Rare cancer, common conversation

A case of T-cell prolymphocytic leukemia with end-of-life discussions

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INTRODUCTION

Cancer in its many forms is particularly common in elderly populations. For females over the age of 80 in Canada, approximately 2% will have a new diagnosis of cancer each year.¹ With thousands of types and subtypes, cancer is a heterogeneous spectrum of diseases, each with its own difficulties in establishing a diagnosis and an effective management strategy.

The diagnosis and treatment of cancer in the elderly is fraught with additional challenges. Symptoms in the elderly may be atypical or less pronounced compared to younger patients. Seniors often have multiple pre-existing conditions and comorbidities in addition to their presenting complaint. Most geriatric patients take numerous medications, complicating a straightforward diagnosis and confounding a simple treatment plan.²⁻⁴ Cognitive impairment, whether due to pathology or physiological decline, can be a complicating factor, hampering physician-patient interactions.² Even good clinicians can still struggle with the complexities of common malignancies in an elderly patient due to these additional factors. Rarer malignancies can be that much more challenging.

Here, we present a case of a patient diagnosed with an exceptionally rare hematologic cancer in combination to other comorbidities, and explore how the health care team and the family was able to collaborate to develop a treatment plan acceptable to both parties.

INITIAL PRESENTATION AND DIAGNOSIS

The patient, CB, was an 83-year-old female retired hairdresser who presented with her daughter to her primary care provider with a 1-2 month history of left upper quadrant pain. Initially, CB's pain was ill-defined, intermittent, and did not limit her activities, but worsened significantly over the few days before the visit.⁵

On presentation, CB was holding her left side and grimacing in pain. CB had an extensive past medical history headlined by mild vascular dementia and heart block requiring a pacemaker. She also had a history of hypertension, hyperlipidemia, bilateral carotid stenosis, and scoliosis. CB's medications included aspirin 81 mg daily, metoprolol 100 mg twice daily, verapamil 240 mg daily, donepezil 10 mg daily, ezetimibe 10 mg daily, fluvastatin XL 80 mg daily, and memantine 10 mg twice daily. CB's adult children who lived nearby provided assistance with medications and meals during daily visits, resulting in good compliance to her prescriptions and reasonable nutrition status. CB also retained many of her activities of daily living despite her conditions; she dressed, bathed, toileted, and ambulated without assistance. CB was a nonsmoker and consumed 3-4 beers per day. Despite her dementia CB had some ability to make decisions regarding her life and health, relying on her daughter more in an advisory capacity on matters needing clarification.⁵

On physical examination CB did not appear ill. However, the exam revealed positive bilateral lymphadenopathy in the neck, axilla, and inguinal regions. Fine inspiratory crackles were noted in the left lower base of the lung. Tender splenomegaly, palpable down to the left lower quadrant, was also found. No hepatomegaly was noted.⁵

After being admitted to hospital, computed tomography revealed an enlarged spleen occupying two-thirds of the left abdominal cavity, a small pleural effusion at the left lung base, and enlarged lymph nodes along the gastro-hepatic ligament, the porta hepatis, the mesentery, and both groins. Complete blood count was remarkable for a white blood cell count exceeding 70 000 with atypical lymphocytes and 20% blasts. Platelets were low at 60 000. A referral to hematology/oncology was made to investigate possible lymphoma or leukemia. Peripheral smears revealed lymphocytes with nuclear contour irregularities, cytoplasmic border irregularities, and rare nuclear clefts. Prominent nucleoli were lacking in most cells. Bone marrow biopsy revealed significantly increased hypercellularity consisting primarily of small lymphocytes. Flow cytometry detected aberrant CD4+/CD8- T-cells and was positive for clonal rearrangement of the TCR- β gene, suggesting T-cell leukemia. CB was negative for human T-cell lymphotropic virus-1, ruling out adult T-cell lymphocytic leukemia. A final diagnosis of T-cell prolymphocytic leukemia (T-PLL) was made.⁵

T-CELL PROLYMPHOCYTIC LEUKEMIA

T-PLL is a rare malignancy, typically affecting those 65 or older, with males somewhat more affected than females. Previously described as a variant of chronic lymphocytic leukemia (CLL), it represents less than 1% of all mature lymphocytic leukemia diagnoses.^{5,6} While most forms of PLL are malignancies of B-cells, T-PLL is a malignancy of mature T-cells. It is a particularly aggressive form of lymphocytic leukemia, with reported median survival times after diagnosis counted in months.⁷

