Hypothesis

Hypertension-Tachycardia Duet in Acute Lymphoblastic Leukemia, Is It Due to Catecholamine Hypersecretion, Highlighting a Gap of Literature

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Hypertension-Tachycardia Duet in Acute Lymphoblastic Leukemia, Is It due to Catecholamine Hypersecretion, Highlighting a Gap of Literature

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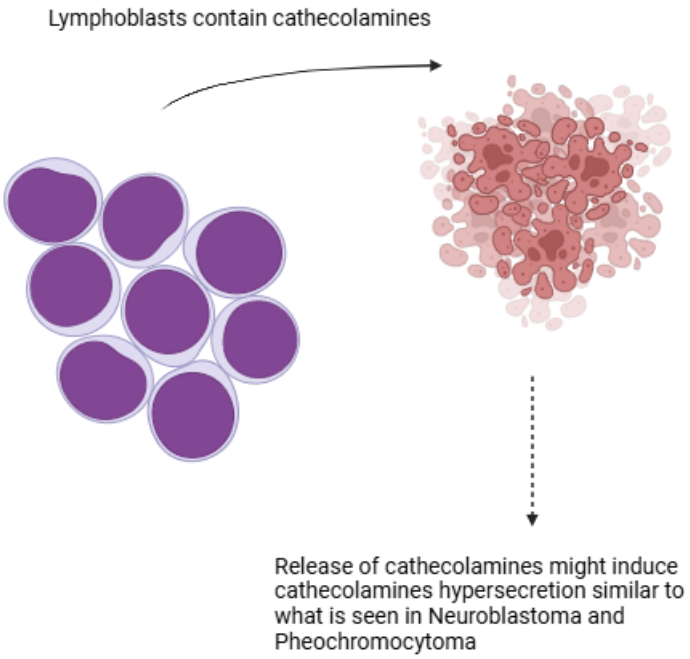
Abstract: Patients with Acute lymphoblastic leukemia (ALL) commonly present with tachycardia and or hypertension. There is little focus in the literature on the pathogenesis of this duet. It is currently established that ALL are catecholamine-secreting cells, and this means that ALL might induce hypertension and tachycardia via catecholamine hypersecretion. Proving the latter hypothesis can help in better treatment of ALL associated inappropriate tachycardia and systemic hypertension using combined alpha and beta blockers.

(A graphical abstract summarizes the hypothesis)



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Combined Hypertension and Tachycardia in Acute Lymphoblastic Leukemia: An Overlooked Problem in Literature

Acute lymphoblastic leukemia (ALL) is the most common malignancy diagnosed in children, representing more than a quarter of all pediatric cancers. The incidence of ALL follows a bimodal distribution, with the first peak occurring in childhood and a second peak occurring around the age of 50. [1]

Literature particularly focuses on hypertension in ALL patients, stating that 45% of patients with ALL develop hypertension after initiation of therapy. They attribute this hypertension to either steroid therapy or acute kidney injury. [2]

While systemic hypertension can be justifiable by steroid use, tachycardia, commonly accompanying hypertension in ALL patients, is less commonly understood. Pulse steroid therapy is known to induce sinus bradycardia, as it is speculated that steroids reduce myocardial cell sensitivity to catecholamines thus leading to sinus bradycardia.[3]

Few studies have focused on sinus tachycardia prevalence in ALL patients and none of them have considered its cohabitation with systemic hypertension. Some of the proposed pathogeneses include anemia, infection, and third-space loss. [4]

A recent large systematic review by Bertrand and colleagues, reported that only five studies have focused on heart rate abnormalities in ALL, and two of them reported an unrealistically wide range, 8-505, of prevalence of tachycardia in ALL patients. But this article does not discuss if this tachycardia was associated with blood pressure abnormalities or not. [4–6]

There is a gap in the literature regarding the prevalence of tachycardia-hypertension syndrome, which largely resembles the catecholamine syndrome seen in neuroblastoma.

Catecholamine Levels and Paracrine Regulation in ALL

On a molecular basis, catecholamines are increasingly recognized as paracrine mediators between different subsets of lymphocytes. Lymphocytes secrete catecholamines and these catecholamines are used to modulate their functions. [7–10]

Of note, Hanns and colleagues have highlighted the importance of use of catecholamines for regulation of tumorigenesis in blood malignancies, catecholamines' receptors are expressed by immune cells, more abundantly on T-lymphocytes. [11]

Another interesting study by Paczulla et al. showed how catecholamines have the potential to induce tumorigenesis and facilitates bone marrow colonization by leukemic cells and inhibiting retention of healthy cells.[12]

Despite the above data on the paracrine and autocrine role of catecholamines in lymphocytes and in leukemic cells regulation, no study to date investigated if serum and urinary catecholamines are significantly increased in leukemia overall and particularly in acute lymphoblastic leukemia.

Choice of Antihypertensives in Cancer-Related Hypertension and Implications of This Hypothesis

The drug group of choice in guidelines of antihypertensive treatment in cancer-related hypertension are RAAS blockers (renin-angiotensin-aldosterone system), whether angiotensin converting enzyme inhibitors or angiotensin receptor blockers; except in cases with a known association to high catecholamines yield.[13]

This observation and hypothesis are not only of academic interest but can potentially tailor better treatments for inappropriate tachycardia and hypertension in ALL. Proving the presence of catecholamine hypersecretion in such patients may render beta-blockers a more favorable treatment modality in ALL.

Therefore, more studies are needed to determine the circulating catecholamine levels in ALL and to rule out or confirm this hypothesis.

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preparation, AFA, BK, CS; writing—review and editing, AFA, BK, CS; supervision, AFA; project administration, AFA; funding acquisition, (none). All authors have read and agreed to the published version of the manuscript.

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Abbreviations

ALL: acute lymphoblastic leukemia

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