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IMMUNOLOGY

A CASE OF LATE-ONSET ADOPTIVE AUTOIMMUNITY IN AN ALLOGENEIC STEM CELL TRANSPLANT RECIPIENT

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Summary

A major complication of allogeneic hematopoietic stem cell transplant (allo-HSCT) is the potential transfer of autoimmune conditions from the donor to the host. We describe a case of a Non- Hodgkin's Lymphoma patient who received an allo-HSCT from her HLA-matched brother who had psoriasis. Her transplant course was complicated by graft-versus-host disease, managed with prednisone and tacrolimus. Nearly two years post-transplant, she developed psoriatic arthritis. We highlight a rare case of late-onset or masked adoptive autoimmunity presenting as psoriatic arthritis post-allo-HSCT. This case demonstrates a need to monitor delayed autoimmune presentations in transplant patients who develop graft-versus-host disease.

Key words: hematopoietic stem cell transplant, autoimmunity, psoriatic arthritis, graft versus host disease

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INTRODUCTION

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a procedure in which a patient's own stem cells are replaced with stem cells from a healthy donor to treat hematologic disorders, autoimmune disorders, or malignancies such as leukemia and lymphoma. Graft-versus-host disease (GvHD) is a major complication of allo-HSCT, whereby graft cells recognize the host cells as foreign and attack them in a T-cell mediated reaction. GvHD can present in various organ systems including diarrhea, arthralgias, and skin rashes, and is commonly managed with immunosuppressive medications [1].

After receiving a transplant, the host immune system is gradually replaced by the donor's immune system in an intricate process that spans months to years to completion, beginning with early reconstitution of the innate immune system (e.g., natural killer cells, neutrophils) and late reconstitution of the adaptive immune system (B and T cells). This forms the basis of adoptive autoimmunity, a major complication of allo-HSCT wherein the host develops autoimmune diseases that were present in the donor. In both GvHD and adoptive autoimmunity, symptoms generally present within twelve months post-transplant [1,2].

Psoriatic arthritis is a chronic autoimmune disease, characterized by combined T-cell-mediated joint inflammation and psoriasis. Genetics plays an important role in its development, and the presence of either psoriatic arthritis or psoriasis in a family member can strongly support its diagnosis [3]. Currently, there are no published cases of adoptive autoimmunity presenting as psoriatic arthritis post-allo-HSCT.

We describe a rare case of an allo-HSCT recipient who had a unique, late-onset presentation of psoriatic arthritis as a form of adoptive autoimmunity, originally masked by immunosuppressive medications.

CASE DESCRIPTION

A 33-year-old woman at our cancer center was diagnosed with Stage IV low-grade follicular non-Hodgkin's lymphoma and was treated with several courses of chemotherapy. Her disease relapsed four years later, and she underwent an allo-HSCT from her 6/6 HLA match brother, who had psoriasis but not arthritis. Her post-transplant course was complicated by GvHD presenting eight months post-transplant as profuse diarrhea, elevated liver enzymes, xerosis of the skin and conjunctiva, and xerostomia. GvHD prophylaxis was unknown. She was subsequently stabilized with tacrolimus and prednisone.

Almost two years post-transplant, the patient developed new onset axial and large joint arthralgia and stiffness affecting the neck, jaw, shoulder, elbow, hands, wrists, and knees bilaterally, shortly after her prednisone was discontinued. Her tacrolimus was also being weaned during this time. Concurrently, she also developed new onset bluish-purple discolouration and swelling at the proximal interphalangeal joint of her left fourth finger, and the third metatarsophalangeal joint of her left foot. Two months later, she experienced worsening pain and swelling of the small joints of her hands and feet, hips, shoulders, as well as cervical and lumbar axial skeleton stiffness. In addition to her arthritic symptoms, a patch of psoriasis was found in the peri-umbilical area. As these issues were initially thought to be related to chronic GvHD (i.e. lichen planus), high dose prednisone and tacrolimus were re-initiated, but with no symptomatic benefit. Initial bloodwork showed elevated c-reactive protein, erythrocyte sedimentation rate and positive rheumatoid factor. She was subsequently referred to a rheumatologist, who diagnosed her with psoriatic arthritis. Through management with sulfasalazine, hydroxychloroquine and methotrexate, her symptoms became controlled within two years. The case timeline is summarized in Figure 1.

