CISPLATIN IN RENAL TRANSPLANT RECIPIENTS: NOT AN ABSOLUTE CONTRAINDICATION

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Abstract

The chemotherapeutic agent cisplatin is usually contraindicated in renal transplant recipients due to its well-known side effect of nephrotoxicity, but is an important (and sometimes irreplaceable) drug in the management of cancer. We report a case of cisplatin usage concurrently with radiation (CRT) in unresectable head and neck cancer, along with a review of the literature.

A 52 year old lady with unresectable T4N2bMx extensive oropharyngeal squamous cell cancer was on immunosuppression with tacrolimus x 6 years following a cadaveric kidney transplant. She was treated with definitive concurrent CRT with cisplatin. She received prophylactic intravenous saline three times a week. She received 6 weekly doses of 40mg/m2 cisplatin (cumulative dose 240mg/m2) I.V with no significant change in renal function (creatinine between 0.5-0.8mg/dl). She is now 6 months out, without any evidence of nephrotoxicity. She has had a complete response to therapy.

Upon extensive literature review, we found 11 other reports of cisplatin use in renal transplant recipients: 5 patients with testicular cancer, 4 with bladder cancer, 1 each with T-ALL and ovarian cancer. Only two patients with testicular cancer developed renal failure, 6&7 years after chemotherapy (unlikely to be related to cisplatin).

We conclude that cisplatin can be safely used in patients with renal transplant recipients with preserved renal function, with no acute nephrotoxicity.

Background

Patients who undergo renal transplantation (or any other organ transplant) are on chronic immunosuppression to prevent graft failure and are at high risk of malignancy, with incidence as high as 20% in some series. The incidence of non-cutaneous head and neck cancer is reported to be 0.2-0.9% in patients with renal transplantation, and may be higher with other risk factors.

Concurrent CRT with cisplatin is the standard first line therapy for unresectable locally advanced head and neck squamous cell cancer (HNSCC), and is also used as a common adjuvant therapy for high risk resected locally advanced head and neck cancer.[1,2] Another alternative is cetuximab with RT, but we found case reports of fatal BOOP in lung transplant recipients and no data on use in renal transplant.

Due to its nephrotoxic potential, cisplatin is usually contraindicated in patients with pre-existing renal impairment. In fact, the dose dependent and cumulative nephrotoxicity of cisplatin is its major toxicity, with 25-35% incidence of renal failure with a single dose. Cisplatin causes renal failure by multiple mechanisms, including tubular epithelial toxicity, vasoconstriction of renal microvasculature, and proinflammatory effects.[3]

Our patient

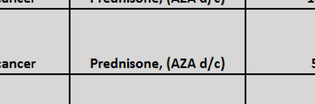
I. HPI:
52 y/o WF, smoker, presented to ENT in Jan 2012 with c/o hoarseness of voice, odynophagia, dysphagia x 5mo. Panendoscopy demonstrated a large mass extending from the oropharynx to larynx with fixation of the hemilarynx along with a R level III LN. Biopsies of base of the tongue and left false vocal cord showed well-differentiated SCC. PET CT also showed b/l neck adenopathy, bilateral ground glass lung opacities and a 1.7cm cavitary lesion in L midlung. Bronchoscopy with biopsy of lung lesion revealed no malignancy. She was staged cT4aN2cMx, and was deemed unresectable due to extent of disease.

II. PMH:
- Cadaveric Renal Transplant for ESRD of uncertain etiology in October, 2006
- T2DM, HTN, HLD, GERD, insomnia, chronic leukocytosis following traumatic splenectomy

III. Meds:
- Tacrolimus 2mg every 12 hours
- Mycophenolate (cellcept)
- Metformin, glyburide, procardia, atenolol, neurontin, myfortic, flexeril, claritin, ASA, multivitamin

IV. Social Hx: chronic smoker, 50-60ppy (1-2ppd x 30+years), married

V. Labs:



VI. Imaging: MRI neck, PET CT: which confirmed the extent of the disease and demonstrated non FDG avid bilateral lung nodules with ground glass opacities, along with slightly avid (SUV 2.6) 1.4 x1.2cm cavitary lung lesion.

