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REVIEW ARTICLE

A SYSTEMATIC REVIEW ON ACUTE LYMPHOBLASTIC LEUKEMIA

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Abstract

Acute lymphoblastic leukemia (ALL) comprises a group of lymphoid neoplasms that are morphologically and immunophenotypically similar to B and T lineage progenitors. The pathogenesis of ALL involves the abnormal proliferation and differentiation of clonal populations of lymphoid cells. Studies in pediatric populations have identified genetic syndromes that predispose to a small number of ALL cases, including Down's syndrome, Fanconi's anemia, Bloom's syndrome, ataxia-telangiectasia, and Nijmegen's breakdown syndrome. Acute lymphoblastic leukemia has been hailed as a major success story in pediatric oncology with the advent of dose-escalating chemotherapy and allogeneic SCT. However, the high risk of this disease and the significant toxicities associated with chemotherapy in adults make the results less promising. Because some studies have shown benefits of pediatric-inspired therapies, much uncertainty remains about how adults with ALL can best be managed.

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Introduction:-

Acute lymphoblastic leukemia (ALL) comprises a group of lymphoid neoplasms that are morphologically and immunophenotypically similar to B- and T-lineage progenitors. These neoplasms present primarily as leukemic processes with extensive myeloid and peripheral blood involvement, or no or confined to limited (<25%) tissue invasion with no myeloid involvement. The latter case is commonly referred to as lymphoblastic lymphoma (LBL) (Paul et al., 2016).

Leukemia is a cancer of the blood and bone marrow. Bone marrow is the spongy tissue in the center of most bones where blood cells are formed. Leukemia begins in one of the immature cells in the bone marrow(Obeagu et al. 2020; Obeaguet al., 2022; Obeagu and Babar, 2021; Obeagu, 2022). One or more changes (mutations) occur in the cell's DNA, causing it to become a type of cancer cell called a "leukemic cell." Leukemic cells do not mature into healthy, functioning blood cells. They grow faster and live longer than normal blood cells. They divide and copy themselves to create more and more leukemia cells. Over time, the leukemia cells prevent or suppress the development of normal, healthy blood cells in the bone marrow. These cells enter the bloodstream from the bone marrow and can spread to organs such as the liver and spleen (Vardiman et al., 2009).

There are many different types of leukemia, divided mainly by whether the leukemia is acute (rapidly growing) or chronic (slow-growing) and whether it begins in myeloid or lymphoid cells. Knowing the specific type of leukemia can help doctors better predict an individual's prognosis (outlook) and select the best treatment (Shah et al., 2013).

There are four main types of leukemia, including acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myelogenous leukemia (AML) and chronic myelogenous leukemia (CML). There are three

main types of blood cells: red blood cells, white blood cells, and platelets. Red blood cells carry oxygen throughout the body. White blood cells help fight infections. Platelets help stop bleeding by clumping (clotting) at the site of injury. Blood cells begin as hematopoietic stem cells in the bone marrow. Hematopoietic stem cells are immature (underdeveloped) blood cells(Obeagu and Obeagu, 2018; Obeagu, 2018; Obeagu et al., 2021; Obeagu et al., 2022). In healthy bone marrow, these hematopoietic stem cells ultimately develop into red blood cells, white blood cells, and platelets through a process called 'differentiation' (National Cancer Institute, 1975).

In patients with ALL, a mutation or series of mutations in the DNA (genetic material) of lymphoid stem cells (or "lymphoblasts") leads to the formation of leukemic cells. Leukemia cells are immature cells stuck in early cellular development. These leukemia cells, also known as ALL blasts, fail to mature into fully functional leukocytes (German, 1997).

Due to genetic errors in mutated cells, cells continue to grow and divide, while healthy cells usually stop dividing and eventually die. All cells emerging from the original leukemia blast also have mutated DNA. When leukemic cells grow uncontrollably and accumulate rapidly in the bone marrow, production of normal, healthy red blood cells, white blood cells, and platelets slows or stops. The result is too many immature leukemic blasts that are unable to fight infection and too few mature, functional red blood cells and white blood cells and platelets (Roberts et al., 2012).

