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Percutaneous Cryoablation of a Relapsed Mantle Cell Lymphoma: A Case Report

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Abstract

Relapsed/refractory mantle cell lymphoma (MCL) is an aggressive, non-Hodgkin's B-cell lymphoma with a poor long-term survival rate and suboptimal responses to multiple conventional treatments. This case report will detail a case of a patient with relapsed/refractory MCL that was treated with percutaneous cryoablation for a localized recurrence and no evidence of further relapse two years post-ablation.

Introduction

Mantle cell lymphoma (MCL) is a rare and aggressive form of non-Hodgkin lymphoma (NHL) arising from cells of mantle zone origin. MCL accounts for 3-6% of adult-onset NHL cases in western countries and is associated with a considerably poor long-term survival rate [1-3]. Pathogenesis is wide-ranging and includes aberrant cell cycle regulation, DNA damage response, molecular and genomic alterations, BCR signalling, and interactions with the lymphoid tissue microenvironment [1,4]. The majority of MCL cases are characterized by constitutive expression of cyclin D1 with translocation t(T11;14) [1,4]. Other major molecular aberrations have been identified, such as SOX-11 overexpression, TP53 mutations, epigenetic aberrations and micro environmental impact. While MCL growth cannot be attributed to a single cause, a combination of these factors is thought to determine clinical course and prognosis for patients [1]. MCL is also associated with early relapse, which has an even worse overall survival of less than 3 years along with a poor response rate to current therapies [1,4]. A patient may be asymptomatic in the early stages of MCL, which could delay the diagnosis until later stages when disease has already metastasized to regional lymph nodes or extra nodal sites [1,5].

Thorough work up is critical to tailor therapies to each patient's unique disease and MCL factors. Age, patient performance status, comorbidities and symptoms all need to be considered when determining course of treatment for each patient [1,4]. Intensive chemo immunotherapy with or without autologous stem cell transplant (SCT) plus rituximab maintenance is standard of care first line treatment for fit patients [6,7]. A meta-analysis reported that rituximab maintenance therapy improved the progression-free survival and overall survival of patients with previously untreated MCL who had induction chemo immunotherapy followed by

an autologous stem cell transplantation [8]. More recently, new drugs have been added to the arsenal to treat MCL, which include proteasome inhibitor Bortezomib, Bruton's Kinase (BTK) Inhibitors and immunomodulatory agents [6,7].Therapies for mantle cell lymphoma have made substantial improvements with advancements in the study of the biology of the disease, however, MCL still remains incurable and further research is necessary in fighting this disease. Development of new and effective therapies for systemic and local control of the disease is vital.

Cryoablation, intraoperative or percutaneous, is a well-established procedure, which utilizes extremely cold cytotoxic temperatures for cell destruction [9-12]. Multiple cryoprobes can be utilized to sculpt an ice ball to cover specific tumour size with lethal ice in nearly any location [13]. Percutaneous image guided cryoablation is a minimally invasive technique which has been highly successful as a feasible treatment option for the local treatment of soft tissue tumours. Cryoablation does not discriminate between cell types, as long as lethal temperature isotherm guidelines are met [9-12]. Herein, we detail a case of a patient with refractory MCL, who had multiple failed rounds of chemotherapy and radiation and then was successfully controlled with CT-guided percutaneous cryoablation.

Case Presentation

A 57-year-old female presented to our institution after referral from her primary care physician. Initially, she presented with severe night sweats, weight loss and splenomegaly for which she underwent complete workup and bone marrow biopsy. After thorough evaluation, she was diagnosed with aggressive variant MCL with bone marrow involvement. Assessment of detailed cytogenetic test results confirmed a translocation (T11;14). Initially, the patient received hyper-CVAD (Cyclophosphamide, vincristine, doxorubicin, and dexamethasone) 1A and 1B chemotherapy, but had inadequate response to the treatment and progressed. She was then started on bendamustine, rituximab and bortezomib and showed a marked response, after which she underwent allogenic stem cell transplant using a match-related donor and achieved complete remission. Subsequently, almost three years post-transplant, imaging demonstrated a new left perinephric mass. CT-guided biopsy of this left perinephric retroperitoneal mass confirmed MCL recurrence. The patient was enrolled in a new clinical trial using a PI3 Kinase drug, however, had to be taken off the trial due to adverse event of persistent severe cytopenia. She was then started on lenalidomide and rituximab and achieved complete remission. Two years later, a new retroperitoneal soft tissue mass recurrence along the left psoas muscle was detected via PET/CT scan (Figure 1) and was different from the prior perinephric recurrence. This new recurrence was also pathologically confirmed with CT-guided biopsy. This new retroperitoneal mass was subsequently treated with and failed localized radiation therapy. Post-therapy PET scan continued to show an FDG avid 1.1 cm soft tissue nodule along the lateral margin of the left psoas muscle. Additional systemic therapy options were limited, and resection was deemed difficult. After discussion at our Multidisciplinary Tumor Board (MDT), the decision was made to proceed with percutaneous cryoablation of the recurrent soft tissue nodule. This decision was extrapolated based on our previous success with a large series (>500) of soft tissue mass cryoablation procedures of multiple other different tumour types (metastases and primary soft tissue tumours) for local disease control.

