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 important (and sometimes irreplaceable) drug in the management of cancer. We report a case of cisplatin usage concurrently with radiation (CRT) in unacceptably head and neck cancer, along with a review of the literature.

A 52 year-old lady with unacceptably T4N2Mx extensive oropharyngeal squamous cell cancer was on immunosuppression with tacrolimus for 6 years following a cadaveric kidney transplant. She was treated with definitive concurrent CRT with cisplatin. She received prophyactic intravenous saline three times a week. She received 6 weekly doses of $40mg/m^2$ cisplatin (cumulative dose $240mg/m^2$) 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 (HNSSC), and is also used as a common adjuvant therapy for high risk resected locally advanced head and neck cancer. 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 makes it a 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.

Our patient

**I. HPI:**

52 yo FE, smoker, presented to ENT in Jan 2012 with c/o hoarseness of voice, odynophagia, dysphagia x 3mo. 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 mid lung. Bronchoscopy with biopsy of lung lesion revealed no malignancy. She was staged T4aN2Mx, 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, GFR, insomnia, chronic leukocytosis following traumatic splenectomy

**III. Meds:**

- Tacrolimus 2mg every 12 hours
- Mycophenolate (cellcept)
- Metformin, gluburide, procutia, atenolol, neurotin, mycortic, flexeril, claritin, ASA, multivitamin

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

**V. Labs:**

- Creatinine (mg/dL)
- 0.6 (baseline)
- 0.8 (pre chem)
- 0.8 (1st month)
- 0.8 (3rd month)
- 0.8 (6th month)

**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 x 1.2cm cavitary lung lesion.

**VII. Plan:** Definitive concurrent CRT with weekly cisplatin $40mg/m^2$ IV along with prophylactic IF 0.9%NS M-W-F and PRN

**VIII. Course of treatment:**

Treated between March 2 and April 24, 2012. Creatinine monitored weekly. The patient tolerated the first 6 weekly doses of cisplatin (total dose of $240mg/m^2$) 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)

By 3 mo post therapy, she had improvement in dysphagia, but was using PEG tube for nutrition. Hoarseness had improved, exam d

**IX. Follow up:**

- By 3 mo post therapy, she had improvement in dysphagia, but was using PEG tube for nutrition. Hoarseness had improved, exam d

**References**

- Diagnosis of Cancer (Years after transplant) Treatment for cancer Dose of Cisplatin Survival after chemo Renal Failure

<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>Immunosuppression following renal transplant</th>
<th>Diagnosed of Cancer (Years after transplant)</th>
<th>Treatment for cancer</th>
<th>Dose of Cisplatin</th>
<th>Survival after chemo</th>
<th>Renal Failure</th>
<th>Measures to prevent renal failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oropharyngeal cancer</td>
<td>Tacrolimus</td>
<td>6 years</td>
<td>Cisplatin 1 cycle</td>
<td>60mg/m2</td>
<td>Still living</td>
<td>No</td>
<td>IV</td>
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<tr>
<td>Bladder cancer</td>
<td>Cytosporine, Prednisone, (AZA 4/6)</td>
<td>6 months</td>
<td>M-VAC+IV</td>
<td>70mg/m2</td>
<td>6 months</td>
<td>No</td>
<td>IV, mannitol</td>
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<tr>
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<td>(AZA 2/6)</td>
<td>8 years</td>
<td>M-VAC+IV</td>
<td>20mg/m2</td>
<td>6 months</td>
<td>No</td>
<td>None reported</td>
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<tr>
<td>Bladder cancer</td>
<td>ATX, Prednisone</td>
<td>5 years</td>
<td>M-VAC+IV</td>
<td>Fluorouracil 6 x 75mg/m2 x 3</td>
<td>6 months</td>
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<td>None reported</td>
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<td>ATX, Prednisone</td>
<td>1.5 years</td>
<td>PEV (3rd post chem)</td>
<td>20 mg/m2</td>
<td>5 years</td>
<td>No</td>
<td>IV, Cisplatin-fluorode (10-15), ILD, mannitol, furosemide</td>
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<td>Prednisone, (AZA 4/6)</td>
<td>10 months</td>
<td>PEV</td>
<td>10-15mg/m2, 10-15mg/m2</td>
<td>7 years after chemo</td>
<td>No</td>
<td>IV, mannitol, at 8 ppp</td>
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<td>Cytosporine, Prednisone, (AZA 4/6)</td>
<td>1 year</td>
<td>PEV+IV</td>
<td>10-15mg/m2</td>
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<td>Prednisone, (AZA 2/6)</td>
<td>18 months</td>
<td>VIPs33</td>
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<td>6 years</td>
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<td>mannitol, furosemide</td>
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<td>Prednisone, (AZA 4/6)</td>
<td>3 months</td>
<td>VIMs + 5FU in initial 9th cycle</td>
<td>10mg</td>
<td>Died during 6th cycle due to metastasis</td>
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<td>None reported</td>
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<td>Acute T-Cell lymphoma</td>
<td>Cytosporine, Prednisone</td>
<td>4 years</td>
<td>Cisplatin + several other chemotherapy agents</td>
<td>10mg/m2</td>
<td>1 year</td>
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<td>Ovarian cancer</td>
<td>Cytosporine, Prednisone</td>
<td>7 years</td>
<td>Cisplatin</td>
<td>50mg/m2</td>
<td>2 months</td>
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