Allochronic Overlapping Malignancies After Renal Transplantation in a Patient with p53 Gene Mutation: Report of a Case

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Abstract
We report a rare case of the development of various tumors over a 16-year period after renal transplantation. A 56-year-old woman underwent renal transplantation using a US kidney. Immunosuppressive treatment consisted of a triple regimen of methylprednisolone, azathioprine, and mizoribine. Left breast cancer was diagnosed 9 years after the renal transplantation, then colon cancers and meningeal epidermal meningioma were diagnosed, 10 years and 12 years post-transplant, respectively. During the investigations for the breast and colon cancers, a p53 gene mutation was detected. A deterioration of renal function was found 16 years after the transplant and graft biopsy confirmed chronic rejection. We suggest that the effects of the immunosuppressive drugs combined with the p53 gene abnormality accelerated tumor development in this patient.

Key words Renal transplantation · Allochronic overlapping tumor · p53 gene mutation · Immunosuppression

Introduction
There are many reports of allochronic overlapping tumors developing after renal transplantation, most of which are progressive and associated with a poor prognosis.¹ We report the case of a patient in whom various tumors developed over a 16-year period after renal transplantation, until renal failure occurred due to chronic rejection, but whose post-transplantation course was good because the tumors were detected early. We also discuss the possible association of p53 mutation, with references to the literature.

Case Report
The patient was a 56-year-old woman who had undergone renal transplantation, using a US kidney, at our hospital when she was 37 years old. She had been diagnosed as having chronic glomerulonephritis when she was 22 years old and commenced on hemodialysis when chronic renal failure was confirmed at the age of 29 years old. Her family history was unremarkable. Immunosuppressive treatment consisted of a triple regimen of methylprednisolone 6mg, azathioprine 50mg, and mizoribine 100mg daily. The patient had a history of blood transfusion and was positive for hepatitis C virus antibodies. Her postoperative course after renal transplantation was uneventful. She noticed a nodule under her left breast 8 years later when she was 44 years old, and ultrasound showed a single low-echoic-mass lesion with a diameter of 0.8 cm, under the skin (Fig. 1). Aspiration biopsy cytology confirmed class V left breast cancer (T1aN0M0 stage I), and a modified radical mastectomy was performed. The pathological diagnosis was invasive ductal carcinoma. Abdominal computed tomography (CT) performed at the same time to check for possible metastasis in the liver showed a space-occupying lesion, about 5 cm in diameter, in the lateral region of the liver, which was diagnosed as a benign liver hemangioma based on its nature and appearance on the CT images. This hemangioma started to grow, but is now becoming smaller. At the age of 48 years, 4 years later, a regular checkup examination detected occult blood in the stool, and she underwent colonic double-contrast examination and total colonoscopy. The colonic double-contrast examination demonstrated a translucent image, about 1 cm in diameter, in the sigmoid colon, and the total colonoscopy showed a
subpedunculated polyp, located about 25 cm on the oral side of the anal verge (Fig. 2). About 3 months later, colonoscopic polypectomy was performed. The final pathological diagnosis was adenocarcinoma in adenoma. Furthermore, immunostaining of paraffin-embedded sections prepared from previously resected specimens using the p53 gene revealed mutations of the p53 gene in both the left breast cancer and sigmoid colon cancer (Fig. 3). No residual cancer was detected in the cut end, and no further resection has been performed. The dosages of the immunosuppressive drugs were reduced 3 years later, following the detection of cryptococcosis in the left lung. About 5 months later, at the age of 52 years, she felt weakness in her left lower leg and experienced difficult walking. She was admitted to the Department of Orthopedic Surgery in our hospital where CT and magnetic resonance imaging examinations were done. These examinations showed a subdural tumor in the extraspinal at Th3–6 (Fig. 4). The tumor was resected and the pathological diagnosis was meningeal epidermal meningioma, but no malignant change was found. Deterioration of renal function became evident about 2 years later and graft biopsy confirmed chronic rejection reaction. Hemodialysis was recommenced 2 months later.

Discussion

The development of malignant tumors after renal transplantation is common. In 1993, Penn reported the incidence to be about 100 times higher than that of the age-matched general population, with an overall 3- to 4-fold increased incidence of cancer in transplant patients compared with age-matched controls. Moreover, malignant tumors are the major cause of death (26% of cases) in patients whose transplanted kidney has remained functional for more than 5 years. The possible reasons for this include: