Donor-transmitted melanoma case study

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Introduction

Organ transplant recipients are at an increased risk of developing malignancy, estimated to occur in 15-20% of graft recipients after 10 years. Most malignancies occur de novo or as recurrence of previously treated disease, related to immunosuppression and oncogenic viruses.

Donor-transmitted tumors are rare. From 1994 – 2001, the US Transplant tumor registry reported 18 donor-related cancers in 108, 062 recipients.

Case Presentation

History

- A 66-year-old female presents with abdominal fullness, fevers, chills and malaise for 1 week’s time. Admitted to transplant service to rule out rejection.

Past Medical History

- End Stage Renal Disease status post cadaveric renal transplant 3 months prior
- Hypertension
- Diabetes Mellitus Type 2 -Anemia of chronic disease

Social History:

- No tobacco, alcohol, or drug abuse

Medications: (do I really need strength and frequency?)

Amlodipine 10 mg daily

Aspirin 81 mg daily

Bactrim 160 mg daily

Carvedilol 25 mg twice daily

Clotrimazole 10 mg troche three times daily

Insulin Lispro 10 units with meals

Lantus 20 units in AM

Myofortic 360 mg 2 tablets twice daily

Prednisone 10 mg daily

Tacrolimus 2mg twice daily

Valcyte 450 mg 2 tablets daily

Physical exam

VITALS: T 100. 1, BP 133/60, HR 71, Resp 18, SpO2 99% on RA, nonoliguric

Neck: no lymphadenopathy, no carotid bruits

Cardiovascular: regular rate and rhythm, no clicks, gallops, rubs, no lower extremity edema

Lungs: clear to auscultation bilaterally, no rales or wheezes

Abdomen: soft, well healed Gibson incision in RLQ, no graft tenderness, no organomegaly

Skin: no rashes or lesions noted on skin

Laboratory and Diagnostic Studies (insert images)

WBC 3. 94 K/mcl; Hgb 9. 8 g/dL (patient’s baseline); platelets 104 K/mcl

LDH 747 U/L

Creatinine 1. 72 mg/dL on the day of admission (baseline 1. 02 two months prior, after transplant). During the hospital course, her renal failure worsened with creatinine reaching 8. 08 mg/dL and patient requiring intermittent hemodialysis

CT of the abdomen with contrast and PET scan

Findings compatible with metastatic disease to the liver, spleen, bones, and probably lungs.

MRI Abdomen/pelvis

A few indeterminate T1 and T2 hyperintense lesions in the periphery of the transplant kidney, suspicious for neoplasm. Innumerable bone marrow and splenic lesions, suspicious for hemorrhagic metastasis

MRI of brain

Diffuse bony metastases, no signs of intraparenchymal metastasis

PET:

Positive for multiple lesions in the transplant kidney, bone, and spleen.

CT guided Bone marrow biopsy:

Metastatic malignant neoplasm, quite consistent with metastatic malignant melanoma

**Within days of patient's admission, it was discovered that the recipient of the liver from the same donor developed melanoma within the transplanted liver and the recipient of the mate kidney had developed melanoma in the renal allograft.

**The transplant center reported no known history of donor melanoma and normal visual inspection of donor organs at time of transplant.

Clinical Course

- Patient elected to undergo allograft nephrectomy. Surgical pathology of removed donor kidney confirmed malignant melanoma that was BRAF-V600E mutation positive (insert histo slide of melanoma in kidney)
- Patient was taken off of all immunosuppressive therapy and was started on chemotherapy with zelboraf and immunotherapy with ipilimumab (completed 4 months of zelboraf and 4 cycles of ipilimumab)
- Patient currently off of chemotherapy, and undergoes repeat imaging every month.
- At 6 months, CT body from 6 months " demonstrates basically stable disease."

- This patient is now undergoing hemodialysis for her end stage renal disease
- The two other recipients died from metastatic melanoma found in the transplanted liver and renal allograft; this patient is the sole survivor of the transplanted melanoma.

Transmission of melanoma by organ transplantation (VIPER)

- Not only is melanoma the most common fatal form of skin cancer, it is the most common tumor responsible for donor-derived malignancy.
- The late disease recurrence of melanoma is related to the dormancy of melanoma. Major theories for the dormancy of melanoma include cell-cycle arrest and blocked angiogenesis. Per Lancet article entitled " Transmission of donor melanoma by organ transplantation," late recurrence of dormant melanoma can occur because of micrometastases or solitary dormant cells. Dormant micrometastasis occurs because of the inability for angiogenesis; therefore there is an equilibrium between cell proliferation and apoptosis and thus an inability of malignant cell growth. In dormant solitary cells, there is an absence of proliferation or apoptosis, in essence a pause in cell growth. Because of these theories, it is possible that these dormant cells stay latent in immunocompetent individuals for decades and even forever, but the immunosuppression of the organ recipient can reactivate the melanoma cells.
- Transplantation for end-stage organ disease has become routine care with resultant increased demand for donor organs.

- With increased public awareness and donor pool expansion, many transplant programs are easing criteria for selection by accepting older donors and those with remote history of low-grade skin cancers and/or remote “ cured cancers.”
- A recent study reported 23 cases of donor-transmitted melanoma from 12 separate donors between 1972 and 2006. Only 2 donors had known history of melanoma and one case of fatal melanoma occurred from a donor who had surgically removed melanoma sixteen years prior to donation.
- History of melanoma remains a contraindication to organ donation given melanoma high transmission rate of 74% and mortality of 58%.
- Treatment of donor-related melanoma involves withdrawing immunosuppression and allowing the body to reject the transplanted organ, followed by explantation of the allograft carrying the melanoma cells.

Summary

- Melanoma incidence in the general population is increasing, but whether this will translate into increased incidence of donor-transmitted melanoma and resultant increased mortality remains to be determined.
- Physicians must not only discuss risks of malignancy with transplant candidates, but also carefully question all donors and their family about recent and remote malignancy, particularly melanoma, given its high transmission rate and mortality.

- Patients with any history of melanoma, whether it be in the early stages or cured, showed not be considered as organ donors.

References

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