Case report

Concurrent toxoplasmosis in a patient with Hodgkin lymphoma A case report

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Abstract

A 14-year-old previously healthy boy was investigated for unilateral cervical lymphadenopathy. The biopsy of the posterior cervical lymph node was suggestive of toxoplasmosis. Polymerase chain reaction on blood for *Toxoplasma gondii* was also positive, however, his serology was negative for *T. gondii*-specific antibodies. A repeat cervical lymph node biopsy performed in a different hospital revealed classic Hodgkin lymphoma with co-existent toxoplasmosis thus the child was transferred to the National Cancer Institute, Sri Lanka for further management. He was started on anticancer chemotherapy as well as pyrimethamine-sulfadiazine and folinic acid for toxoplasmosis. As the child was intolerant to the pyrimethamine-sulfadiazine combination, he was started on co-trimoxazole and is on further follow-up. This case reiterates the importance of promptly ruling out sinister diagnoses such as malignancies when presenting with lymphadenopathy, and the need for concurrent management of co-existent, opportunistic infections that would impair the clinical outcome of the immunocompromised host.

Key words: *Toxoplasmosis, immunocompromised host, Hodgkin lymphoma, lymphadenopathy*

Introduction

Toxoplasma gondii is an obligate, intracellular parasite capable of infecting nucleated cells in nearly all warm-blooded animals, with domestic cats and their relatives serving as definitive hosts.[1] While toxoplasmosis may be asymptomatic in immunocompetent individuals, it poses significant risks in immunocompromised patients, including potentially fatal encephalitis and pneumonitis.[1] Misdiagnosis of serious conditions such as malignancies as toxoplasmosis[2,3] can have detrimental consequences. This case report details a child initially diagnosed with acquired toxoplasmosis, who was subsequently found to have Hodgkin lymphoma.

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Case Report

A 14-year-old, previously healthy boy from a village near Matale town, presented to the local hospital in November 2023 with gradual, painless enlargement of left-sided cervical lymph nodes since October 2023. He denied constitutional symptoms such as fever, weight loss, anorexia, night sweats, fatigue, or respiratory issues, and had no neurological manifestations or allergies. His birth and developmental history were unremarkable, and he has been maintaining satisfactory academic performance in ninth grade at a local school. His father is an army officer, his mother a housewife, and he has two healthy younger siblings. There was no contact history of tuberculosis, but he had several pet cats and occasionally consumed unwashed garden fruits. Despite treatment at the local hospital his condition did not improve. Concerned, his mother sought further medical evaluation at District General Hospital, Matale in December 2023, where the otolaryngology (ENT) unit suspected lymphoma.

Ultrasound scan (USS) of the neck revealed altered architecture in a left-sided lymph node cluster, prompting histological assessment to exclude neoplasia. The biopsy indicated reactive lymphoid follicular hyperplasia with encroaching granulomata and myeloid cell sheets suggestive of toxoplasmosis. Blood polymerase chain reaction (PCR) confirmed *Toxoplasma* DNA positivity. Treatment was not deemed necessary upon Parasitology referral as the child was immunocompetent. Subsequent serological evaluation revealed negative *Toxoplasma*-specific IgG and IgM antibodies. Due to persistent lymph node enlargement, a repeat ultrasound was scheduled for June. However, his mother independently took him to the Sirimavo Bandaranaike Children's Hospital (SBSCH) in Peradeniya for re-evaluation.

A repeat ultrasound scan at Peradeniya revealed altered architecture and the biopsy revealed mixed cellular classic Hodgkin lymphoma alongside positive blood PCR for toxoplasmosis and micro-granulomata, indicating co-existent toxoplasmosis. He was subsequently transferred to the National Cancer Institute, Sri Lanka. On admission, he presented with firm, non-tender left submandibular and posterior cervical lymph node enlargement without systemic abnormalities. Laboratory investigations including full blood count, renal functions, erythrocyte sedimentation rate, and liver profile were normal, with fluctuating white blood count upon treatment and mild eosinophilia noted in the blood picture. Mantoux test and sputum acid-fast bacilli were negative, and chest x-ray and abdominal ultrasound were unremarkable.

The computed tomography (CT) scan of the neck, chest, abdomen and pelvis scan revealed multiple enlarged cervical and axillary lymph nodes indicative of Hodgkin lymphoma. Chemotherapy with vincristine sulfate, etoposide, prednisone, and doxorubicin hydrochloride commenced, followed by anti-toxoplasma therapy after the first cycle. This included oral pyrimethamine 200 mg single dose followed by 75 mg/day 6 hourly and sulfadiazine 1 g daily with folinic acid 25 mg daily for six weeks, monitored with weekly full blood counts. Due to severe vomiting following anti-toxoplasma treatment, he switched to co-trimoxazole; trimethoprim 10 mg/kg/day + sulfamethoxazole 50mg/kg/day in two divided doses for six weeks. Neurological and ophthalmological screenings were recommended, and serological/molecular tests were planned to monitor treatment response. The family received education on disease transmission, complications, and preventive measures. The timeline of events is shown in Figure 1.

