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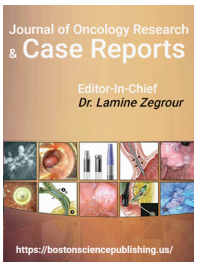

Extranodal Primary Adrenal Lymphoma – A Case Report

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A R T I C L E I N F O

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A B S T R A C T

Abstract: Primary adrenal lymphoma (PAL) is a highly invasive and an extremely rare malignant disease, accounting for <1% of non-Hodgkin lymphomas. The overall survival (OS) rate is poor and only a few cases of PAL are reported in medical literature. Due to the rarity of the condition, no standardized treatment is available.

Introduction

Adrenal Lymphomas are of two types – primary and secondary adrenal lymphoma. Secondary adrenal lymphoma accounts for 4-5% of all NHL cases. PAL predominantly occurs in males in their sixth to seventh decade of life and involvement of bilateral adrenal glands (70%) is a common finding. The two most common WHO defined PAL subtypes are diffuse large B cell lymphoma (78%) and peripheral T cell lymphoma (7%).PAL is a histologically confirmed lymphoma involving 1 or 2 adrenal glands, with no prior history of lymphoma and if there is involvement of other tissues or lymph nodes in addition to adrenal glands, adrenal lesions should be significantly dominant.[2] Patients commonly present with abdominal pain, fever, night sweats and weight loss (B symptoms).

Case

A 37 year old male with no comorbidities was evaluated for complaints of repeated episodes of fever since 3 months and history of weight loss (5kgs) in 6 months. USG was suggestive of possible liver lesion. PET CT showed 12.2x9.1x12cm hypo enhancing mass arising from suprarenal region with non-visualised adrenal gland separately, mass effect on the right lobe of liver with intrahepatic right portal vein, significant compression of infrahepatic IVC was noted, likely primary adrenal neoplasm with no lymphadenopathy and distant metastases. USG guided biopsy of the right adrenal mass reported features in favour of Non-Hodgkin's lymphoma. IHC done on the block showed atypical lymphoid cells diffusely positive for CD20, CD10, BCL6 and MUM1, negative for CD30, BCL2 and CD34 with a Ki-67 of 70%. Morphology and IHC feature were suggestive of Diffuse B-cell Lymphoma – GC type. FISH negative for MYC and BCL-2 co-expression. Patient was diagnosed as Adrenal Lymphoma stage IV, RIPI – good risk, CNS-IPI – intermediate risk. Patient underwent prephase chemotherapy with cyclophosphamide and steroid following which patient was treated with course A3, course B2 and course B3 – modified R-G MALL chemotherapy. PET CT done after chemotherapy showed complete response.

Patient planned for consolidative radiotherapy (RT) to a dose of 30.6Gy/17fractionsusing IGRT technique with CTV including spaces adjacent to right kidney, right adrenal gland, thin margin of the liver including porta hepatis; superiorly – IVC and surface of liver; inferiorly – right hilum till the renal vessels; anteriorly – surface of liver; posteriorly – space between the liver and kidney; medially – retrocaval and para-caval regions were included. A PTV margin of 1cm and 1.5cm given circumferentially and craniocaudally respectively. Patient was advised to be in a state of fasting 4 hours prior to radiation. During the course of the treatment patient developed grade 1 Gastrointestinal toxicity and was treated symptomatically.

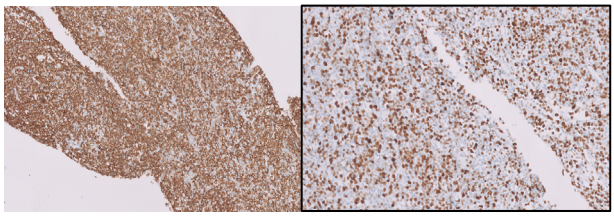

Figure 1: IHC slide stained positive for CD20 and reported Ki-67 proliferation index of 70%.

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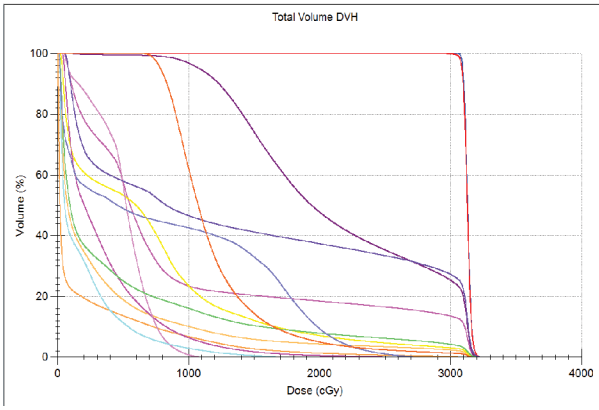

