with no differences in specific geographical distribution and climate. It, most commonly manifested as abdominal masses, such as small intestinal, mesenteric and ovarian masses. Approximately 25% of sporadic BL could have great impacts on the head and neck, especially on cervical lymph nodes. Immunodeficiency-associated BL mainly occurs in HIV-infected patients and organ transplant recipients, mainly involving lymph nodes and bone marrow [4,5,6]. There are several oral symptoms of BL, including tooth mobility, pain, gingival swelling, maxillofacial swelling and pain, and facial sensory disturbances. [6]. In this paper, we report a case of BL in a 4-year-old child who initially presented with gingival swelling. The presentation and treatment of such cases are rare. The second recurrence of this case also had oral manifestations of right gingival swelling on the right side of the mouth, and the prognosis of the case was poor. Under the exclusion of the etiology of simple periodontal inflammation, if the patient presents with excessive tooth mobility and severe alveolar bone resorption around the eruption of permanent teeth, dentists should attach great importance to the examination of the general condition.

3. Case Report

Consent for publication in this report was obtained from the patient's parents. The patient (male; aging 4-year-old) with a 2-week history of swelling on the right cheek and swollen gums was diagnosed in the Department of Oral Medicine in August 2018 Past medical history. In January 2018, the patient visited another hospital due to gingival swelling, and was given "antibiotics" for "acute periodontal abscess", but the effect was poor. In February 2018, the patient was admitted to the Department of Pediatric Internal Medicine due to persistent low-grade fever. The diagnosis of BL/leukemia (stage IV) was confirmed by the bone marrow examination, bone marrow flow cytometry, and B lymphocytoma mutation gene screening test. The condition was improved after anti-infection and chemotherapy. When the patient suffered from swelling and pain of the right cheek and gingival swelling and pain of the right lower posterior tooth again, he visited the Department of Oral Medicine. After reexamination of Positron emission tomography-computed tomography (PET-CT), considering the recurrence of the disease, there was no significant improvement after chemotherapy. The family gave up treatment, and the patient died half a year later **(1)**. Clinical examination: A lymph node about 2.5 * 3 cm in size was palpable in the submandibular region. The throat of the child was congested with I° tonsillar enlargement. Neurological examination showed that the right frontal striae became shallower when lifting the eyebrows. The right eyelid could not be completely closed when closing the eyes. The right nasal striae were shallower when shrugging the nose. The drumsticks could be drummed, the neck was soft, and the corneal reflex existed. Dental examination revealed fair oral hygiene and essentially normal occlusal relationship. The buccal lingual gingiva of the lower right first deciduous molar and the lower right second deciduous molar were red, swollen and bright with diffused swelling according to the palpation (+). The erosive surface was observed on the far middle buccal side that was covered with a pseudomembrane of the lower right second deciduous molar. A lingual deviation and detectable periodontal pockets with percussion (+ +) were found, which indicated the grade Ⅱ loosening (Figure 1). The buccal lingual gingiva of the lower left second deciduous molar was mild red and swollen with percussion (-), which indicated the grade I loosening **(2)**. Auxiliary examination: Laboratory tests showed white blood cells of 8.69×10^9/L (normal range 8-10×10^9/L), hemoglobin of 85g/L (normal range 120-140g/L), platelets of 352×10^9/L (normal range 100-300×10^9/L), lactate dehydrogenase of 1503 U/L (normal range 100-300U/L). Examination and analysis of myelogram displayed that the lymphocyte system was highly proliferative. The cells were large and blue with coarse chromatin, nucleoli in some cells, small cell mass, vacuoles in the nucleus and cytoplasm in most cells, prolymphocytosis, and prolymphocytosis, considering the possibility of BL (Figure 2). Bone marrow fluid flow cytometry results: CD45dimCD19 + cells about 18.9%; CD20:96.3%, Kappa: 86.5%; CD10:56.2%; CD22dim: 44.6%; CD79b: 85.3%; CD23:96.2%; FMC: 97.7%; CD24:61.5%. It should be reminded that some abnormal B lymphocytes were found. Genetic screening for B lymphocytoma mutations: detection of MYC gene p.Y89H, p.P78T, D236H site mutation. Abdominal ultrasound displayed several lymph nodes with heterogeneous hypoechogenicity in the right abdomen. Cerebrospinal fluid cytology revealed multiple heterosexual cells, including lymphoma, suggesting involvement of the central nervous system. PET-CT (February 27th, 2018, Figure 3): ① Increased diffuse metabolism of the whole-body bone marrow. Lymphoma may involve bone, bone marrow, lymph nodes, pancreas, and both kidneys. ② Significant bone destruction of the mandible and filling of the surrounding soft tissue shadows. PET-CT (August 24th, 2018, Figure 4) reexamination showed that there was no abnormality in the metabolism of the whole-body bone marrow, multiple bones, submandibular lymph nodes, pancreas, or both kidneys. The right mandible was still hypermetabolic with visible bone destruction, soft tissue mass formation, unclear boundary, and heterogeneous density. Panoramic radiography before treatment (January 1st, 2018, Figure 5) showed low-density destruction of the mandibular body, low-density shadows in the apical region of the lower right second deciduous molar and the lower left second deciduous molar, and loss of mandibular second premolars. Panoramic radiography reexamination with chemotherapy showed (August 17th, 2018, Figure 6) that there was root apical truncating resorption of the lower right second deciduous molar and bone destruction edge affected tooth germs of the lower right first permanent molar and the lower right first premolar, which led to compression displacement. Compared with before treatment, the degree of bone destruction around the apical region of the lower right second deciduous molar and the lower left second deciduous molar was improved with increased bone mineral density.

