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EDITORIAL COMMENTARY

Empirical Antitubercular Treatment for Lymphadenopathy: A Luring Trap!

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Hodgkin lymphoma (HL) and tuberculosis share a few similar clinical features, laboratory and imaging findings that can result in misdiagnosis or delay in diagnosis. The best efforts must be undertaken to confirm the diagnosis of tuberculosis before being lured by the temptation of empirical antitubercular therapy (ATT).

It is a considerable effort by Mahajan et al. to highlight the practice of initiating empirical ATT before the definitive diagnosis of HL [1]. An alarming 29% of patients in the multicentric, prospective study received empirical ATT prior to the diagnosis of HL [1]. In similar data from the country, 28 (20.3%) and 32 (19%) patients had received ATT prior to a referral from centers in Chandigarh and Chennai, respectively [2, 3].

Rarely tuberculosis can coexist with HL. In a study from Kidwai Cancer Institute, Bengaluru, 42 (9.1%) among 462 patients with HL had received empirical ATT [4]. Five of the 42 (12%) patients had histologically proven tuberculosis along with HL [4]. Simultaneous occurrence of HL and tuberculosis has been reported among 12 children and adolescents from Guatemala and Argentina [5]. However, the coexistence of tuberculosis and HL at diagnosis is a rarity, and most cases have been reported in adults. None of the earlier-mentioned studies from India had the coexistence of tuberculosis with HL [1–3]. Strenuous efforts must be made to establish the diagnosis of tuberculosis prior to embarking on empirical ATT.

It is apt to refer to the National Tuberculosis Elimination Programme guidelines. Though histological demonstration of tuberculosis by biopsy or fine needle aspiration cytology (FNAC) is the gold standard for establishing the diagnosis, there are alternative tests that are adequate and correlate well. The availability of an experienced pathologist is indeed a challenge in the periphery, particularly in reference to the reporting of FNAC. FNAC is often an easy tool for investigating cervical lymphadenopathy in children. However, experience and expertise are crucial for reporting FNAC. Indeed, the authors recall several cases in practice where ATT was started based on FNAC reported in the periphery health care facility; the diagnosis later being revised to HL.

With the decentralization of the diagnosis of tuberculosis, the demonstration of acid-fast bacteria, culture, or cartridge-based nucleic acid amplification test (CBNAAT) are available at district hospitals and medical colleges. Suspected cases with negative initial tests can be referred to higher centers for FNAC or histopathology [6]. The temptation for the stereotyped behavior of starting empirical ATT must be avoided. ATT has inherent adverse effects besides diverting attention from the correct diagnosis.

The late effects of chemotherapy have not been discussed in the paper [1]. The cohort that had received prior ATT presented with advanced disease and B symptoms at diagnosis, warranting more intensive treatment. The cumulative anthracycline dose is 300 mg/m^2 for 6 cycles of adriamycin, bleomycin, vinblastine, and dacarbazine (ABVD). The risk of anthracycline-induced cardiotoxicity and bleomycin-induced interstitial pulmonary fibrosis increases with increasing cumulative dose [7–9]. It is plausible that empirical ATT contributes to delayed diagnosis and higher stage of disease, warranting more intensive chemotherapy resulting in a greater risk of late effects. In addition, radiotherapy administered typically for bulky disease or inadequate response, contributes to late effects, including hypothyroidism and second cancers. However, the information on the administration of radiotherapy in the two cohorts is not included in the paper.

The authors have admitted that the study was limited in that it was not designed to look at the duration, the basis of, and the details of empirical ATT prior to treatment, nor the toxicity associated with ATT [1]. Indeed, additional information on the duration and basis of ATT would have helped better understand the circumstances and the implications of empirical ATT and the real-life impact of this practice on delay in diagnosing HL.

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The team deserves accolades for highlighting the inappropriate practice of empirical ATT. The need for practice-changing behavior of confirming the diagnosis of tuberculosis before starting ATT is well emphasized.

Declarations

Conflict of Interest None.

References

1. Mahajan A, Bakhshi S, Singh M, et al. Empirical antitubercular treatment for lymphadenopathy: Are we missing lymphoma? Indian J Pediatr. 2022. https://doi.org/10.1007/s12098-022-04180-6.
2. Palayullakandi A, Trehan A, Jain R, et al. Retrospective single-center experience with OEPA/COPDAC and PET-CT based strategy for pediatric Hodgkin lymphoma in a LMIC setting. Pediatr Hematol Oncol. 2022;39:587–99.
3. Radhakrishnan V, Dhanushkodi M, Ganesan TS, et al. Pediatric hodgkin lymphoma treated at cancer institute, Chennai, India: Long-term outcome. J Glob Oncol. 2016;3:545–54.
4. Padma M, Kumar N, Munireddy J, Kumar A, Gujjal PC, Premalata SC. Tuberculosis coexistence in pediatric hodgkin's lymphoma: a tropical country experience. South Asian. J Cancer. 2020;9:236–9.
5. Obando P, Verón DA, Castellanos M, Fernández KS. Simultaneous occurrence of Hodgkin lymphoma and tuberculosis in children and adolescents. Pediatr Blood Cancer. 2020;67:e28405.
6. Paediatric TB Management Guideline 2022. National Tuberculosis Elimination Programme. Diagnosis of Extrapulmonary TB. New Delhi: Central TB Division, Ministry of Health and Family Welfare. 2022. p. 29–30.
7. Ali N, Selim M, Salah Z, El Nabarawy NM, Hussein H, Sidhom I. Cardiovascular and thyroid late effects in pediatric patients with hodgkin lymphoma treated with ABVD Protocol. J Pediatr Hematol Oncol. 2023;45:e455–63.
8. Zheng K, Bassal M, Mitsakakis N, et al. A longitudinal analysis of early lung function trajectory in survivors of childhood Hodgkin lymphoma. Cancer Rep (Hoboken). 2023;6:e1661.
9. Radhakrishnan V, Kapoor G, Arora B, et al. Management of Hodgkins lymphoma: ICMR consensus document. Indian J Pediatr. 2017;84:371–81.