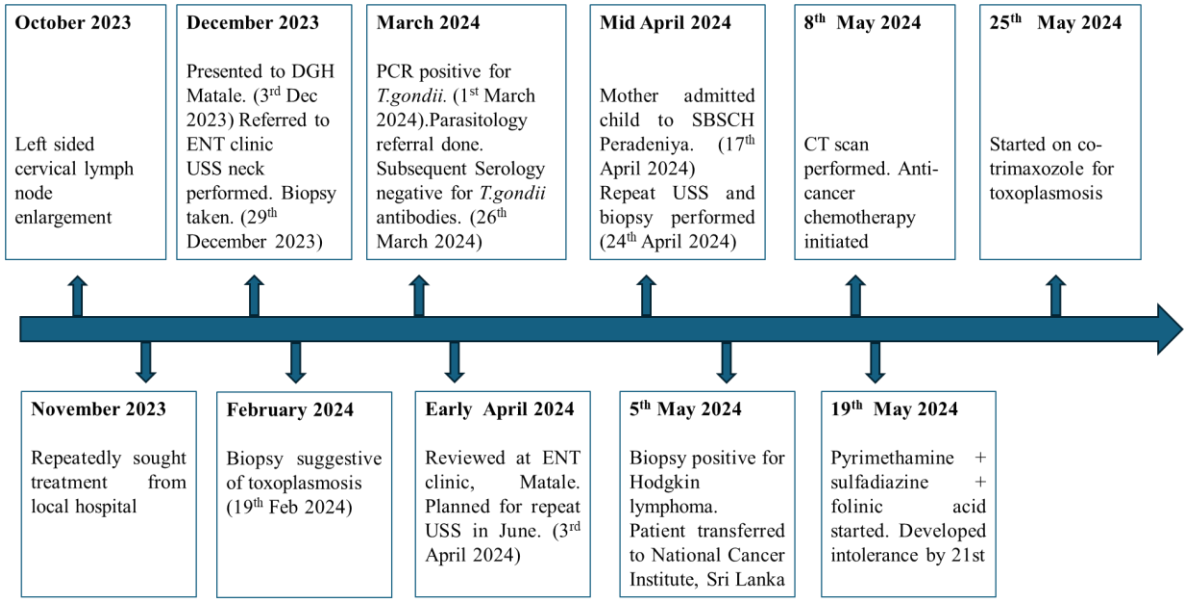

Figure 1. Timeline of events.

Discussion

Our diagnosis involves concurrent toxoplasmosis in a child with Hodgkin lymphoma, illustrating a classic example where the toxoplasmosis diagnosis obscured a more severe pathology. In Hodgkin lymphoma, malignant cells disrupt normal immune function, reducing functional T cells and altering cytokine production.[4] Patients are thus susceptible to infections due to both disease and treatment-related immunosuppression. The cellular immune response plays a critical role in immunity against toxoplasmosis, with the Interferon-Gamma producing functional CD4 and CD8 T cells playing an important part.[5] The humoral immunity alone is insufficient against the protection from the parasite.[5]

A positive blood PCR indicates active infection, though whether primary or reactivated from latency remains unclear. At the first evaluation by a specialist Parasitologist, the child was deemed immunocompetent (March 2024), as Hodgkin lymphoma had not been diagnosed yet. Treatment for toxoplasmosis in immunocompetent people, unless they are pregnant, is usually not warranted.[1] Negative serology reflects the child's inability to produce antibodies, however, repeat serological assessment, and testing paired samples to assess seroconversion is recommended. Upon the subsequent evaluation in May 2024, the child was regarded as having high risk of immunosuppression due to the Hodgkin lymphoma and the anti-cancer chemotherapy, thus, anti-Toxoplasma treatment was initiated, starting with pyrimethamine-sulfadiazine plus folinic acid.[1] Although classic Hodgkin lymphoma has a high cure rate with chemotherapy, 10-30% of patients do experience relapse or refractory disease depending on the stage.[6] Relapse of Hodgkin lymphoma may warrant haemopoietic stem cell transplantation, which would also require immunosuppression for a successful outcome. The parasite persists in the stage of bradyzoites-i.e., tissue cysts in muscles, central nervous system and other tissues and forms lifelong infection. This latent stage can be reactivated in the presence of immunosuppression, and give rise to severe manifestations such as encephalitis, pneumonitis and chorioretinitis. Monitoring at regular intervals for symptoms, for serological and molecular evidence of infection and even

chemoprophylaxis for prolonged periods may be required to prevent the occurrence of severe toxoplasmosis in this patient.[1]

The child's intolerance to pyrimethamine-sulfadiazine remains unexplained; potential reasons include sulfur intolerance or drug interactions with anti-cancer agents. Tolerance to co-trimoxazole suggests pyrimethamine intolerance. Despite challenges, it proved a valuable alternative for this high-risk patient.

This case underscores several crucial aspects of patient care. Firstly, the need to consider a broad differential diagnosis for cervical lymphadenopathy, especially in non-resolving cases as not to miss sinister pathologies. Secondly, the importance of molecular diagnostics for toxoplasmosis in immunocompromised patients. Thirdly, the necessity for accessible treatment for parasitic diseases (notably, pyrimethamine-sulfadiazine is unregistered in Sri Lanka and poses procurement challenges). Fourthly, the consideration of patient-specific factors influencing medication tolerance and the use of alternative regimen and finally, paramount importance of a multidisciplinary approach to ensure comprehensive care.

Declaration

Acknowledgement: All health professionals involved in the management of this patient are gratefully acknowledged.
Conflicts of Interest: None
Funding: None.
Ethics statement: Informed consent was obtained from the parents of the child and assent was obtained from the child. All identifiers of the child have been removed.
Authors' contributions: The data collection was done by YKP, CJW, MADPKW, MPKG, WKM, MMIRS, SMM and MSVBP. The patient management was by MS and SPG. The manuscript was drafted by YKP and CJW. Overall supervision was by SPG.

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