(3) Diagnosis: *1.* BL/leukemia (stage IV) *2.* periodontal abscess

(4) Treatment: *1.* The child was treated with China Net-Childhood Lymphoma (CNCL)-HL GroupC regimen. *2.* Oral local treatment: the child was gargled with Kangfuxin liquid (KFX) solution and treated with gingiva wiping, pseudomembrane washing, 3% hydrogen peroxide pericoronal irrigation, and education to maintain oral hygiene. In addition, after communication with the physician, the supportive treatment and systemic antibiotics were recommended to reduce systemic infection and periodontal inflammation.

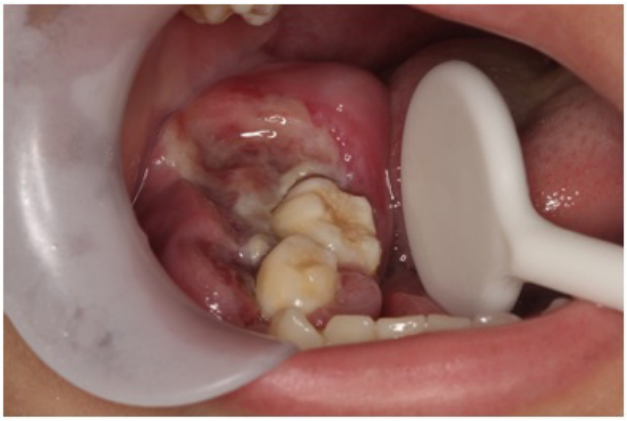

Figure 1: The buccal lingual gingiva of the lower right first deciduous molar and the lower right second deciduous molar were diffused swelling. Lingual deviation of the lower right second deciduous molar.

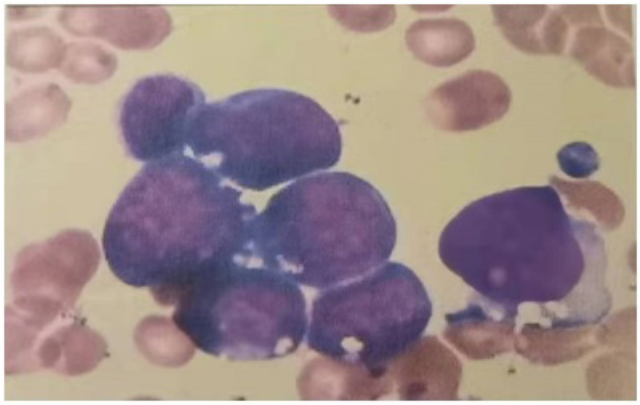

Figure 2: Increased pro- and prolymphocytes by Myelogram examination. (Wright Giemsa staining, 10×100).

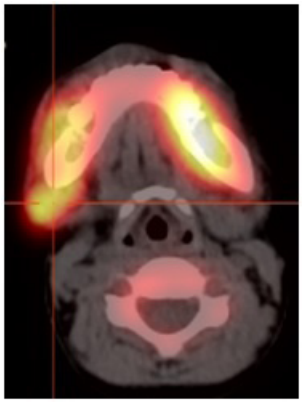

Figure 3: Systemic increased bone metabolism and bone destruction in both mandibles by PET-CT.

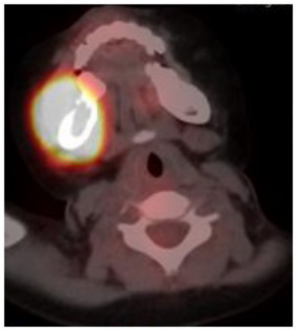

Figure 4: Increased metabolism in the right mandible with visible bone destruction and soft tissue formation by PET-CT.

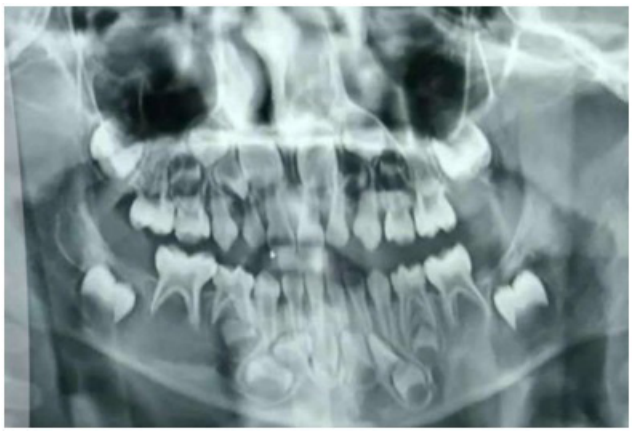

Figure 5: Panoramic radiography (January 1, 2018): low-density destruction of the mandibular body.

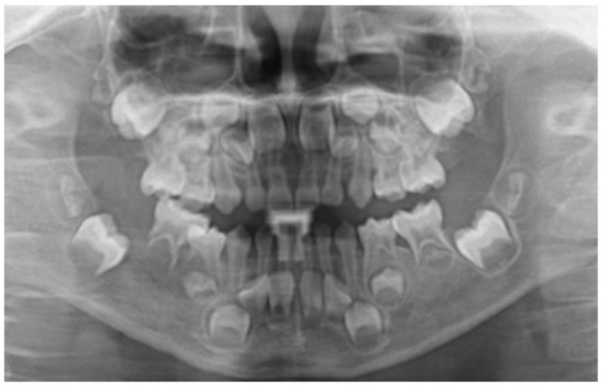

Figure 6: Panoramic radiography (Aug. 17, 2018): there was root apical truncating resorption of the lower right second deciduous molar and bone destruction edge affected tooth germs of the lower right first permanent molar and the lower right first premolar, which led to compression displacement.

4. Discussion

BL has unique clinical and morphological characteristics with rapid development, short course of disease, and high degree of malignancy, accounting for 30-50% of pediatric non-Hodgkin's lymphoma [7]. BL is extranodal or characterized by leukemia. Due to the short doubling time of tumor cells, most patients suffer from bone marrow involvement and progress to leukemia stage (tumor cells > 25%), which is called BL/leukemia (BL/B.AL). BL is mostly characterized by high tumor burden at initial diagnosis and more prominent symptoms of abdominal and maxillofacial tumor masses [8]. Thrombocytopenia is the most common hemogram in patients. Anemia or leukopenia may occur, and high white blood cell count may occur in some patients. The varied number of tumor cells may be seen in the peripheral blood. BL/B.AL is more prevalent in pediatric non-Hodgkin's lymphoma. The diagnosis of BL requires a comprehensive analysis combined with cytomorphological, immunophenotypic and genetic characteristics [9]. Pathological findings are mainly composed of poorly differentiated lymphocytes, mixed with phagocytic histiocytes with clear cytoplasm, leading to typical "starry sky" images [10]. On the immunophenotyping, IgM and B cell-associated antigens (e.g., CDl9, CD20, CD22, CD79a), CDl0, and BCL-6 were mostly expressed, but CD5, TdT, and BCL-2 were not expressed [11]. In addition, almost 100% of Ki-67 was positive, CD45 was highly expressed, and cD34 and TdT were often negative. These findings were consistent with the high expression of CD19, CD20, CD10, CD22, and CD79b in this case. Cytogenetically, the characteristic change is a translocation of the C-myc gene [12]. In this case, changes in MYC gene locus were detected in genetic screening. Mutations in the MYC gene can be found in about 40% of BL. MYC gene is an oncogene encoding nuclear protein. MYC gene product, C-myc gene can affect the protein transcription levels of apoptosis, cell growth, differentiation, and other biological processes. The three c-myc translocations that often occur in BL accelerate malignant tumor growth by facilitating cell proliferation [8]. It is interesting to note that the occurrence of sporadic BL is mostly affected by the relationship between oncogenes and cancer-suppressor gene mutations. P53 mutation, the most common secondary change in sporadic BL, is closely related to MYC dysregulation and abnormal activation of the PI3K-AKT signaling pathway [13]. Mutation of p53 to an oncogene is essential for the occurrence and development of BL [14]. In addition, the content of miRNAs was different in BL tumor cells and lymph node reactive proliferative cells, and miR-155 is correlated with poor prognosis in lymphoma and leukemia [15,16]. PET-CT is known with its sensitive, specific and accurate characteristics in localization, which can be used for early diagnosis and staging of tumors. Due to its prominent role in disease assessment, it is now widely used in the examination of most lymphoma subtypes [17]. In this case, the right gingiva swelling was the first symptom. PET-CT (February 27th, 2018) showed increased diffuse metabolism of the whole-body bone marrow with evident bone destruction of the mandible. After chemotherapy, reexamination of PET-CT (August 24th, 2018) exhibited the increased metabolism of the right mandible and volume of soft tissue mass, and relieved other parts. Clinically, it is considered that the possibility of recurrence was very high. Through the comparison of two PET-CT, it was found that effective treatment alleviated the bone destruction of the left mandible, and suppressed the gingival inflammation. In the right mandible, although the extent of bone destruction was reduced, the increase of bone metabolism was associated with soft tissue mass formation. It can be explained that the exposed periodontal pocket communicated with the outside world is not conducive to the inhibition of inflammation. In addition, primary malignant lymphoma of the jaw irregularly destroys the cancellous bone of the jaw in the early stage, then penetrates the dense bone to invade the soft tissue, leading to facial swelling. Because the patient's physical condition was not suitable for tooth extraction treatment, it is essential to control inflammation and strengthen the hygienic care of the oral cavity. Chemotherapy is the first choice for the treatment of BL, which is combined with other therapies, including monoclonal antibody therapy, immunotherapy, bone marrow transplantation, surgical treatment, and radiotherapy. According to different types, different stratified chemotherapy regimens have been adopted by major international treatment centers, and the 5-year event-free survival (EFS) rate has increased to over 80% [18]. At present, the multi-center cooperative group treatment regimen adopted in China is the modified protocol CN-CL-NHL-B-2017 of the internationally accepted basic protocol LMB89/96. A total of 488 children with mature B-cell lymphoma were treated in a multicenter study by the Chinese Children's Lymphoma Collaborative Group (CNCL) during a 3-year period, and the overall 2-year progression-free survival (PFS) reached 88.7% [19]. The prognosis of BL is closely related to the type of disease, the age of patients, tumor size, diagnostic stage, and hemoglobin level [20]. In this case, there are multiple indicators of poor prognosis, such as bone marrow and central nervous system involvement, tumor mass > 10 cm in diameter, abnormal C-myc gene, and high serum level of lactate dehydrogenase (LDH). With the wide application of short-course and high-dose chemotherapy regimens, the prognosis of children with BL has been significantly improved, but there are still a few children who progress or relapse during treatment, and the prognosis of children with relapsed and refractory disease is poor. After high-intensity chemotherapy in 100 children with BL in an Italian center, the recurrence rate was about 7% [21], close to 8.9% that reported by Beijing Children's Hospital [22]. At present, relapsed and refractory BL in children has been improved by rituximab combined with high-intensity chemotherapy in the first-line treatment at home and abroad [23]. In the future, the treatment of BL will be more inclined to promote the molecular characteristics of tumorigenesis through molecular biology, genomics, etc., and targeted immunotherapy is a potential strategy for relapsed and refractory patients [20]. For children

with malignant tumors, oral conditions should be paid close attention. Throughout the whole course of treatment, it is imperative to monitor oral mucosal changes timely and to implement early intervention and nursing. In addition, strengthening the oral health education of patients and their families is helpful to prevent and treat oral problems in patients with cancer and to reduce the risk of oral infection. Tumor cell infiltration of the disease itself and drug treatment reduced child's own resistance with the destroyed tissue structure of oral mucosal cells, reduced salivary secretion, which is very likely to be secondary to oral infection. Poor oral environment and oral self-cleaning habits arethe essential factors of oral infection following chemotherapy in patients with hematological malignancies. Kangfuxin liquid (KFX) for traditional Chinese medicine, the main ingredient is alcohol extract of Periplaneta americana, containing polyols, sticky sugar amino acid, epidermal growth factor and other active substances [24]. KFX can effectively shorten the healing time of ulcers and relieve the pain of Oral ulcer induced by chemotherapy, with no adverse drug reactions. Cleaning the mouth, protecting the oral mucosa, and keeping the oral cavity moist are essential to control infection [25].

5. Conclusions

As a unique B-cell tumor, BL develops rapidly. The comprehensive understanding of the disease is conductive to improve the vigilance and emphasize the important role of physicians in early detection of systemic disease. For patients with recurrent gingival swelling, the general condition should not be ignored, and the primary disease should be found as soon as possible to confirm diagnosis and to refer in time, thereby improving the quality of life of patients.

References

1. Biko DM, Anupindi SA, Hernandez A, Kersun L, Bellah R. Childhood Burkitt lymphoma: abdominal and pelvic imaging findings. AJR Am J Roentgenol. 2009; 192(5): 1304-15.
2. Ryland GL, Jones K, McBean M, Khot A, Seymour JF, Blombery P. Comprehensive genomic characterization dissects the complex biology of a case of synchronous Burkitt lymphoma and myeloid malignancy with shared hematopoietic ancestry. Leuk Lymphoma. 2018; 59(4): 992-995.
3. Hoelzer D, Walewski J, Döhner H, Viardot A, Hiddemann W, Spiekermann K. Improved outcome of adult Burkitt lymphoma/leukemia with rituximab and chemotherapy: report of a large prospective multicenter trial. Blood. 2014; 124(26): 3870-9.
4. Rebelo-Pontes HA, Abreu MC, Guimarães DM, Fonseca FP, Andrade BA, Almeida OP, et al. Burkitt's lymphoma of the jaws in the Amazon region of Brazil. Med Oral Patol Oral Cir Bucal. 2014;19(1): e32-8.
5. Cho BH, Shin DH, Jung YH, Park HR. Widely disseminated sporadic Burkitt lymphoma initially presented as oral manifestations in a 6-year-old boy. J Oral Biol Craniofac Res. 2018; 8(2): 140-142.
6. Jan A, Vora K, Sándor GK. Sporadic Burkitt's lymphoma of the jaws: the essentials of prompt life-saving referral and management. J Can Dent Assoc. 2005; 71(3): 165-8.
7. Said J, Lones M, Yea S. Burkitt lymphoma and MYC: what else is new? Adv Anat Pathol. 2014; 21(3): 160-5.
8. Campo E, Swerdlow SH, Harris NL, Pileri S, Stein H, Jaffe ES. The 2008 WHO classification of lymphoid neoplasms and beyond: evolving concepts and practical applications. Blood. 2011; 117(19): 5019-32.
9. De Coninck W, Govaerts D, Bila M, Vansteenkiste G, Uyttebroeck A, Tousseyn T, et al. Burkitt lymphoma in children causing an osteolytic lesion in the mandible: A case report. Clin Case Rep. 2020; 9(2): 938-943.
10. Ren G, Cheng A, Reddy V, Melnyk P, Mitra AK. Three-dimensional fold of the human AQP1 water channel determined at 4 A resolution by electron crystallography of two-dimensional crystals embedded in ice. J Mol Biol. 2000; 301(2): 369-87.
11. Dozzo M, Carobolante F, Donisi PM, Scattolin A, Maino E, Sancetta R, et al. Burkitt lymphoma in adolescents and young adults: management challenges. Adolesc Health Med Ther. 2016; 8: 11-29.
12. Ambinder RF, Griffin CA. Biology of the lymphomas: cytogenetics, molecular biology, and virology. Curr Opin Oncol. 1991; 3(5): 806-12.
13. Sander S, Calado DP, Srinivasan L, Köchert K, Zhang B, Rosolowski M, et al. Synergy between PI3K signaling and MYC in Burkitt lymphomagenesis. Cancer Cell. 2012; 22(2): 167-79.
14. Kanungo A, Medeiros LJ, Abruzzo LV, Lin P. Lymphoid neoplasms associated with concurrent t(14;18) and 8q24/c-MYC translocation generally have a poor prognosis. Mod Pathol. 2006; 19(1): 25-33.
15. Leucci E, Cocco M, Onnis A, De Falco G, van Cleef P, Bellan C, et al. MYC translocation-negative classical Burkitt lymphoma cases: an alternative pathogenetic mechanism involving miRNA deregulation. J Pathol. 2008; 216(4): 440-50.
16. Seto AG, Beatty X, Lynch JM, Hermreck M, Tetzlaff M, Duvic M, et al. Cobomarsen, an oligonucleotide inhibitor of miR-155, co-ordinately regulates multiple survival pathways to reduce cellular proliferation and survival in cutaneous T-cell lymphoma. Br J Haematol. 2018; 183(3): 428-444.
17. Carrillo-Cruz E, Marín-Oyaga VA, Solé Rodríguez M, Borrego-Dorado I, de la Cruz Vicente F, Quiroga Cantero E, et al. Role of 18F-FDG-PET/CT in the management of Burkitt lymphoma. Eur J Haematol. 2015; 94(1): 23-30.
18. Mangani D, Roberti A, Rizzolio F, Giordano A. Emerging molecular networks in Burkitt's lymphoma. J Cell Biochem. 2013; 114(1): 35-8.
19. Liu Y, Zhang Y H. [Prospect of targeted immunotherapy for mature B-cell non-Hodgkin's lymphoma in children]. Journal of China Pediatric Blood and Cancer. 2020; 25(5): 249-252..
20. Casulo C, Friedberg JW. Burkitt lymphoma- a rare but challenging lymphoma. Best Pract Res Clin Haematol. 2018; 31(3): 279-284.

21. Intermesoli T, Rambaldi A, Rossi G, Delaini F, Romani C, Pogliani EM, et al. High cure rates in Burkitt lymphoma and leukemia: a Northern Italy Leukemia Group study of the German short intensive rituximab-chemotherapy program. Haematologica. 2013; 98(11): 1718-25.

22. Huang S, Jin L, Yang J, Duan YL, Zhang M, Zhou CJ. [Clinical pathologic characteristics and treatment outcomes of 19 relapsed pediatric B-cell lymphoma]. Zhonghua Er Ke Za Zhi. 2017; 55(10): 748-753.

23. Ganjoo KN, de Vos S, Pohlman BL, Flinn IW, Forero-Torres A, Enas NH, et al. Phase 1/2 study of ocaratuzumab, an Fc-engineered humanized anti-CD20 monoclonal antibody, in low-affinity FcγRII-Ia patients with previously treated follicular lymphoma. Leuk Lymphoma. 2015; 56(1): 42-8.

24. Zhu S, Shi Q, Lu J. Curative effect of oral ulcer powder on the treatment of recurrent aphthous ulcer. Pak J Pharm Sci. 2018; 31(3(Special)): 1175-1178.

25. Linyu Bo, Yulin Zhang, Xiumei Wu, Ancui Ma; Yu Zhao, Heng Liu, et al. Effect and mechanism of Kangfuxin liquid on oral ulcer in patients with chemotherapy treated hematologic malignancies: Network pharmacology study and clinical observations. Informatics in Medicine Unlocked. 2021; 100693.