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Case report

Successful treatment of refractory chylous ascites due to follicular lymphoma with very low-dose radiotherapy

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ABSTRACT

Chylous ascites is an extremely rare complication of lymphoma. Here, we discuss the case of a patient presenting with refractory chylous ascites due to a massive retroperitoneal follicular lymphoma, staged as IVB. The patient was unresponsive to chemoimmunotherapy, which prompted us to consider alternative treatment strategies. Low-dose radiotherapy was initiated and resulted in a marked decrease of the lymphadenopathy and complete regression of the peritoneal fluid. Low-dose radiotherapy represents a well-tolerated, highly effective treatment and should remain an important modality in cases of follicular lymphoma-associated chylous ascites.

1. Introduction

Lymphoma-associated chylous ascites results from impaired lymphatic drainage by external pressure and consequent chyle leakage from dilated subserosal lymphatics into the peritoneal space.[1] Conservative management strategies are not successful and treatment of the underlying lymphoma should be immediately started. Radiotherapy is an established treatment option in follicular lymphoma. The adoption of lower doses and smaller treatment fields have notably decreased the associated toxicity. This translates into an increasing number of patients who are candidates for radiotherapy, especially in indolent non-curable disease.

2. Case report

A 60-year-old man was admitted to our department because of persistent chylous ascites and a bulky retroperitoneal mass. He had a history of alcohol abuse, persistent psoriasis and smoking habits. He was generally well until approximately six

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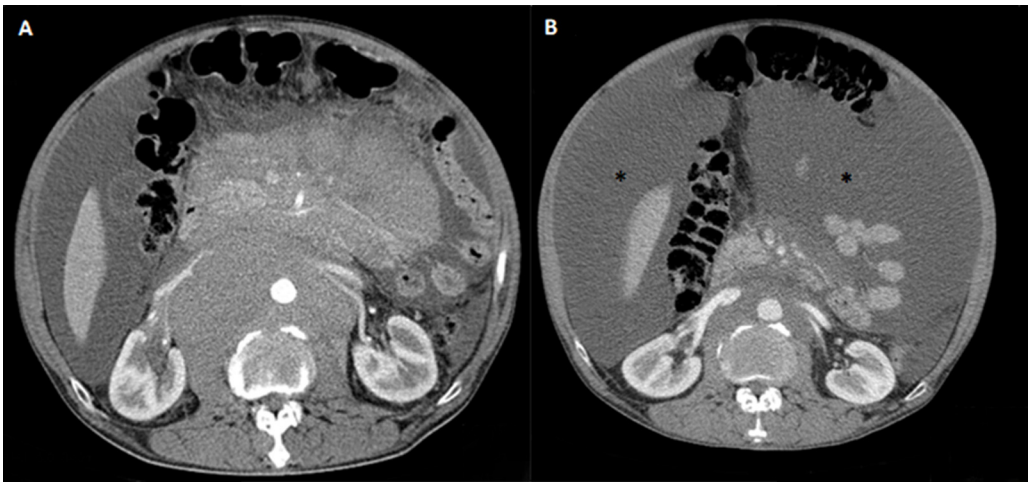

Fig. 1 – Coronal section from contrast-enhanced abdominal CT scan. (A) initial diagnosis showing a bulky, irregular, retroperitoneal mass encasing the inferior vena cava, abdominal aorta and renal vessels. There is anterior displacement of the renal vessels. (B) Reassessment 6-weeks after radiotherapy with a residual densification in the retroperitoneal compartment and persistent massive ascites (*).

weeks before admission when weakness, unexplained weight loss of 8 kg, night sweats and abdominal distention occurred. For the past three weeks, multiple recurrent paracentesis were performed at an emergency department of another hospital with an approximate drainage of 10 L of a milky fluid per week. An abdominal ultrasound revealed hepatomegaly without cirrhosis and a computerized tomography (CT) scan showed an irregular retroperitoneal mass ($17 \times 20 \times 18$ cm) extending along the root of the mesentery accompanied by enlarged mesenteric nodes and massive ascites (Fig. 1A). No pleural or pericardial effusions were observed.

