"Literature Review"

Oral Malignant Burkitt’s Lymphoma and It’s Problems

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Abstract

A non-Hodgkin lymphoma with rapid growth and aggressive behavior is Burkitt’s lymphoma. Burkitt’s lymphoma (BL) is also an oral cancer of lymphoid origin with a high percentage of occurrences and includes an advanced B-cell neoplasm. Fundamentally, the exact cause of BL is unknown. This disease commonly occurs in people with weakened immune systems or children related to the Epstein-Barr virus (EBV) and chronic malaria. Burkitt lymphoma can be fatal. Burkitt lymphoma is a rare but highly aggressive (fast-growing) B-cell non-Hodgkin lymphoma (NHL). This disease may affect the jaw, central nervous system, bowel, kidneys, ovaries, or other organs Cancer cells in BL can spread to all parts of the body. Inhibiting the proliferation of BL oral cancer cells requires a viable and efficient plan. One of them is using medicinal plants whose antitumor potential needs to be scientifically tested. However, Burkitt lymphoma is often very responsive to the currently recommended intensive chemotherapy regimens, and cure rates for this disease remain high. Studies show people who receive treatment right away have high rates of remission, meaning after treatment they don’t have symptoms or signs of the condition. The aim of this review is to discuss Burkitt’s lymphoma (BL) in diagnosis and treatment. Burkitt's lymphoma, or Raji cell, is a B-cell non-Hodgkin lymphoma that is very aggressive.

Keywords: Burkitt’s lymphoma, oral cancer, antitumor

INTRODUCTION

Introduction On One of the diseases that lead to death in large numbers worldwide is cancer. Not only found in adults, cancer also potentially develop in children. The World Health Organization (WHO) projects that there will be an increase in the number of new cancer cases to over 35 million in 2050, a 77% increase from the 20 million cases in 2022.1 Choosing Burkitt lymphoma for research is important because it represents an aggressive form of non-Hodgkin lymphoma that has a high impact on patient outcomes. One form of malignancy (cancer) in the oral cavity is Burkitt’s lymphoma.2

Raji cell, another name for Burkitt’s lymphoma, is a B-cell non-Hodgkin lymphoma which is very aggressive by having a doubling time of 25 hours. The term Burkitt's lymphoma itself started in 1887, which Sir Albert Cook put forward, and then in 1950, Dr. Dennis Burkitt explained this disease. Burkitt's lymphoma has three subtypes, i.e., sporadic Burkitt's lymphoma, endemic Burkitt's lymphoma (Africa), and Burkitt's lymphoma associated with immunodeficiency.3 Lymphoma occurs in less than 5% as a form of malignancy in the oral cavity. Waldeyer's ring is the primary area of lymphoid tissue in the oral cavity. The oral cavity’s other places having lymphoid tissue include the minor and major salivary glands, the soft palate, the tongue’s base, and not encapsulated lymphoid tissue. Alveolar bone destruction and tooth mobility can be seen when the lymphoma is in the bone.2

DISCUSSION

Burkitt's lymphoma characteristics are uniform monomorphic cells, medium in size with round nuclei, and many nucleoli as well as little cytoplasm. It also has the fastest rate of cell division compared to other tumors, one of which is the presence of growth cells with a high fraction. In addition, Ki-67 which is a specific marker for cell cycle, is showed more than 95% in BL cells.4
One treatment that can be done for BL is chemotherapy by utilizing cisplatin. Cisplatin is one of the chemotherapeutic agents used to treat Burkitt’s lymphoma. This medication exhibits anticancer activity by interacting with the nucleophilic bases of purine DNA. Both oxamate and galloflavin are lactate dehydrogenase inhibitors, which can increase the effectiveness of cisplatin in Burkitt’s lymphoma culture, and it is not administered in normal lymphocyte proliferation. Lactate dehydrogenase inhibitors increase cisplatin activity only in neoplastic cells.\(^5\) whereas, in cervical cancer, cisplatin induces cytoplasmic acidification at the start of therapy. After acidification, the ability of cells to restore as well as keep an alkaline pH is essential as a mediator in the decision of cells to survive and proliferate until they eventually experience cell death.\(^6\)

Cancer is also a genetic disorder caused by DNA mutations, mostly occurs by a spontaneous what or due epigenetic effect. Which influences to DNA methylation increasing, e.g., increased DNA methylation as well as histone modifications resulting from gene mutations. Changes in epigenetics, as well as genetics, can change the gene expression that acts as a regulator in the body's fundamental processes, such as growth, survival, and aging.\(^7\)

Further, cancer growth occurs uncontrollable. Three groups of genes that regulate normal growth include growth-promoting proto-oncogenes, growth-inhibiting cancer suppressor genes (antioncogenes), and genes involved in cell death (apoptosis). Other genes are responsible for DNA repair, which affects cell proliferation. Failure of the DNA repair phase can lead to malignancy. The malignancy (cancer) process is called carcinogenesis.\(^8\)

**Cancer Cell Cycle**

The stage of cell development and division is known as the cell cycle. Phases G1 and G0, as well as the resting phases S, G2, and M, make up the cell cycle.\(^9\) At the G1, the cell will increase it’s size as preparing for S phase when the DNA was synthesized. In addition to increasing DNA cell size, the S phase allows cells to replicate or duplicate their genetic material. Meanwhile, the G2 phase is the stage that cells go through after the S phase (synthesis) is complete. When a cell is in the G2 phase, it prepares itself to carry out the cell division in the M phase (mitosis).\(^10\)