DISCUSSION

In certain presentations such as skin lesions, it can be difficult to distinguish whether an allo-HSCT patient's signs and symptoms are due to GvHD or adoptive autoimmunity, as they may mimic one another with considerable overlap. For example, George et al. described a case of psoriasis that developed in a nine-year-old boy who received an allo-HSCT from his sister who had no history of psoriasis. In their case, GvHD was excluded through multiple skin biopsies and his psoriasis was thought to be due to adoptive autoimmunity [4]. In our case, it is possible the patient may have developed her psoriatic arthritis regardless of whether she received the allo-HSCT, as her autoreactive T-cells may have been present in low titers due to the tenuous balance between autoreactivity and tolerance with no clinical evidence of disease [5]. However, this is unlikely to occur, and the replacement of her immune system by allo-HSCT suggests that her autoimmunity was most likely donor-derived (i.e. adoptive). This is further supported by the fact that her donor brother developed psoriatic arthritis simultaneously with the patient.

There are currently no reported cases on the development of psoriatic arthritis as a form of adoptive autoimmunity. Daikeler et al. (2011) described a case of psoriatic arthritis that developed in a three-year-old boy after allo-HSCT, however it is unclear whether this disease developed *de novo* [6].

Adoptive autoimmunity and GvHD generally present within twelve months post-allo-HSCT [2]. We highlight a patient with a late presentation of psoriatic arthritis nearly two years after receiving an allo-HSCT from her HLA-matched brother. Given that her psoriatic arthritis development coincided with the discontinuation of immunosuppression, it was likely delayed by her medications. Li et al. (2015) highlighted a similar patient who was treated with prednisone for nine months for GvHD and immediately developed psoriasis after prednisone was discontinued [7]. It is possible that the combination of tacrolimus and prednisone rather than prednisone alone, led to a delayed presentation of psoriatic disease (> 20 months post-transplant) in our case.

In conclusion, we describe a unique case of a patient who developed psoriatic arthritis as a form of adoptive autoimmunity nearly two years post-allo-HSCT, delayed by immunosuppressive medications for GvHD. We demonstrate a need for extended monitoring for delayed autoimmune presentations in allo-HSCT recipients whose post-transplant course is complicated by GvHD.

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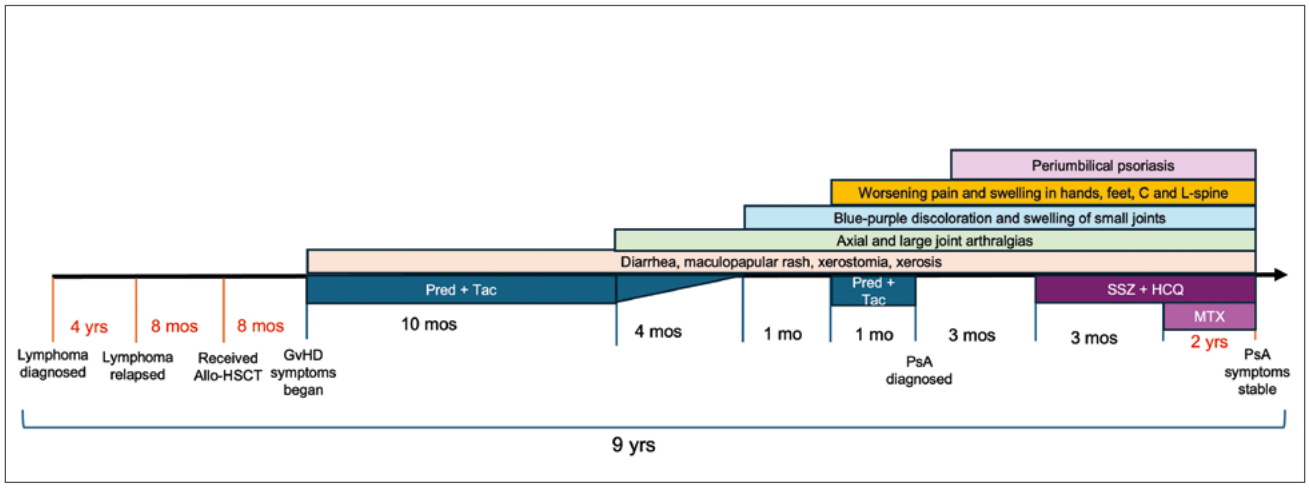

Figure 1. Timeline of patient course. Timeline presented as red text is not to scale.
yrs: years; mos: months; Pred: prednisone; Tac: tacrolimus; SSZ: sulfasalazine; HCQ: hydroxychloroquine; MTX: methotrexate.

Conflict of interest statement

The authors declare no conflict of interest.

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Ethical consideration

Our institution does not require formal ethics approval for individual cases or case series. Verbal informed consent was obtained from the patient through a legally authorized representative for anonymized patient information.

Author contributions

AYW: collected data, literature review, drafted the manuscript, and completed the submission process; AX: responsible for critical assessment and providing clinical details, drafting and review of manuscript, UD: critical assessment, idea generation, providing clinical insights, drafted and reviewed the manuscript and corresponding author; AA: drafting, reviewing of the manuscript. All authors have read and approved the final manuscript.

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