Background. Malakoplakia is an unusual chronic inflammatory disease with distinctive histopathological features rarely involving the parenchyma of a transplanted kidney, and to date less than ten cases have been reported. 

Methods and results. We present a case of malakoplakia of a kidney graft in a 31 year old woman after simultaneous kidney and pancreas transplantation, which was successfully treated with quinolones. After the treatment of malakoplakia, she was monitored regularly, and her renal and pancreas grafts functioned well for the following 9 years, which is 12 years post transplantation. Moreover, 1 year after treatment of malakoplakia she became pregnant and gave birth to a healthy child.

Conclusion. Evaluation of a kidney biopsy sample represents the key to diagnosis of malakoplakia which is important for correct patient management. Treatment with antibiotics with intracellular penetration (quinolone type) may result in curing the disease. According to our knowledge, this is the first case of allograft renal malakoplakia after combined kidney and pancreas transplantation.

Key words: malakoplakia, renal allograft, combined kidney and pancreas transplantation

INTRODUCTION

Malakoplakia is a rare inflammatory disorder frequently associated with Escherichia coli infection in immunocompromised patients in whom defective bacterial killing by macrophages leads to the manifestation of the disease. The term malakoplakia is derived from the Greek words “malakos” which means soft, and “plakos”, meaning plaques.

Malakoplakia was originally described in the urinary bladder, but can involve many other organs. However, renal parenchymal involvement is rare and to date less than ten cases have been reported in renal allografts. The diagnosis can be confirmed only histologically and depends on microscopic detection of so-called Michaelis-Gutmann bodies. Before 1990, malakoplakia was a serious disease with a high mortality rate. Quinolones, antibiotics with high intracellular penetration are used in treatment and can cure malakoplakia.

CASE REPORT

A 31 year old woman had been suffering from diabetes mellitus (DM) type I since the age of 16. Because of severe organ complications of DM, she underwent cadaveric kidney-pancreas transplantation 12 years ago (in February 1999). She was immnosuppressed with Tacrolimus and Mycophenolate Mofetil. The patient had a histologically verified episode of acute rejection of the pancreas on the 15th day after transplantation (grade II, using Drachenberg’s criteria) and was treated with steroids with good response. During the following 3 years she was treated for repeated urinary tract infections. She was admitted to the hospital for the same complaints in 2001. Her serum creatinine level was 147 μmol/L (one month before admission, her creatinine level was 104 μmol/L). There was no proteinuria, and an examination of spun urine sediment showed the presence of 5-10 leukocytes and no red cells or cellular casts. There was evidence of repeated bacteriuria, and Escherichia coli and Staphylococcus aureus had grown from cultures of the urine 3 times during the last 2 years, and were also growing at this time. Her hypertension was under control (with blood pressure 120/80 mm Hg). The level of blood glucose was 5.7 mmol/L (normal range 3.6–5.59), and the glycated hemoglobin value was 7.1% (normal range less than 6%). The values for total protein, albumin, electrolytes, and lipids were normal. There was no recent history of anorexia, nausea, vomiting, fever, lymphadenopathy or systemic disease. Hematologic and liver laboratory tests were normal. Tests for viral hepatitis B, and C were negative. Testing for CMV and EBV were also negative. Ultrasonographic examination of the kidney and pancreas grafts showed normal pancreas and normal kidney graft with “forgotten” double pig-tail stent in the pelvis. The
Clinical diagnostic suspicion was rejection, and biopsies of both grafts were performed. There were no pathologo-
logical findings in the pancreas graft.

The kidney biopsy sample was divided for immuno-
fluorescence (IF) and light microscopy (LM). The sample
for IF contained 2 glomeruli, both were negative for im-
umoglobulins. Peritubular capillaries were C4d negative.
In light microscopy, the kidney biopsy was 23 mm long,
and the normal kidney cortex appeared only in a small
part of the sample. The remainder revealed completely
destroyed renal parenchyma. This area showed predomi-
nantly mesenchymal tissue with chronic inflammatory
cells, histiocytes and numerous PAS and von Kossa’s
positive Michaelis – Gutmann (MG) bodies with typical
targetoid appearance (Fig. 1, 2). MG bodies were con-
firmed ultrastructurally (Fig. 3). Focally there was active
inflammation with formation of microabscesses. Muscle
arteries showed muscular hypertrophy, and arterioles
showed mild hyalinosis.

The diagnostic conclusion was: Malakoplakia in the
renal allograft, and active infection with micro-abscess
formation.

Follow-up

The patient was treated with antibiotics with intracel-
lar penetration (quinolone type), and simultaneously
immunosuppression was reduced. Her renal functions im-
proved during the following month (with a serum creati-
nine level of 105 μmol/L).

Six months later, she suffered from short-term nausea
and vomiting, and was admitted to the hospital. Her S-Cr
had increased to 145 μmol/L, and a second renal biopsy
was performed.

The sample obtained for IF contained cortex of kidney
tissue with 5 gli, and staining for immunoglobulins, and
for C4d in PTCs were negative. In light microscopy, there
were 8 gli which were unremarkable. There was no inflam-
mation, and focal interstitial fibrosis was recognized. The
diagnostic conclusion was: nonspecific focal interstitial
scarring, no morphological features of rejection, no mala-
koplakia.

Her renal function improved spontaneously with only
supportive therapy within several days after rehydration.
She has been monitored regularly and her renal and pan-
creas functions are stable. Both grafts have remained in
situ. Her S-Cr level was 110 μmol/L after the treatment
of malakoplakia and remained at the same level for the
following 9 years, which is 12 years post transplantation.
Moreover, 1 year after treatment of malakoplakia she be-
came pregnant and gave birth to a healthy child.

DISCUSSION

Malakoplakia represents an uncommon form of chron-
ic inflammatory disease with distinctive histopathological
features. Diagnosis can be determined only histologically.
The targetoid structures, so-called Michaelis-Gutmann
bodies which represent the key diagnostic marker, were
in fact discovered in human medicine by Prof. von Hansemann, in 1901 (ref.4). Prof. von Hansemann read about a similar disease in a veterinary journal. Then he discussed this with his assistant Dr. Gutmann and provided him with details of this case. Dr. Michaelis was an expert biochemist, and Michaelis and Gutmann agreed to study this new disease in co-operation. Finally they published their results in 1902, one year before von Hansemann’s paper. Both papers were published in German, and the error probably occurred because the texts were never translated completely4. Now, Hansemann’s histiocytes and Michaelis-Gutmann bodies are known.

The precise pathogenesis of malakoplakia is still unknown. A favorite theory assumes an abnormal macrophage response because of defective lysosomal function5. It has been suggested that macrophages in malakoplakia are capable of phagocytosis but unable to digest the bacteria. There is general agreement that a patient with malakoplakia has an underlying disease involving an abnormal or altered immune response, and that microorganisms also play a role in the pathogenesis, especially E. coli which is found in more than 80% of cases6. Before 1990, malakoplakia was a serious disease with a high mortality rate and poor recovery of renal function. At that time, early nephrectomy represented the recommended treatment of choice with subsequent withdrawal of immunosuppressive therapy7. In the 90s, quinolones, antibiotics with high intracellular penetration, were first reported to cure malakoplakia8.

Malakoplakia can affect many organs and soft tissues but most frequently involves the urinary tract. However, renal parenchymal involvement is rare and accounts for only 15% of the urinary tract cases. Malakoplakia in renal allograft patients only rarely affects the renal allograft itself, and to date less than ten cases have been reported. According to our knowledge, this is the first case of allograft renal malakoplakia after combined kidney and pancreas transplantation.

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REFERENCES