According to Several factors often inhibit cell division in the M phase. The final limit of cell division can be inhibited at the boundary point (restriction point) around the G1 phase. When cell division is inhibited after exceeding the cutoff point, division cannot stop until it continues to produce two cells, and the phase repeats.\(^11\)

**Epidemiology**

Early estimates of Burkitt’s lymphoma incidence in children vary from 1 per 100,000 cases, increasing to 18 per 100,000 cases. This figure implies a similar incidence with cases of acute lymphoblastic lymphoma (ALL) in developed countries, but in Africa, ALL incidence is lower than Burkitt's lymphoma.\(^16\) The incidence of Burkitt's lymphoma in other countries is summarized in the following diagram.\(^17\)
Chemotherapy is also a therapy for cancer by using drugs to kill cancer cells. Chemotherapy can be used as a single therapy or a combination of various forms of therapy. Neoadjuvant chemotherapy is a form of chemotherapy given before surgery to reduce tumor size, while adjuvant chemotherapy is a drug given after surgery to prevent cancer recurrence. The side effects of chemotherapy vary from person to person. Anticancer drugs generally affect cell division which occurs rapidly. Anticancer drugs also work on the cells of blood that transport oxygen around the body, fight off infection, and aid in blood coagulation. Cells of blood that anticancer drugs have impacted make the patient susceptible to infection, bruising or bleeding easily, and the patient's physical condition is weakened.

3) Hormonal Therapy

Hormonal therapies used in cancer treatment are classified into hormone analogs, inhibitors of hormone synthesis, and inhibitors of hormone receptors. Hormone analogs occur naturally from hormones or their derivatives that directly have antineoplastic effects or inhibit the synthesis of other hormones when administered in supraphysiological amounts. Corticosteroids are widely used in cancer therapy due to the side effects of lymphoid malignancies, but they cause complications, such as pneumatosis, osteoporosis, and osteonecrosis. Progestins are used for endometrial and breast cancer with thromboembolic complications. Hormone receptor inhibitors are equipped with physiologic hormones to bind to the receptor and block it. The two most common types of hormone receptor inhibitors are estrogen and androgen receptor inhibitors. Tamoxifen is used as a selective estrogen receptormodulator.
for breast cancer, but there is a chance of anomalies in the uterine wall with the appearance of endometrial polyps, hyperplasia, carcinoma, sarcoma, and thromboembolic phenomena.²¹

In this case, a malignancy of B lymphocytes is Burkitt's lymphoma.²² Burkitt's lymphoma is a lymphoid tumor with the characteristics of chromosomal translocations, especially translocations in MYC.²³ Burkitt's lymphoma is also the most quickly expanding tumor in terms of activity, doubling the number of cells, namely 24-48 hours.

Three virologists, including Yvonne Barr, Michael Anthony Epstein, and Bert Achong, discovered the Epstein-Barr Virus (EBV) in tumor tissue in 1964. Then, Burkitt was found in many malaria cases spread in various countries, especially in Africa. EBV was also linked to Burkitt's lymphoma, which was noted as an endemic subtype. In cases of somatic mutations, EBV positive for Burkitt's lymphoma occurs more frequently than EBV negative.²⁴ Endemic and sporadic subtypes experience translocations in the distal part of chromosomes 8 and 14. This translocation process is directly involved in increasing the proliferation of Burkitt's lymphoma tumor cells; with a possible doubling time of 24 hours and a growing proportion of almost 100%, they have the highest rate of proliferation of all human neoplasms.²

4) Other Therapy

Treatment for Burkitt's lymphoma is currently very limited. Various kinds of therapy proposals are currently being developed, one of which is gene therapy. Several studies have been conducted and show promising results. Previous studies on oral Burkitt's lymphoma demonstrated that in oral Burkitt lymphoma cells, p45Skp-2 inhibits migration and metastatic chemotactic activity by downregulating MTA-1 and inducing the protein E-cadherin, which is a target of this molecule. Skp, Cullin, and F-box (SCF)-Skp-2 form the ubiquitin ligase complex known as S-phase kinase-associated protein-2 (p45Skp-2 or Skp-2). In this case, Skp-2 controls the G1-to-S transition favorably and participates in the ubiquitin-mediated degradation of the CDK p27Kip1 cyclin-dependent inhibitors kinase.²⁵ In addition, further studies have been carried out, and the results show that the oligonucleotides KIP-1 S and SKP-2 AS have the ability to stimulate cell growth and inhibit chemotactic migration, which results in apoptosis. Cell growth and apoptosis induction are suppressed by downregulating MTA-1, CDK2-cyclin E complex, and NF-κB protein. Upregulation of KIP-1 S and SKP-2 AS can be useful for modulating apoptosis to treat Burkitt's lymphoma.²⁶

According to other investigations, the oral malignant Burkitt's lymphoma cells exhibited a robust probable anticancer response to the ethyl acetate portion of the ant nest plant which was demonstrated by the induction of cell cycle arrest and apoptosis by downregulation of the cyclin E-CDK-2 complex.²⁷

CONCLUSION

Burkitt's lymphoma, or Raji cell, is a B-cell non-Hodgkin lymphoma that is very aggressive. Lymphoma occurs in less than 5% as a form of malignancy in the oral cavity. Characteristics of Burkitt's lymphoma are uniform monomorphic cells, medium in size with round nuclei, and many nucleoli as well as little cytoplasm. Due to uncontrolled cell cycle development, loss of checkpoints occurs in
tumor development (tumorigenesis). Various therapies that can be performed on Burkitt's lymphoma are surgical therapy, chemotherapy, hormone therapy, and other therapies such as gene therapy. Gene therapy is a treatment developed with promising results based on the studies conducted.

REFERENCES
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