The pathogenesis of ALL involves the abnormal proliferation and differentiation of clonal populations of lymphoid cells. Studies in pediatric populations have identified genetic syndromes that predispose a small number of ALL cases, including Down's syndrome, Fanconi's anemia, Bloom's syndrome, ataxia-telangiectasia, and Nijmegen's breakdown syndrome (Mullighan et al. 2007). Other predisposing factors include exposure to ionizing radiation, pesticides, certain solvents, or viruses such as Epstein-Barr virus and human immunodeficiency virus. However, it most often occurs as a new malignancy in previously healthy individuals. Chromosomal abnormalities are characteristic of his ALL, but not enough to cause leukemia. Characteristic translocations include t(12;21)[ETV6-RUNX1], t(1;19)[TCF3-PBX1], t(9;22)[BCR-ABL1], and similar gene expression profiles It includes a reorganization of MLL.11, which is (Philadelphia) have identified Ph-positive ALL without BCR-ABL1 rearrangements. In more than 80% of cases of this so-called Ph-like ALL, the IKAROS family zinc finger 1 (IKZF1), transcription factor 3 (E2A), former B-cell factor 1 (EBF1) and paired box 5 (PAX5). Similarly, kinase-activating mutations are observed in 90% of Ph-like ALL (Bielorai et al., 2013).

Acute lymphocytic leukaemia (ALL)

Acute lymphoblastic leukemia (ALL) is also known as acute lymphoblastic leukemia. "Acute" means that leukemia can progress rapidly and is likely to cause death within months if left untreated. By "lymphocyte" is meant that it arises from an early (immature) form of a lymphocyte, a type of white blood cell. ALL starts in the bone marrow (the soft inner part of certain bones where new blood cells are made) (Arber et al., 2016).In most cases, leukemia cells invade the blood fairly quickly. It can also spread to other parts of the body, such as the lymph nodes, liver, spleen, "brain and spinal cord" of the central nervous system, and testicles (in men). Some cancers start in these organs and can then spread to the bone marrow, but these cancers are not leukemias. Leukemias like ALL affect mainly the bone marrow and blood, but lymphomas mainly affects lymph nodes or other organs (but can also affect the bone marrow). It may be difficult to tell whether lymphocytic cancer is leukemia or lymphoma. When at least 20% of the bone marrow is composed of cancerous lymphocytes (called lymphoblasts or simply blasts), the disease is usually considered leukemia (Geriniere et al., 2010).

Most cases of his ALL in the United States occur in children, with an incidence of 3–4/100,000 in patients aged 0–14 years and w1/100,000 in patients aged 15 years and older. In children, ALL accounts for 75% of all acute leukemias (and 34% of all cancers in this age group), with peak incidence between 2 and 5 years of age. This rate is much lower in adults, where acute myeloid leukemia (AML) and chronic lymphocytic leukemia are more common. There is a slight male predominance across all age groups, with significantly more white children. ALL primarily occurs as a de novo disease, with only rare cases manifesting as secondary neoplasms (Berry et al., 2020). Various genetic and environmental factors are associated with ALL. It is more common in patients with Down's syndrome, Bloom's syndrome, type I neurofibromatosis, and ataxia telangiectasia. In addition, exposure to ionizing radiation, pesticides, and solvents in utero are also associated with an increased risk of childhood leukemia. Leukemia-specific fusion genes or immunoglobulin (Ig) and clonal Ig gene rearrangements have been identified in the neonatal spot map (Guthrie) of a patient who later developed her ALL (Chessells et al.

When evaluating cells, the percentage of blasts identified in a sample is another important finding. There are usually no blasts in the blood and less than 5% of the cells in the bone marrow are blasts. In general, the diagnosis of ALL requires that at least 20% of the cells in the bone marrow be blasts. Most people diagnosed with ALL have a myeloblast rate well above 20%, but a high myeloblast rate does not necessarily mean a poor prognosis (Roberts et al., 2014). .

If leukemia is diagnosed, additional tests are done on blood and bone marrow samples to gather information about the type and subtype of ALL. Other tests that may be done include flow cytometry, a laboratory test used to detect certain types of cancer cells based on cell surface antigens or proteins. The pattern of surface proteins is called the "immunophenotype". It helps diagnose certain types of leukemia and lymphoma cells. Cytogenetic testing can also be done using bone marrow or blood samples. The leukemic cells in the sample are cultured in the laboratory and stained prior to testing. After examining the stained sample under a microscope, a photograph is taken to confirm the arrangement of the chromosomes (called a karyotype). Karyotype indicates whether there are abnormal changes in the size, shape, structure, or number of chromosomes in leukemic cells (Holmfeldt et al., 2013).

