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Malignancy in solid organ transplantation

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Solid organ transplantation provides life-saving therapy for patients with end organ disease. Solid organ transplant recipients are at increased risk of developing cancer compared with general populations. Tumors can arise de novo, as a recurrence of pre-existing malignancy or from the donated organ. Immunosuppression plays a major role in oncogenesis in transplant recipient both through immunosurveillance and through direct oncogenic activity. Post-transplant malignancy is the third major cause of patient death with graft function after cardiovascular disease and infection. Since management and outcome of cardiovascular and infection complications improving, malignancy become more important. First year survival rate of grafts rising over 90%. However long-term survival rate changed a little in the last 20 years, because of chronic rejection and complication of immunosuppression such as nephrotoxicity, cardiovascular disease, infection and malignancy. United States Renal Data System (USRDS) on more than 35,000 renal transplant recipients after 3 years showed cumulative incidence of 7.5% for non-skin malignancy and 7.4% for skin cancer. Compared to general population there was especially an increase in incidence of Kaposi's sarcoma, non-Hodgkin lymphoma and non-melanoma skin cancers (more than 20 folds) and kidney cancer (approximately 15 folds). By contrast the more common solid cancers in general population (ex. breast, lung, prostate, colorectal, uterine and ovarian cancers) were increased only two folds. The Standardized Incidence Ratio (SIR) is a ratio of the number of cancers seen in study population compared with an age & sex match general population and is best measure of increased risk for cancers. SIR for Kaposi's sarcoma, Non-Hodgkin lymphoma and non-melanoma skin cancer is more than 20 (SIR) in following renal transplant vs general population whereas tumor of colon, lung, prostate, stomach, esophagus, pancreas, ovary & breast is 2 (SIR) in transplant recipient compared with general population. The six multistep biological hallmarks mechanism of oncogenesis in transplantation are sustained proliferative signalling, evasion of growth suppressors, resistance to cell death, enabled replicative immortality, induced angiogenesis and activated invasion and metastasis. Chronic immunosuppression predisposes transplant patient to a variety of viral infections. There are several viruses with oncogenic potential such as Human Papillomavirus (HPV) causing cervical carcinoma, human polyoma viruses (BKV, JCV, SV40, MCV) causing mesothelioma, brain tumor, markel cell carcinoma, Epstein Barr Virus (EBV) causing Post-Transplant Lymphoproliferative Disorder (PTLD), Human Herpes Virus (HHV8) causing Kaposi's Sarcoma, Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) causing hepatocellular carcinoma, Human T cell Lymphotropic Virus Type 1 (HTLV-1) causing T cell leukemia. Risk of recurrence with preexisting malignancies after renal transplantation is divided low recurrence rate (0%-10%), intermediate recurrence rate (11%-25%) and high recurrence rate (>26%). Recurrence rate of incidental RCC (0%), colorectal cancer (20%), breast cancer (24%), non-melanoma skin cancer (60%), melanoma skin cancer (24%). Risk of Squamous Cell Carcinoma (SCC) of skin is 60 to 100 times greater than general population and basal cell carcinoma (BCC) 10 to 16 times greater in transplant patients. Kaposi's sarcoma (KS) is vascular neoplasia occurs early in transplantation within 1 to 2 years, common in male person. Post-Transplant Lymphoproliferative Disorder (PTLD) is heterogeneous group of disease after transplantation characterized by abnormal lymphoid proliferation. It is second most frequent cancer after skin cancer. According to WHO classification PTLP can be divided into three distinct morphological groups' namely early disease (55%), polymorphic PTLD (30%) and monomorphic PTLD (15%). Prognosis of PTLD varies according to clonality and extend of disease. However, in general PTLD has a poor prognosis with 1 year mortality of approximately 40%. The principal factor influencing the role of post-transplant malignancy is the overall level of immunosuppressive treatment. Azathioprine associated with increased risk of skin cancer. Calcineurin inhibitor cyclosporins and tacrolimus promote cancer progression. Inhibitor of mammalian Target of Rapamycin (mTOR) sirolimus and everolimus has antioncogenic properties and thereby reduce malignancy. KDIGO (Kidney Disease Improving Global Outcome) and EBPG (European Best Practice Guideline) general recommendations for cancer screening after renal transplantation 1). Annual examination of skin & lip by dermatologist, 2) Abdominal surveillance USG at least every three years, 3) Standard cancer surveillance include a) colorectal cancer: colonoscopy every 5 years, b) breast cancer: screening mammography every year, c) cervical cancer: pap smear every year of onset of sexual activity or from age of 21 years (whichever comes first), d) Prostatic Cancer: digital rectal examination and PSA every year, e) hepatocellular cancer: abdominal USG and alphafetoprotein every 6-12 months. In conclusion, clinicians should be aware of risk of post-transplant malignancies making primary prevention a major concern. In addition, they should consider and follow a cancer screening plan.

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