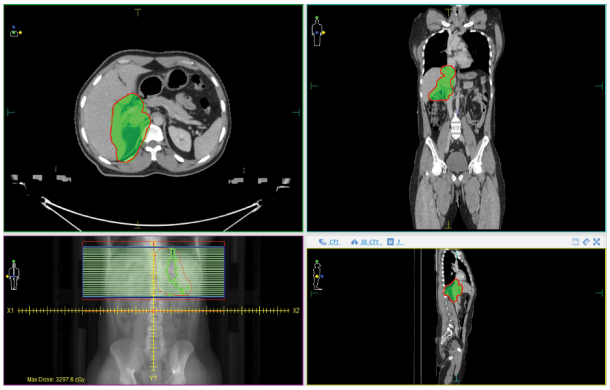

Laboratory Findings

Tests	Results	References
Biochemical Marker		
aPTT	29.0	25-35 seconds
Bilirubin	0.8	<1.2 mg/dl
Calcium	8.8	8.5-10.2 mg/dl
Ceruloplasmin	29mg/dl	14-40 mg/dl
Creatinine	0.85	0.75-1.35 mg/dl
Ferritin	362	24-335 mcg/l
Free Metanephrine	91.66pg/ml	12-60 pg/ml
Free Nor Metanephrine	13.3pg/ml	18-111 pg/ml
INR	1.20	0.8-1.1
LDH	392	110-220 (IU/L)
PT	16.6	11-35 seconds
Serum Ferritin	362	24-336 mcg/l
Serum Iron	61	60-170 mcg/dL
Serum Potassium	4.79	3.5-5.3 (mmol/L)
Serum Sodium	134	137-147 (mmol/L)
Serum Transferrin	214.44	215-380 mg/dl
TIBC	319	240-450 mcg/dL
Transferrin Saturation	19.12	20-50%
UIBC	258	111-343 mcg/dL
URIC ACID	6.0	3.5-7.2 mg/dl
Serum Tumour Markers		
AFP	<0.908ng/ml	0-40 ng/ml
CA19.9	16U/ml	0-37 U/ml
CEA	2.12ng/ml	0-2.5 ng/ml

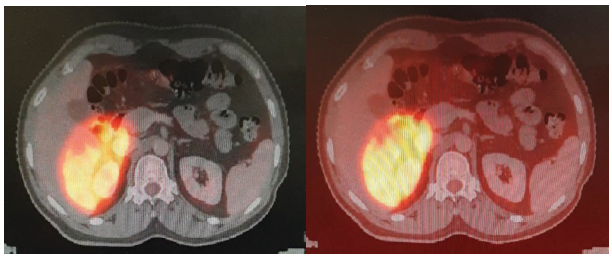

Figure 2: Initial PETCT scan showing the extent of the disease.

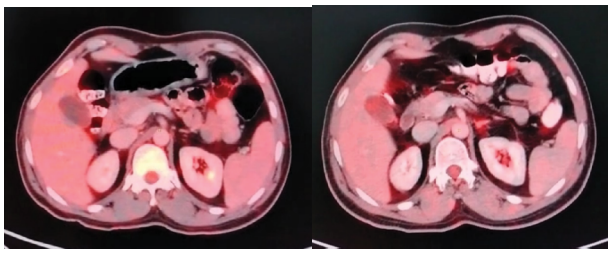

Figure 3: PETCT done post chemotherapy regimen showing complete response.

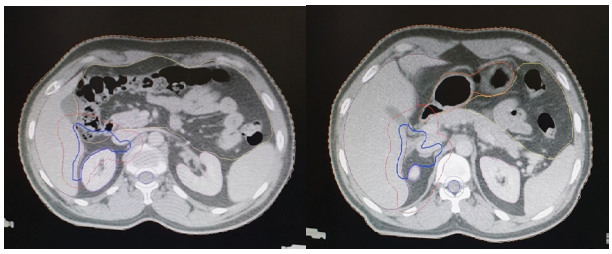

Figure 4: Contouring done on the planning CT scan.

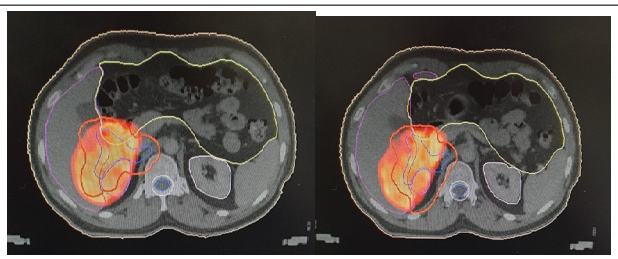

Figure 5: Planning CT scan fused with initial PETCT scan showing contour coverage of the initial disease.

Discussion

The case reported here was of a 37-year-old male who manifested with repeated episodes of fever in the last 3 months and weight loss in the past 6 months. Laboratory tests showed increased levels of LDH with all other investigations being within normal limits. There was no evidence of active tuberculosis or other opportunistic infections such as HIV. PET CT showed 12.2x9.1x12cm hypo enhancing mass arising from the right suprarenal region likely to be primary adrenal neoplasm with no lymphadenopathy and distant metastases. USG guided biopsy of the right adrenal mass reported features in favour of non-Hodgkin's lymphoma. IHC done on the block showed atypical lymphoid cells diffusely positive for CD20, CD10, BCL6 and MUM1. The clinical, imaging and pathological characteristics of the case were consistent with Primary Adrenal Lymphoma.

Other causes of adrenal masses include – metastatic disease (lung cancer, renal cancer, ovarian cancer, lymphoma and melanoma), pheochromocytoma, adrenocortical carcinoma, adrenal hyperplasia, functioning adenomas, infiltrative causes (sarcoidsosis and amyloidosis) and infections such as tuberculosis and cryptococcosis.

Several blood tests done on the patient revealed normal sodium and potassium levels and his plasma total cortisol and ACTH did not indicate adrenal insufficiency (AI). Studies have shown that 61%

patients with PAL could develop AI. AI caused by malignant tumours requires approximately 90% destruction of the adrenal glands.

An interesting feature of this case was the complete radiological response post chemotherapy. Several studies have reported rapid increase in PAL tumours due to overexpression of Ki-67, an important indicator that signifies tumour cell proliferation. In this patient the Ki-67 was 70%. In addition, the patient's IHC revealed negative co-expression of BCL-2 and MYC in lymphoma tissues. BCL-2 and MYC co-expression indicates double expressor lymphoma (DEL). Studies have shown most of DLBCL patients with DEL usually have an aggressive clinical course characterized by poor prognosis, advanced stage, more extranodal involvement (bone marrow, central nervous system, lung, liver etc), high serum LDH levels and an intermediate to high international prognostic index (IPI) score.

A systematic review of 3-, 6- and 12-months survival rates of PAL were found to be 67%, 46%, and 20%. Other studies have reported the 2-year, 5-year overall survival and progression free survival rate to be 61.6% and 49.9%, 52.5% and 53.2% respectively. The estimated 5 year and 10-year overall survival rates of PAL were 19.17% and 3.33% respectively.[2]Factors such as older age, bilateral adrenal involvement, adrenal insufficiency, B symptoms, large tumour size, elevated LDH levels, CNS relapse and non-GCB type are identified as poor prognostic factors for the overall survival and progression free survival in patients with PAL.

Compared to patients who do not receive chemotherapy, patients who receive chemotherapy have a good prognosis. Chemotherapy with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone) is the most commonly recognized strategy for PAL. For this patient pre-phase chemotherapy with cyclophosphamide and steroid followed by a more extensive chemotherapy regimen, i.e., the R-G MALL regimen was chosen. Timely diagnosis and treatment with chemotherapy is the key to improving the prognosis of PAL.

This patient showed complete response post chemotherapy and was followed with consolidative radiotherapy to the region of initial mass.

Radiotherapy is one of the most powerful and most effective NHL therapeutics. RT is used as either a primary therapy (particularly for indolent ENL) or as a consolidation after systemic therapy or as salvage therapy or for palliation. Consolidative therapy is used to kill any cancer cells that may be left in the body. Consolidative RT improves isolated local control. Studies show patients receiving consolidative RT show improved PFS, OS and local control compared with chemotherapy group.[3]Initital bulk (variable diameters of 5-7cms) portends poorer prognosis with greater relapse even after adjusting for rituximab. The RICOVER-60 trial studied 6-8 cycles of CHOP chemotherapy with or without rituximab for elderly patients of all stages and recommended Involved Field Radiotherapy (IFRT) to 36Gy to bulky sites >7.5cm. The patients where RT was omitted had significantly poorer EFS, PFS and OS supporting the need for CMT therapy.[1]Patient tolerated the treatment well and is in a stable condition presently.

Conclusion

PAL is an aggressive, metabolically hyperactive, and a high-grade lymphoma with poor prognosis. Primarily affects the elderly males and presents with large bilateral adrenal masses. Studies have suggested BCL-2 and MYC co-expression to be poor prognostic factors in patients with DLBCL. The average 1-year survival is as low as 20%. Rituximab containing chemotherapy such as R-CHOP has shown to increase the overall survival of patients with this disease. R-CHOP combined with CNS prophylaxis and autologous stem cell transplant further increases the overall survival. RT is often used to consolidate the results of systemic therapy, it reduces the risk of local failure, provides improvement in progression-free and overall survival. Larger sample studies are needed to establish the best treatment option and role of surgery and radiation in the management of PAL.

Conflict of Interest: This case report has no potential competing interests, all authors have approved the manuscript for submission

Ethical Consideration: None

Abbreviations:

ACTH – adrenocorticotropic hormone; AI – adrenal insufficiency; CTV – Clinical target volume; DLBCL – diffuse large B-cell lymphoma; EBV – Ebstein-Barr virus; ENL – Extranodal lymphoma; LDH – lactate dehydrogenase; NHL – Non-Hodgkin lymphoma; PAL – primary adrenal lymphoma; PTV – Planning target volume;

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