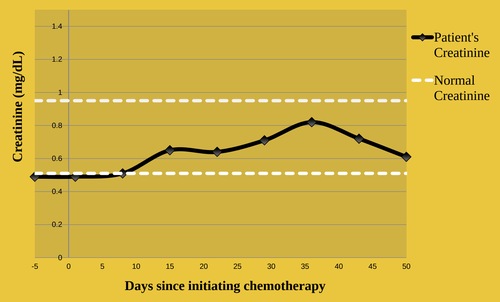
VII. Plan: Definitive concurrent CRT with weekly cisplatin 40mg/m2 IV along with prophylactic IVF 0.9%NS M-W-F and PRN

VIII. Course of treatment:
Treated between March 7 and April 24, 2012. Creatinine monitored weekly. The patient tolerated the first 6 weekly doses of cisplatin (total dose of 240mg/m2) without major complaints. Chemotherapy was held after 6 weeks due to Grade 3 fatigue, nausea, vomiting, overall deconditioning, and patient request. Radiation was completed by the end of April with 68 Gy/34 fractions (planned 70Gy/35) .

IX. Follow up:
By 3 mo post therapy, she had improvement in dysphagia, but was using PEG tube for nutrition. Hoarseness had improved, exam did not reveal any residual disease. PET CT in July 2012 demonstrated resolution of the large oropharyngeal mass and adenopathy, with mild SUV uptake in the oropharynx. Subsequent ENT eval and bx did not reveal malignancy. However, she was admitted to ICU with severe urosepsis in the last week of September, ARF with Cr of 3.5, requiring temporary hemodialysis and intubation. She recovered completely with abx and Cr was 0.81 when last seen in clinic in November. Additionally, a repeat bronchoscopy showed no signs of malignancy.

Type of cancer	Immunosuppressant following renal transplant	Diagnosis of Cancer (Years after transplant)	Treatment for cancer	Dose of Cisplatin	Survival after chemo	Renal Failure	Measures to prevent renal failure
Oropharyngeal cancer	Tacrolimus	6 years	Cisplatin (+ concurrent Rd)	60mg/m2	Still living	No	IVF
Bladder cancer	Cyclosporine, Prednisone, (AZA d/c)	6 months	M-VACx4	70mg/m2	8 months	No	IVF, mannitol
Bladder cancer	(AZA d/c)	18 years	M-VACx1	20mg/m2	6 months	No	None reported
Bladder cancer	AZA, Prednisolone	5 years	M-VAC x 1; Cisplatin + fluorouracil x 6	70mg/m2; 30mg daily	8 months	No	None reported
Testicular cancer	AZA, Prednisone	1.5 years	PEx3 (+Rd post chemo)	20 mg/ m2	5+ years	No	IVF, Cisplatin infused w/ 3% NS, mannitol, furosemide
Testicular cancer	Prednisone, (AZA d/c)	10 years	PEx4	20mg/m2	6+ years	6 years after chemo	IVF, mannitol, tx at 9pm
Testicular cancer	Cyclosporine, Prednisolone, (AZA d/c)	1 year	PEx4; CVB	10-15mg/m2; 10-15mg/m2	[-]	7 years after chemo	Maintain diuresis above 100ml/hr., furosemide
Testicular cancer	Prednisone, (AZA d/c)	10 months	VPBx3	Not reported	6+ years	No	mannitol, furosemide
Testicular cancer	Prednisone, (AZA d/c)	5 months	VAB6 x 5 (Cisplatin during 5th course)	180mg	Died during 6th course due to metastasis	No	None reported
Acute T-Cell Lymphoma	Cyclosporine, Prednisolone	4 years	1 dose of Cisplatin + several other chemotherapy agents	100mg	1+ years	No	None reported
Ovarian cancer	Methylprednisolone, (AZA d/c)	7 years	Cisplatin + cyclophosphamide X 8	50mg/m2	2 months	No	None reported

Chart 1: Creatinine Levels During Treatment



Conclusion

- The use of cisplatin in renal transplant patients is not an absolute contraindication.
- Cisplatin can safely be administered to renal transplant recipients across a wide range of cancers and renal failure is a rarely reported side effect.
- This is the first case report that describes the use of cisplatin in a renal transplant patient with unresectable oropharyngeal squamous cell cancer.
- It is imperative to monitor renal function and we would recommend prophylactic IV fluids given with cisplatin at least three times per week and on an as needed basis.
- Future studies should continue to evaluate the long-term response to cisplatin in renal transplant patients.

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