中文題目：腎臟移植漿細胞急性排斥反應：個案報告

英文題目：Plasma cell-rich acute rejection in kidney transplant: a case report

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***Introduction****:* Plasma cell-rich acute rejection (PCAR) is a relatively rare type of acute allograft rejection with higher rate of graft failure. The most commonly used classification to define PCAR was plasma cell account for more than 10% of graft infiltrating cells. We reported a case of a 45-year-old woman with a kidney transplant who had PCAR and then kidney failure.

***Case Report****:* This is a 45-year-old woman received a kidney transplant on 2019/12. The patient received induction immunosuppressive therapy of basiliximab and methylprednisolone pulse therapy followed by maintenance therapy of prednisolone 10 mg/day, mycophenolate mofetil (MMF) 500 mg twice daily, and tacrolimus 2.5 mg twice daily initially. Based on stable kidney function (creatinine: 0.76 mg/dl), prednisolone was discontinued and tacrolimus was tapered down to 4mg/day. MMF was tapered to 250 mg twice daily. However, the patient's serum creatinine level increased to 1.74 mg/dl. Serum immunology test showed normal immunoglobin level. Nor cytomegalovirus (CMV) or BK virus infection was noticed in serum. No hydronephrosis was noticed by sonography.

Kidney biopsy revealed interstitial fibrosis in 35 % of cortical area, inflammation at 60 % of the scarred area, moderate chronic inflammatory infiltration involving 40 % non-scarred cortex, tubular atrophy detected at 35 % of area. Immunohistochemistry (IHC) study highlighted the scattered T lymphocytes in interstitial space, glomeruli and renal tubules with CD3 staining. There was plenty of plasma cells (>10 % of graft infiltrating cells) distributes through kidney tissue under CD138 staining. The patient was diagnosed with PCAR and chronic active T-cell mediated rejection (CATCMR), grade IA.

After the diagnosis was made, immunosuppressant was escalated to tacrolimus 2 mg twice daily and prednisolone 15 mg/day. Her serum creatinine level increased to 6.76 mg/dl later. She was declared impending graft-failure.

***Discussion:*** Multiple factors, such as infection, drug hyperreactions, post-transplant lymphoproliferative disorders (PTLD) nephropathy, and reflux nephropathy, would result in the plasma cell rich feature. We excluded CMV and BK virus by serology and IHC staining. PTLD was excluded due to lack of typical histological findings and absence of EBV encoded-RNA (EBER) stain. The patient can be diagnosed with CA TCMR and classified into PCAR since other etiology was not likely.

A study on 50 patients discussed the histological feature with PCAR. 42 in 50 cases showed severe interstitial inflammation (i3). 38 in 50 showed severe tubulitis. 28 in 50 showed moderate interstitial fibrosis, and 28 in 50 patient's showed i-IFTA II lesion. A case series of six PCAR cases found out that both moderate tubulointerstitial and microvascular inflammations may relate to worse graft function.

Poor drug adherence of medication and reduced dosage of immunosuppressant may be risk factors to PCAR. A study showed the average density of plasma cell in inflammatory infiltrates in non-compliant patients were higher than compliant patients but didn't reach clinical significance. Another study noticed that non-adherence with immunosuppressive medications appeared to be a major cause of acute rejection in CD20+ vs. CD20- group as well as CD38+ vs. CD38- group. The case we presented had poor compliance to immunosuppressant, which made her at higher risk of developing PCAR.

Another issue worth discussing was the immunosuppression and monitoring of drug level. Calcineurin inhibitor (CNI) is an extremely effective regimen. It was crucial to monitor tacrolimus trough level in immunosuppression. A study investigated the association between tacrolimus trough on the first month with acute rejection and infection within a year. Tacrolimus trough level between 5.35 to 7.15 ng/ml had less acute rejection rate compared to the < 5.35 ng/ml group and lower infection rate than > 7.15 ng/ml group. Another study revealed that the percent coefficient of variation (%CV) of tacrolimus trough level within 6 months in patients with acute rejection was significantly higher than patients without acute rejection. High variability of tacrolimus trough level is associated mainly to poor drug-adherence and drug-drug interactions. Medication adherence can be improved by altering twice a day (BID) dosage to once a day (QD) dosage in stable patients. In our case, the patient's %CV of tacrolimus trough level within 6 months was 34.9 %. It may contribute to higher rejection rate according the study.

***Conclusion:*** We reported a case of PCAR with treatment failure. The patient's distinctive histological feature was compatible to the group in prior case series with poorer prognosis and may be related to her poor medication compliance. We discovered that high variability of tacrolimus in this patient may be causative to develop graft rejection. Aggressive immunosuppression therapy could be choice of rescue treatment for PCAR. Further multi-centered and randomized-controlled study of treatment and disease prevention may be conducted in the future.