Sezary syndrome, thyroid carcinoma, and renal carcinoma in a patient with Poland syndrome

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Key words: cutaneous T-cell lymphoma; papillary thyroid carcinoma; Poland syndrome; renal cell carcinoma; Sezary syndrome.

INTRODUCTION

Sezary syndrome is a type of cutaneous T-cell lymphoma (CTCL) with aggressive clinical behavior. Although sometimes labeled as a leukemic variant of mycosis fungoides, Sezary syndrome may arise from distinct T-cell subsets, rather than existing on a continuum with mycosis fungoides. We present a case of Sezary syndrome occurring in a patient with Poland syndrome, who, with staging, was found to have 2 additional primary malignancies. Poland syndrome is a rare congenital unilateral aplasia of the chest wall muscles. It can be associated with other features such as symbrachydactyly, nipple underdevelopment, and axillary alopecia, and has also been associated with malignancies. Although the cause of Poland syndrome is unknown, a vascular embryonic origin has been proposed, and no pathogenetic mechanism has been identified.

CASE REPORT

A 50-year-old man was referred for evaluation of erythroderma and progressive lymphocytosis. He had a 20-year history of pruritic scaly erythematous plaques on his scalp, back, and elbows. His rash was treated as psoriasis for many years with topical corticosteroids and topical combinations of corticosteroids and calcipotriol, with minimal improvement. Two years prior to his referral, he began treatment with ustekinumab, and the plaques improved with complete clearance 1.5 years into treatment; however, his pruritus persisted. Almost 2 years after initiation of ustekinumab, he experienced recurrence of erythematous scaly plaques on 50% of his body. The ustekinumab was stopped, and skin biopsies were performed. On referral, he was erythrodermic with greater than 80% of his body surface area covered in confluent scaly erythematous patches and plaques. His physical examination was also notable for onycholysis, subungual hyperkeratosis, splinter hemorrhages of the finger- and toenails, and hyperlinear fissured palms with keratoderma (Fig 1). There was clinically palpable bilateral cervical and axillary lymphadenopathy. He also had congenital right breast aplasia with an intact nipple, consistent with Poland syndrome (Fig 2); this was confirmed by computed tomography of the chest, which illustrated absence of the right pectoralis major and minor muscles. His past medical history was significant for hypertension controlled with amlodipine, cilazapril, and spironolactone; diet-controlled type-II diabetes mellitus; and obstructive sleep apnea; he was not on any other biologics for treatment of psoriasis. There was no family history of dermatologic or malignant conditions.

On presentation, his white blood cell count was elevated at 34.6 × 10⁹/L (normal, 4.0-11.0 × 10⁹/L),...
with an elevated lymphocyte count of $26.5 \times 10^9/L$ (normal, 0.7-3.5 \times 10^9/L). In fact, his blood counts showed mild lymphocytosis 4 years previously (white blood cells, $11.6-16.7 \times 10^9/L$; lymphocytes, $4.5-8.9 \times 10^9/L$). Cells with characteristic cerebriform nuclei consistent with Sezary cells were seen on a peripheral blood smear (Fig 3). Peripheral blood flow cytometry showed lymphocytosis composed of 97% T cells with an increased CD4:CD8 ratio (38:1) with partial loss of CD7, consistent with Sezary cells. The Sezary cell count was $26.2 \times 10^9/L$. Skin biopsies revealed atypical T-cell infiltrates suggestive of a CD4+ T-cell lymphoproliferative disorder (Fig 4). The T cells were positive for CD3 and CD4, scattered-positive for CD30, and negative for CD5 and CD7. Polymerase chain reaction analysis of peripheral blood revealed monoclonal rearrangements of both TCRG and TCRB genes. This atypical T-cell clone was also identified by T-cell receptor studies in skin, axillary lymph node and bone marrow biopsies. His bloodwork was otherwise unremarkable, including normal electrolytes, liver panel, renal function, and human T-lymphotropic virus type 1 serology.

