pla... Future challenges include diagnostic delays, variability in laboratory availability, and unequal global access to advanced therapies. However, rapid integration of genomics, standardized testing protocols, and emerging hemostatic agents promise to redefine clinical management. Collaborative registries and international networks will be essential to accelerate discovery and translate innovation into equitable care. In conclusion, PFDs embody a nuanced and evolving frontier in hematology. By integrating advanced diagnostics with personalized management strategies, hematologists can reduce morbidity, anticipate complications, and contribute to reshaping the future of bleeding disorder care., Türkiye

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Abstract 015

CNS INVOLVEMENT IN PRIMARY AND SECONDARY ALL AND TREATMENT STRATEGIES

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Abstract Central nervous system (CNS) involvement is an important prognostic factor in acute lymphoblastic leukemia (ALL). Both primary and secondary CNS disease are associated with increased relapse risk and inferior survival. In adults, CNS involvement at diagnosis occurs in 5–10% of cases, with relapse rates of 4–15%. Before the introduction of prophylaxis in the 1980s, CNS relapse rates were as high as 30–40%. The pathophysiology of CNS involvement in ALL is complex, involving early migration of leukemic blasts across the blood –brain barrier, facilitated by adhesion molecules, integrins, and vascular endothelial growth factor (VEGF). VEGF-mediated endothelial disruption increases vascular permeability and plays a pivotal role in the development of posterior reversible encephalopathy syndrome (PRES). Targeting VEGF with monoclonal antibodies has been shown to reduce CNS leukemic burden, suggesting a promising future strategy in both pediatric and adult ALL. The immune-privileged microenvironment of the CNS provides a sanctuary for leukemic cells, supporting their persistence and relapse risk. Traditionally, cerebrospinal fluid (CSF) cytomorphology has been considered the gold standard for assessing CNS involvement. However, this method has low sensitivity and specificity, particularly in samples with low cell counts or technical artifacts. In recent years, flow cytometric immunophenotyping of CSF has demonstrated superior sensitivity, identifying CNS disease more frequently and serving as a strong biomarker for relapse prediction. Minimal CNS involvement not only increases the risk of relapse but is also associated with treatment-related neurotoxicities. Data from the NOPHO group indicate that minimal CNS involvement in pediatric ALL is linked to higher rates of seizures and PRES. Standard treatment approaches continue to rely on intrathecal chemotherapy (methotrexate, cytarabine, corticosteroids) and high-dose systemic agents. However, repeated intrathecal administration and cranial irradiation carry substantial risks of long-term neurotoxicity, highlighting the need for more selective and less toxic strategies. Radiation therapy may still be considered in selected cases, particularly in the context of hematopoietic stem cell transplantation (HSCT). HSCT remains a potentially curative option, especially when preceded by effective cytoreduction with immunotherapy. In conclusion, CNS involvement in ALL represents a biologically and clinically distinct entity requiring tailored management. Primary involvement demands sensitive diagnostics and a careful balance between efficacy and neurotoxicity, while secondary CNS relapse necessitates aggressive multimodal therapy, often incorporating novel immunotherapies and HSCT. Advances in CNS-directed diagnostics and therapeutics are expected to further individualize treatment, aiming to reduce relapse risk while minimizing late toxicities.

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Abstract 016

GAUCHER DISEASE

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Gaucher disease is an autosomal recessive lysosomal storage disorder caused by pathogenic variants in the GBA1 gene on chromosome 1q21, resulting in reduced or absent activity of the enzyme glucocerebrosidase. Consequently, glucosylceramide accumulates primarily in macrophages, leading to the formation of Gaucher cells. The disease most commonly presents with anemia, thrombocytopenia, bleeding tendency, hepatosplenomegaly, fatigue, and skeletal involvement. Bone pathology includes decreased mineral density, bone marrow infiltration, infarction, and fibrosis, all of which contribute to impaired hematopoiesis and cytopenias. From a hematological standpoint, bone marrow aspiration may reveal Gaucher cells with the typical “wrinkled tissue paper” cytoplasm; however, this finding is not pathognomonic and may be seen in other lysosomal storage disorders. Definitive diagnosis therefore requires demonstration of deficient glucocerebrosidase activity or identification of pathogenic GBA1 variants through molecular analysis. In clinical practice, hematological parameters remain essential both for diagnosis and longitudinal monitoring. Complete blood counts provide information on cytopenias and treatment response, while coagulation studies and platelet function tests assist in evaluating bleeding risk. Biomarkers such as chitotriosidase and glucosylsphingosine, together with organomegaly assessment, are increasingly employed in follow-up. Historically, hematopoietic stem cell transplantation was considered a potential curative approach but was limited by high morbidity, mortality, and donor-related challenges. With the advent and efficacy of enzyme replacement therapy and substrate reduction therapy, hematopoietic stem cell transplantation is now reserved only for rare, severe cases without access to standard treatment. In summary, Gaucher disease is a multisystemic disorder with prominent hematological manifestations. Early recognition, accurate diagnosis, and systematic monitoring