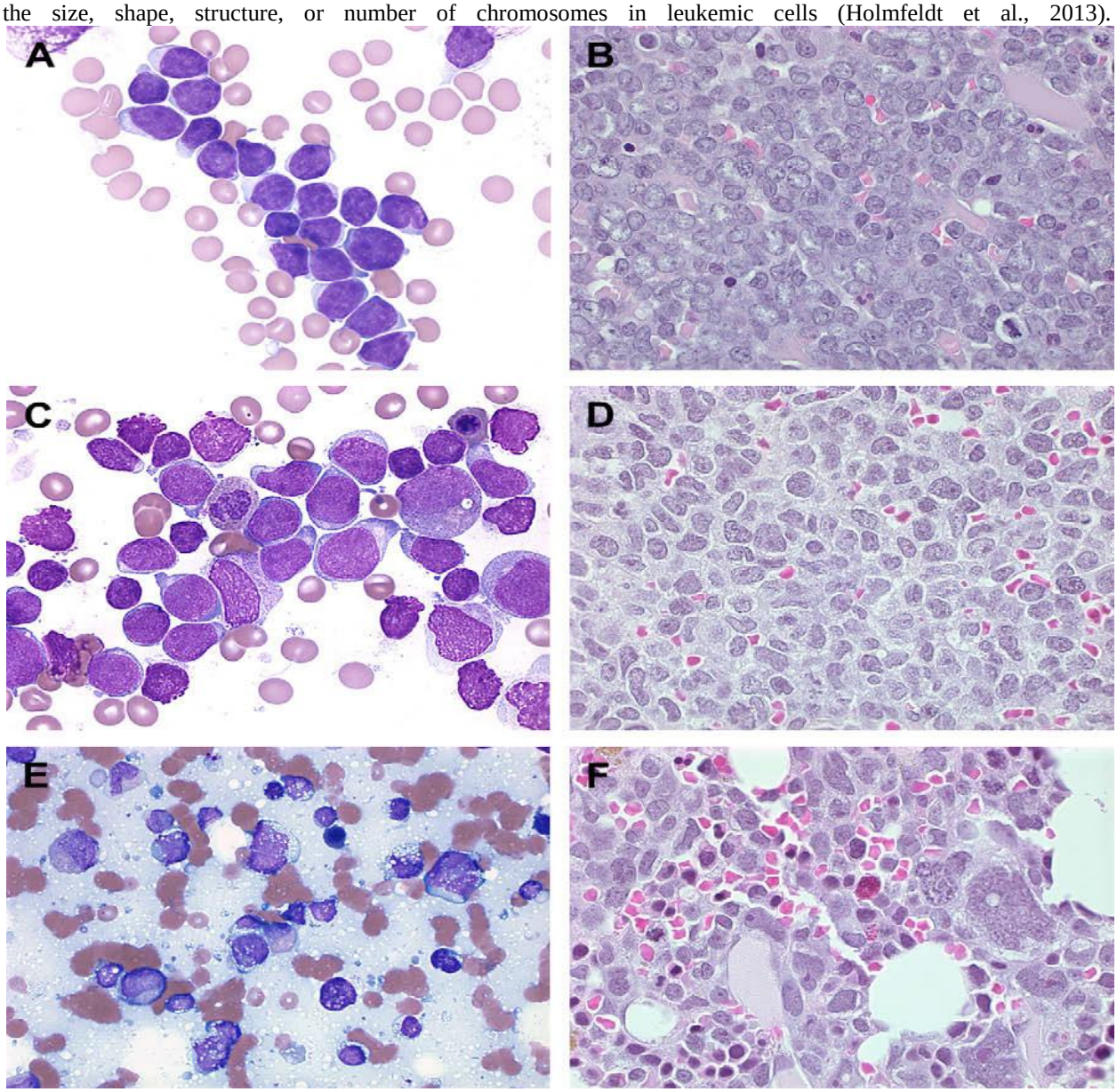

Figure 1:- Showing the morphology of ALL/LBL in smears and paraffin-embedded tissue sections. (A, B) ALL L1. (C–D) ALL L2. (E, F) Morphologic findings in a case of precursor B-ALL with hypodiploidy, resembling a high-

grade, mature B-cell lymphoma (A, C, E, Wright-Giemsa stain) (B, D, F, hematoxylin-eosin; original magnification 60x oil immersion) (Abouet al., 2020).

Conclusion:-

Leukemias like ALL primarily affect the bone marrow and blood, whereas lymphomas primarily affect the lymph nodes or other organs (but can also affect the bone marrow). It may be difficult to tell whether lymphocytic cancer is leukemia or lymphoma. When at least 20% of the bone marrow is composed of cancerous lymphocytes called lymphoblasts or simply "blasts," the disease is usually considered leukemia.

Acute lymphoblastic leukemia is heralded as a major success story in pediatric oncology with the advent of dose-scaling chemotherapy and allogeneic SCT. However, because of the high-risk nature of the disease and the significant toxicities associated with chemotherapy in adults, the results are not very encouraging. Because some studies have shown benefits of pediatric-inspired therapies, much uncertainty remains about how adults with ALL can best be treated.

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