This procedure was conducted under approval of the Institutional Review Board as well as informed written and verbal consent from the patient. The procedure was performed in the CT suite under CT fluoroscopic guidance, conscious sedation was provided by anesthesia staff and lidocaine 1% with epinephrine (Fresenius Kabi USA, Lake Zurich, IL) was utilized for local anesthesia. Prophylactic Cefazolin (Ancef) 1 mg antibiotic was given at the onset of the procedure. The patient was placed in the right lateral decubitus position on the CT table and the overlying skin was marked, prepped, and draped in a sterile fashion. On the initial pre-procedure CT images, it appeared the lesion had doubled in size (Figure 2) since the patient's most recent imaging study, however, it remained amenable to percutaneous ablation. Under CT fluoroscopic guidance, an initial 20-gauge spinal needle (BD Medical, Franklin Lakes, NJ) was advanced to the area adjacent to the mass for probe placement guidance. Two 2.1 mm cryoprobes (Boston Scientific, Marlborough MA) were placed along the upper and lower margins of the left retroperitoneal mass abutting the psoas muscle (about 2 cm apart) making sure to bracket the entire mass (Figure 2). The spinal guidance needle was removed after the first probe was placed. An 18-gauge trocar needle (Cook Medical, Bloomington, IN) was placed under CT fluoroscopic guidance between the mass and adjacent bowel for hydro dissection displacement protection of the nearby vital structures (ie: nerves and bowel) during the procedure. Normal saline/contrast in a 60:1 ratio was utilized for hydro dissection displacement throughout the procedure. A 10-minute freeze cycle was performed, followed by a 5-minute passive thaw (stick) and a 5-minute second freeze cycle, after which the probes were thawed and removed. The ice ball size was monitored continuously throughout the procedure to confirm adequate coverage of lethal ice, which encompassed the entire left retroperitoneal mass. Post-procedure CT images were obtained to document ablation zone size and any immediate procedural complications (Figure 2). The patient tolerated the procedure well without immediate complications. She was then transferred to recovery in stable condition and discharged the next day following overnight monitoring post-ablation. Periodic follow-up PET/CT scans were performed post-cryoablation and demonstrated a resorbing avascular left retroperitoneal ablation zone without evidence of recurrence or suspicious FDG avidity. The patient remains under surveillance and appears to be in remission per

recent PET/CT scan two years post ablation with no clinical evidence of recurrent disease (Figure 3).

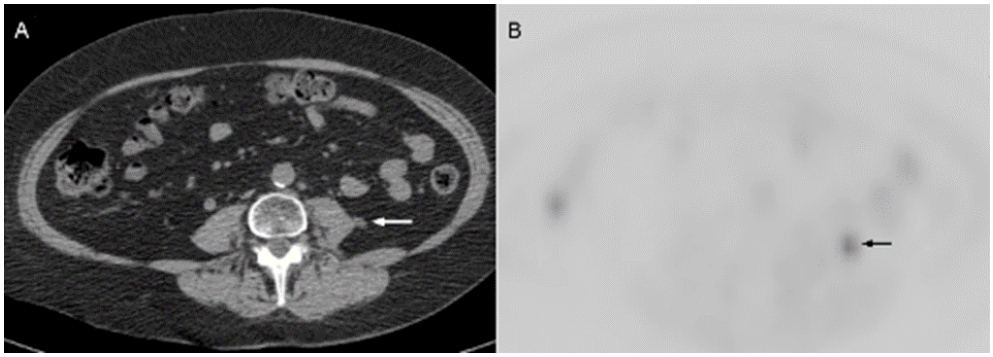

Figure 1: PET/CT scan: A. Axial unenhanced CT image of the abdomen demonstrates a recurrent soft tissue mass (white arrow) abutting the left psoas muscle. B. Axial PET image demonstrates hyper metabolism within a mass (black arrow) along the left psoas muscle.