Physical examination revealed malnutrition, abdominal distention and a palpable abdominal mass. Laboratory investigations showed lymphopenia ($0.32 \times 10^9\ L^{-1}$, normal range 1.5–4.0), hypoalbuminemia (2.4 g/dL, normal range 3.8–5.3) and low serum immunoglobulins (IgG 311 mg/dL, normal range 751–1560). Lactate dehydrogenase and liver function tests were within the normal range. Chylous ascites was confirmed by a triglyceride concentration >1300 mg/dL in the peritoneal fluid. Flow cytometry analysis of the paracentesis specimen revealed the presence of 24% of monoclonal B-lymphocytes with a follicular lymphoma-like phenotypic profile (CD5−, CD10++, CD19+, CD20+/++, CD23−, 1.61% of cells in S-phase). A percutaneous biopsy of the retroperitoneal mass was performed and the histologic analysis was compatible with the diagnosis of follicular lymphoma, grade 1–2, staged as IVB, bulky. Chemotherapy with RCHOP (rituximab, cyclophosphamide, vincristine, doxorubicin, prednisolone) was immediately started. During hospitalization, a percutaneous abdominal drainage tube was inserted. The average daily drainage was 3500 mL. The drainage tube was removed due to infection and the patient was discharged home. Eighteen days after the first cycle of chemotherapy, he was re-admitted due to re-accumulation of massive ascites. Conservative therapy was optimized with diuretics (furosemide and spironolactone) as well as octreotide, but the patient remained unresponsive. Furthermore, there was no reduction of the abdominal mass on physical examination. The case was discussed in the multidisciplinary tumor board and therapy changed to radiotherapy. Radiotherapy was performed with a palliative intent to gross retroperitoneal lymph nodes (GTV – gross tumor volume). Due to the objective of the treatment, no expansion was used for planning target volume (PTV) delineation. A total dose of 4 Gy was administered in two fractions, every other day, 3-dimensional radiotherapy technique, 3 fields, with plan normalization mode – 100% in target mean dose. Patient was treated supine with no immobilization device. Attending to the very low dose, there was no organ at risk (OAR) dose constraint. There was no acute side effect. After radiotherapy, 5 additional weekly doses of rituximab 375 mg/m^2 were administered and no infusion reactions occurred. A CT scan was performed 6 weeks after radiotherapy, disclosing unconfirmed complete response, but large ascites persisted (Fig. 1B). For 16 months, monthly paracentesis were needed for symptomatic relief. There was a progressive decline of chylous ascites and after 36 months of follow-up, the patient remains asymptomatic without recurrence of effusions and with a good quality of life.

3. Discussion

Chylous ascites is associated with depletion of water and electrolytes, proteins and lipids, immunoglobulins and lymphocytes that predispose, respectively, to organ dysfunction, malnutrition and susceptibility to infections.[1] Very limited data are available on the treatment of retroperitoneal lymphoma complicated by chylous ascites and there is no standard therapy established so far. The role of chemoimmunotherapy is controversial. It achieved significant responses in a few reported cases but was unsuccessful in others.[2,3] In the era of modern therapy, radiotherapy remains

the most active single modality in the treatment of follicular lymphoma, leading to a complete remission rate of approximately 60% and providing long-term local control.[4–6] There is a large variability in radiation doses and it is still debatable which patients benefit from higher doses of radiotherapy and which do not. The recommended dose of curative radiotherapy for patients with low-grade, early-stage lymphoma is 24–30 Gy. High doses may also be appropriate for selected bulky, advanced-stage presentations.[2] A prospective, randomized study and a number of retrospective cohort studies demonstrated that low-dose radiotherapy of 4 Gy in 2×2 Gy fractions is an excellent option for advanced or refractory indolent lymphoma with high and sustained response rates.[5–7] Furthermore, it can be repeated as needed. Abdominal irradiation has also been successful in a patient with follicular lymphoma-associated chylothorax.[8] Interestingly, chylous ascites due to other etiologies have also been successfully treated with radiotherapy.[9–10] The combination of radiotherapy with rituximab is a reasonable approach that provides optimum local as well as more widespread disease control. Rituximab monotherapy is a highly active systemic treatment for follicular lymphoma and there is *in vitro* evidence of a strong synergism between radiotherapy and rituximab.[11] It remains unclear if the addition of rituximab and/or the single cycle of chemotherapy had an additional positive local effect in our patient.

In conclusion, the management of follicular lymphoma is challenging. Among several valid treatment options, low-dose radiotherapy has shown to be a well-tolerated, highly effective treatment for follicular lymphoma-associated chylous effusions with long-term remissions. Its omission in favor of alternative managing strategies may compromise patients' outcome.

Authors contributions

Márcio Tavares and Ângelo Oliveira collected the data. Sofia Ramalheira, Sérgio Chacim, Ângelo Oliveira, Rui Henrique and José Mariz analyzed the data and provided menthorship. Sofia Ramalheira, Sérgio Chacim and Ângelo Oliveira cared for the patient. Márcio Tavares wrote the first manuscript (including the first draft). All authors revised the final manuscript.

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Conflict of interest

None declared.

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