His presentation met the criteria for diagnosis of Sezary syndrome: Erythroderma covering greater than 80% of the body, clonal T-cell receptor rearrangement in the blood that matched the skin, and abnormal lymphocytes in the blood with a Sezary cell count of more than 1000 cells/\mu L. In addition to bilateral axillary, external iliac, inguinal, and femoral lymphadenopathy, a staging computed tomography identified splenomegaly, a renal mass, and a thyroid nodule. Further investigation found the renal mass to represent renal clear cell carcinoma, which was treated with cryoablation. Biopsy of the thyroid nodule revealed a third primary malignancy of papillary thyroid carcinoma, for which he is awaiting surgical management.

Staging of his Sezary syndrome was determined to be T4N2bM0B2 or stage IVA1. He was initiated on treatment with extracorporeal photopheresis 2 consecutive days every 2 weeks. He experienced moderate improvement of his pruritus and demonstrated a partial response in the blood. Interferon alfa-2b 1.5 million units thrice weekly were added 2 months later. He also found symptomatic relief of his pruritus with betamethasone valerate 0.1% cream
twice daily. His concurrent secondary malignancies make curative intent allogeneic transplantation for Sezary syndrome a relative contraindication. This may be reconsidered once the renal cell and thyroid malignancies are definitively treated and in complete remission.

DISCUSSION

Both hematologic and solid organ malignancies have been reported in patients with Poland syndrome, including renal cell carcinoma as observed in our case (Table I). These malignancies have been described in both sexes and all ages. None of these cases have arisen in the setting of immunosuppressive or biologic therapy. To the best of our knowledge, there have been no reports of an individual with Poland syndrome developing CTCL or thyroid cancer, as well as no reports of multiple primary malignancies in a single individual.

CTCLs have been associated with an increased risk of second primary malignancies, although no studies have focused on this relationship with Sezary syndrome alone. This is thought to be due to decreased cellular immunity and immune surveillance. A retrospective cohort study of almost 2000 patients with mycosis fungoides or Sezary syndrome found an increased risk of both hematologic and solid organ malignancies, with a standardized incidence ratio of 1.32; included were reports of renal cell, but not thyroid, carcinoma.12

Although tumor necrosis factor inhibitors, have been linked with an increased risk of malignancy, we do not believe that ustekinumab therapy played a role in our patient. This inhibitor of the p40 subunit of interleukin 12 and interleukin 23 has been found to confer no increased risk of malignancy compared with placebo in multiple long-term studies.13

Table I. Malignancies associated with Poland syndrome

| Ductal breast carcinoma (reviewed by Zhang et al)1 |
| Signet cell gastric adenocarcinoma2,3 |
| Head and neck planocellular carcinoma4 |
| Hematologic malignancies (reviewed by Sackey et al)5,6 |
| • Acute lymphocytic leukemia |
| • Acute myelogenous leukemia |
| • Large-cell histiocytic lymphoma |
| Kidney cancer |
| • Nephroblastoma7 |
| • Renal cell carcinoma8 |
| Leiomyosarcoma9 |
| Squamous cell carcinoma of the lung10 |
| Neuroblastoma1 |

Theoretically, inhibition of pro-inflammatory cytokines and T-cells helper type 1 pathways, as a result of initiation of ustekinumab, may have unmasked or accelerated the patient’s presentation of CTCL.14 Interestingly, his lymphocytosis was observed many years prior to the initiation of ustekinumab, and his pruritus persisted despite treatment of his psoriasis, which would suggest that he had longstanding CTCL diagnosed as psoriasis.

In the present case, it is uncertain whether our patient was predisposed to the development of secondary malignancies on the basis of his cutaneous lymphoma, immunosuppressive therapy, or underlying Poland syndrome. Nevertheless, it illustrates the importance of heightened awareness regarding the increased risk for secondary malignancies with Poland syndrome and CTCLs. Thorough investigation of symptoms and age-appropriate cancer screening in these populations is important for comprehensive patient care.

The authors would like to thank Dr. Joyce Wong (Skin Health & Wellness Centre, Calgary, Canada) for her contribution to the case timeline.

Conflicts of interest

None disclosed.

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