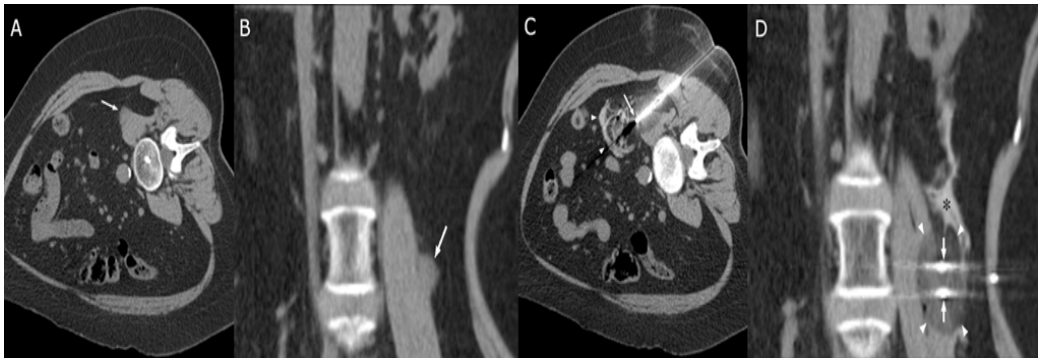

Figure 2: CT-guided Cryoablation Procedure: A. Axial pre-procedure CT image demonstrates interval increase in size of the left retroperitoneal soft tissue mass abutting the psoas muscle (white arrow). B. Coronal pre-procedure CT image demonstrates interval increase in size of the left retroperitoneal mass abutting the psoas muscle (white arrow). C. Intraprocedure axial CT image demonstrates the cryoprobes with surrounding ice ball encompassing the mass (white arrow). Hydro protection fluid (arrowheads) is present between the ablation zone and bowel/ureter. D. Intraprocedure coronal CT image demonstrates two cryoprobes (white arrows), less than 2 cm apart, bracketing the soft tissue mass with surrounding ice ball (white arrow heads) encompassing the nodule. Hydro protection fluid (black asterisk) is present between the ablation zone and bowel/ureter.

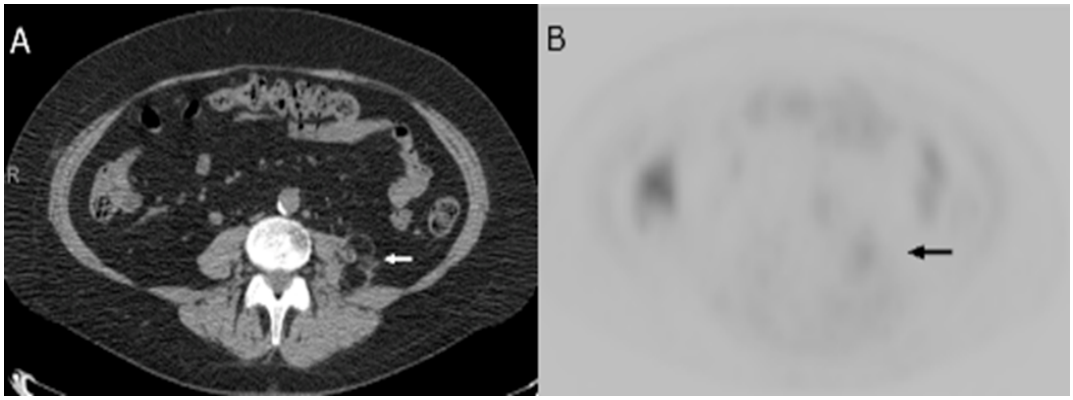

Figure 3: Follow-up: A. Two-year axial CT follow-up image demonstrates a resorbing ablation zone (white arrow) without evidence of recurrent disease. B. Two-year PET axial images demonstrate no significant hyper metabolism in the ablation zone (black arrow) of previous left retroperitoneal mass. Faint metabolism on the medial margin is likely physiologic or related to granulation tissue.

Conclusion

Treating patients with MCL can be challenging due to the aggressive nature of the disease and early relapse [1, 4]. To the best of our knowledge, this is the first report of cryoablation as a treatment for local control of relapsed MCL or any lymphoma. Image-guided percutaneous cryoablation for local tumor control has documented high efficacy and low morbidity across multiple different sites (i.e., kidney, soft tissue, lung and liver) [9-12]. The cytotoxic temperatures of cryoablation freeze/thaw cycles do not discriminate between cell types and are lethal to nearly all cell types, normal and malignant [13]. In conclusion, a comprehensive report of one of the first image-guided cryoablation procedures for local control of relapsed lymphoma (MCL) in the soft tissues was detailed in this report. Ablation therapy, specifically cryoablation, could prove to be a safe and effective way to locally treat relapsed or refractory lymphoma.

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