# Successful Treatment of Hepatosplenic T Cell Lymphoma in an Adolescent with Turner Syndrome Using Ifosfamide, Carboplatin, and Etoposide Followed by Allogeneic Hematopoietic Stem Cell Transplant

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Abbreviations key:

| Abbreviation | Full term/phrase |
|---|---|
| HSTCL | hepatosplenic T cell lymphoma |
| CT | computed tomography |
| PET/CT | positron emission tomography/computed tomography |
| ICE | ifosfamide, carboplatin, and etoposide |
| MRD | minimal residual disease |
| HSCT | hematopoietic stem cell transplant |
| NCCN | National Comprehensive Cancer Network |
| IVAC | ifosfamide, cytarabine, etoposide |
| CHOP | cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, and prednisone |

*MAIN TEXT*

To the editor: Hepatosplenic T Cell Lymphoma (HSTCL) is a rare malignancy that occurs most often in young adult males, and is associated with immunosuppressive medications[1–3]. Less than 10% of patients with HSTCL survive five years after diagnosis[4], and there is no consensus for treatment, particularly for pediatric patients[2].

A 14 year old female with Turner Syndrome and Crohn's disease previously treated with mercaptopurine for seven years presented following two weeks of facial and truncal rash (Figure 1), fatigue, night sweats, and hepatosplenomegaly. Mercaptopurine was discontinued 19 months prior to presentation. Laboratory evaluation revealed blast-like cells, white blood cell count 17500/mm$^3$, hemoglobin 10.7 g/dL, platelet count 119000/ mm$^3$, and lactate dehydrogenase 5,885 u/L. Bone marrow aspirate contained 31% malignant cells—positive for CD3, CD7, and CD56, and negative for alpha/beta T cell receptor—with isochromosome 7q and

8q gain. Computed tomography (CT) and positron emission tomography/computed tomography (PET/CT) confirmed hepatosplenomegaly and hypermetabolic splenic lesions (Figure 2). The diagnostic workup was consistent with HSTCL.

She received induction therapy with ifosfamide, carboplatin, and etoposide (ICE)[5]. After one cycle, rash resolved and splenomegaly markedly improved. She achieved a complete response with negative PET/CT scan and 0.009% minimal residual disease (MRD) after four cycles. She underwent allogeneic hematopoietic stem cell transplant (HSCT) from a matched unrelated donor following conditioning with total body irradiation, thiotepa, and cyclophosphamide. Bone marrow aspirate obtained 30 days after HSCT had rare suspicious cells, but MRD was <0.001%. One year after HSCT, bone marrow evaluation was MRD negative and PET/CT was negative for disease.

Patients with exposure to thiopurines and other immunomodulators have increased risk of HSTCL[1–3,6,7]. However, this is the first reported case of HSTCL in a patient with Turner Syndrome. While patients with Turner Syndrome have increased risk of solid tumors, increased hematologic malignancy is not reported in this group[8,9]. A systematic review of patients with HSTCL following immunosuppressive therapy for inflammatory bowel disease found that this cohort of patients were >90% male[6], an interesting finding considering this female patient had only one X chromosome. Also notable is the development of malignancy after more than a year from discontinuation of immunomodulators, indicating that risk may be sustained over months to years after exposure.

Outcomes among HSTCL case series are dismal[7,10,11], and treatment regimens vary widely. National Comprehensive Cancer Network (NCCN) guidelines revised January 2020 suggest ICE followed by allogeneic HSCT[1]. Ifosfamide, cytarabine, etoposide (IVAC) has been used with some success[4]; while cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, and prednisone (CHOP) has been largely accepted as inadequate[1,10]. While NCCN guidelines recommend allogeneic HSCT, American Society of Blood and Marrow Transplantation recommends autologous HSCT for older adults and those who have achieved complete response prior to transplant[12].

In summary, we successfully treated a 14 year old with Turner syndrome and HSTCL with ICE and allogeneic HSCT. She remains in remission 16 months from diagnosis and 12 months following HSCT. Some patients with this challenging disease can achieve sustained remission with aggressive induction chemotherapy followed by consolidation with allogeneic HSCT.

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*Figure legend:*

Figure 1: Non-blanching violaceous rash at initial presentation. Rash was convalescent on the lower two-thirds of the face (a), and macular over the trunk (b). Rash resolved completely after the first cycle of induction chemotherapy. Her family provided consent to publish these images. Photograph credit: Suhas Radhakrishna.

Figure 2: Diagnostic workup included CT of the neck, chest, abdomen, and pelvis and PET/CT. CT scan, identified the liver 17 cm in superior to inferior dimension without focal lesion and spleen 24 cm in superior to inferior dimension. Spleen was diffusely heterogeneous in attenuation with several large geographic areas of hypoattenuation. No additional areas of lymphadenopathy were identified (a). PET/CT was significant for massive splenomegaly with portions of the spleen intensely hypermetabolic with Deauville Score 5 (b).