As T-PLL is quite rare, diagnosis can be difficult. A key feature of T-PLL is dramatic splenomegaly, palpable 10 cm below the left costal margin in over 80% of patients. Other potential symptoms include hepatomegaly, ascites, lymphadenopathy, lymphocytosis, pleural effusions, skin lesions, and CNS involvement.⁶ Further testing typically involves peripheral smears and bone marrow biopsies. Immunophenotype features of T-PLL include the presence of CD52 as well as T-cell markers CD2, CD3, and CD7.⁷ Genetic features include clonal rearrangement of TCR genes.⁸

Typical cancer treatments such as splenectomy, splenic irradiation, leukaphoresis, or standard chemotherapy are largely ineffective. The primary therapy is a monoclonal antibody called alemtuzumab, which targets CD52 and was created to treat B-cell CLL

resistant to standard chemotherapy. CD52 targeting causes cancer cell lysis by apoptosis through a host effector mechanism. Trials have shown remission rates of up to 30 months in patients with T-PLL, and several further studies found a median survival time of 14.8 months with treatment. Hematopoietic stem cell transplantation is an option for those who achieve complete remission with alemtuzumab. Alemtuzumab is associated with serious toxicities, particularly myelosuppression. Potential adverse effects include severe infections, bleeding crises, and hypersensitivity reactions. Regrettably, in all cases the cancer eventually relapses.^{7,9,10}

TREATMENT AND FOLLOW-UP

The health care team engaged in a detailed discussion with CB and her family regarding beliefs, quality of life, and the options available for palliative and curative treatment. Given CB's advanced age and multiple comorbidities, the likelihood of a negative outcome from toxicities or side effects was significant. Officially, CB's daughter was the surrogate decision maker. However, she wanted CB to be given the opportunity to choose her own treatment, despite the possibility that she may not be fully aware of the risks and benefits of treatment. Ultimately, CB opted for chemotherapy with alemtuzumab, stating that she "just wasn't ready to die yet." A modified treatment regimen with subcutaneous injections and a slow introduction of alemtuzumab was initiated to minimize the potential for side effects.⁵

Cost was another challenge faced by the health care team. A 12-week course of alemtuzumab costs over \$240 000. The oncologist and CB's daughter collaborated closely to find outside sources of funding to help cover this cost. An infusion center was found several days later, and chemotherapy was initiated in a timely manner.⁵

CB tolerated the treatment well, with few side effects. After 6 weeks of therapy there was a significant reduction in splenomegaly and lymphadenopathy, with the white blood cell (WBC) count returning to 2.2, and platelets returning to 176 000. Following the 12-week treatment CB was discharged on antibiotics as a result of T-cell obliteration and followed monthly. At two months post-treatment, she was still asymptomatic, with a WBC count of 6.7 and platelets at 143 000. At three months post-treatment her T-cell counts returned to 200 000 and antibiotic therapy was discontinued.⁵

CB continued to live in her own home post-therapy. She celebrated her 84th birthday with family and friends, and was able to travel to her hometown to visit her remaining family members. However, 4 months post-therapy she began to develop recurring left upper quadrant pain and splenomegaly. Palliative radiation therapy was offered. CB's daughter, after discussion with the rest of the family, refused radiation therapy and other treatment options on grounds that it would not bring CB an acceptable quality of life. CB was kept in her home with hospice care for pain management and end-of-life care. Despite her deteriorating condition, she remained mobile and active until 3 days prior to entering a comatose state. She died shortly thereafter with her family at her bedside.⁵

DISCUSSION

The medical side of this case involves an exceedingly rare, but notably aggressive form of leukemia. Establishing a diagnosis of T-PLL can be troublesome given its rarity and its nonspecific symptoms on presentation. Treatment is frequently minimally effective, with the main prognostic factor being response to alemtuzumab.⁷ As T-PLL is primarily a disease of the elderly, both diagnosis and treatment can be challenging. In this case, dementia proved to be the main hurdle, as concerns of comprehension by CB were noted by the involved clinicians.⁵ Nevertheless, physicians should be aware of this rather unique form of hematologic malignancy, mindful of its defining features on physical exam and be prepared to make appropriate referrals to hematology/oncology when suspicion of T-PLL is high.⁷

However, at its core this case is worth highlighting for the manner in which end-of-life discussions occurred. In an aging society, the strategies for addressing terminal illness in the context of cognitive decline become increasingly important.^{2,4} This case underlines the necessity of including all key stakeholders in the conversation about treatment options, including clinicians, patients, and family members.^{2,5} Not every malady is curable, but all patients can feel cared for by their medical team.

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