Thalidomide induced remission of refractory diffuse large B-Cell Lymphoma post-allogeneic SCT

Patients who relapse after High dose therapy and autologous stem cell transplant (ASCT) for Diffuse large B cell Lymphoma (DLBCL) have a poor prognosis with a median survival of only 3-6 month.[1-2] This case demonstrates the ability of thalidomide at low doses to induce durable response in a patient with DLBCL who relapsed after full intensity allogeneic transplantation.

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A 36 year-old male presented with sciatic pain in July 2000, MRI scan revealed a tissue mass at L4. The diagnosis of stage IV DLBCL was confirmed.

The patient received 30 Gray of radiation to the lumbosacral region followed by 6 cycles of chemotherapy (HOPE- Epirubicin, etoposide vincristine and prednisolone). His disease relapsed 2 months after completing treatment. He was treated with DHAP (Dexamethasone, Cytarabine and Cisplatin) chemotherapy consolidated by an ASCT with BEAM (BCNU, Eotoposide, Ara-C, Melphalan) conditioning. He developed signs of progression 4 weeks post transplant with masses in the right bicep, right molar region and right testicle.

He received two cycles of CHOP-R (cyclophosphamide, doxorubicin, vincristine, and prednisolone and rituximab) followed by full intensity T-cell replete matched sibling allogeneic transplant with Cyclophosphamide (200 mg/kg)/Total Body Irradiation (1200 cGy) conditioning. Restaging CT scan at 3 months showed bilateral symmetrical enlargement of the adrenal glands positive on PET scan (Figure 1). Adrenal biopsy confirmed relapsed disease and the patient subsequently developed swelling in the neck and left testicle.

He underwent rapid tail of immunosuppression but developed hepatic GVHD. Methylprednsiolone was given but despite this his lymphadenopathy progressed. In view of the early relapse and presence of GVHD the use of Donor Lymphocyte Infusions was felt to be contraindicated. He was commenced on thalidomide 200 mg daily, which led to reduction in size of his neck node and testicular swelling within 48 hours. Two weeks later he was given a further 4 cycles of single agent Rituximab.

Repeat PET scan 9 months post transplant showed complete remission (Figure 2).

He continued on low dose thalidomide (50 mg) until November 2002 when he complained of worsening peripheral neuropathy.

Thalidomide was discontinued and he remained in remission for 18 months before his disease relapsed in the original site. Despite further chemotherapy and re-challenge with Thalidomide his disease progressed and he died 29 months post transplant.

Discussion. Thalidomide has been most extensively studied in myeloma where 30% response rate has been documented in refractory and relapsed disease.[3]

It has been used with some success in mantle cell lymphoma.[4] However its use in DLBCL has not previously been reported.

The effects of thalidomide have been attributed to several mechanisms including inhibition of angiogenesis, anti-inflammatory and immunomodulatory effects including inhibition of tumor necrosis factor alpha (TNF-α) production.[5]

The addition of thalidomide may have enhanced CTL

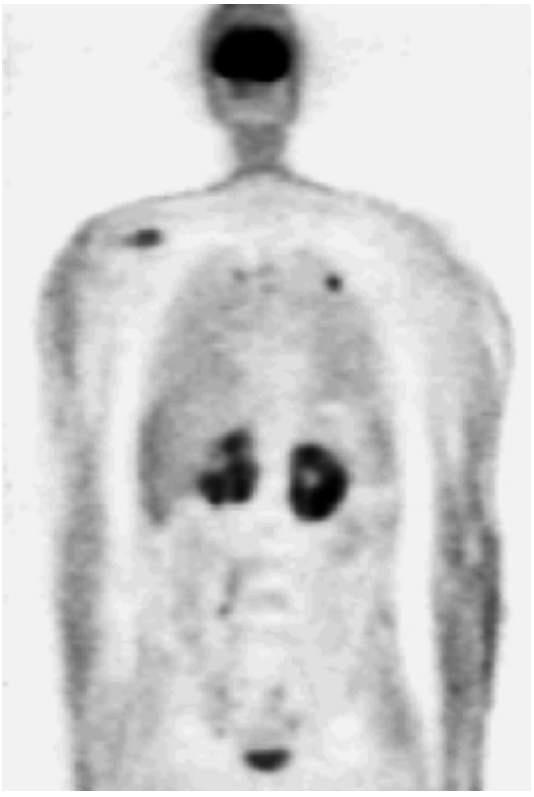

Figure 1. (PET Scan May 2002) demonstrated multiple abnormalities. It illustrates two very large foci in the adrenal glands bilaterally, with necrotic centres. Further foci are seen in the right scapula and left upper lobe of the lung.

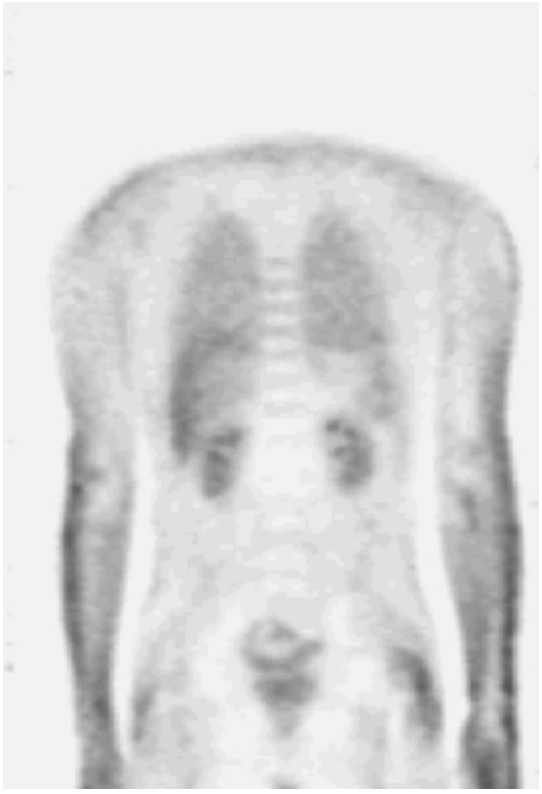

Figure 2. (Sep 2002) Normal PET study showing complete resolution of previous abnormalities.

function through an immunomodulatory effect resulting in an enhanced graft versus lymphoma effect. His disease was progressing despite florid GVHD suggesting that response was not solely due to rapid tail of immunsuppression.The fact that he remained in remission for 18 months argues against a direct effect of thalidomide on lymphoma cells.

This patient highlights the remarkable ability of single agent thalidomide to induce response in a patient with highly aggressive lymphoma who failed allogeneic transplantation and could be considered as an option for treatment in this difficult clinical scenario.

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