出國報告（類別：參加國際醫學會議及發表成果）

班夫移植病理基金會暨西班牙移植醫學會聯合會

成果發表：
移植腎單株免疫球蛋白病所導致的腎絲球足細胞結晶體沉積病變

服務機關：台北榮民總醫院 病理檢驗部
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出國期間：2017/3/25-2017/4/2
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摘要（含關鍵字）

班夫移植病理基金會每兩年召開國際移植病理大會，其所製定的病理診斷共識已成為全球奉行的主流規範，並且廣泛的應用在臨床治療及許多新葯試驗上。此次大會主旨在更新各器官的移植病理診斷指引及發表全球研究的新進展。職以本院病例報告受邀參加此次在西班舉辦的大會，發表罕見的移植腎單株免疫球蛋白病所導致的腎絲球足細胞結晶體沉積病變。我們的報告屬於此次大會的主題之一有關移植腎的再發及新生腎病。此次大會提出許多目前最重要的移植醫學議題及未來移植病理的新展望，尤其在更新病理診斷共識及新穎分子生物技術的應用及發展上，值得我們學習及推展。此次參展最大的感想是除了要確立我們的移植病理診斷能維持在國際尖端水平以上，在研究議題及成果上也要能受到國際同儕的重視。同時國外機構的跨領域合作平台及團隊的建立也可做為我們推動移植醫療及研究的學習對象。

關鍵字：移植病理診斷共識，單株免疫球蛋白病，足細胞結晶體沉積

目次

一、 目的

(1) 受邀參加班夫移植病理基金會暨西班牙移植醫學聯合會並發表本院病例-- "移植腎單株免疫球蛋白病所導致的腎絲球足細胞結晶體沉積病變"。

(2) 學習交流移植病理的新知及技術，尤其在更新病理診斷共識及新穎生物技術的應用及發展，並確立我們的移植病理診斷能力可維持在國際尖端水平以上。

二、 過程

班夫移植病理基金會每兩年召開國際移植病理大會，今年三月二十七日至三十一日在西班牙巴賽隆那大學與西班牙移植醫學會合併舉辦聯合會議。職以本院病例報告受邀參加此次在西班舉辦的大會，發表罕見的移植腎單株免疫球蛋白病所導致的腎絲球足細胞結晶體沉積病變。此次會議有數佰位全球各地專業人士參與，台灣病理醫師除本人外尚有台中榮總文醫師參加。我的報告也是此次大會的主題之一，引起國際同儕的注意及廣泛交流。

三、 心得

此次大會的主要議題涵蓋移植器官老化，抗體性排斥，遠距病理診斷，大數據在移植病理學的應用，移植相關生物標誌的進展，排斥耐受性，腎，肝，心和肺器官移植病理的臨床進展，移植病理數位化，捐贈和倫理，組織配對免疫學，人體移植臨床試驗的關鍵問題，組織再生及修復，同種異體移植的新技術及病理特色和診斷共識，同種異體移植物器官的非特異性損傷及診斷，移植組織病理學之過展及更新，器官採取之病理檢診，免疫抑制和個人化醫療，面部及四肢移植的進展及病理診斷，移植組織工程病理等重要議題。本次大會提出許多未來移植病

理的新展望，尤其在更新病理診斷共識及新穎生物技術的應用及發展上，值得我們學習及推展。其中最值得借鏡之處包含：(1) 鼓勵利用研究成果及本院臨床資源，多參與此類專業科學會議，以提昇我們的移植病理診斷能力在國際尖端水平上。此外也可藉機尋求跨國合作機會來爭取新診斷試劑或儀器的測試機會。此次會議中，許多國外的成果，值得我們學習及推廣。(2). 班夫移植病理基金會國際移植病理大會內容涵蓋各類器官移植如腎臟、心臟、胰臟、肝臟、小腸、以及複合組織（臉以及肢體）等，因時間上各器官系統專業區段討論多為平行進行，個人無法同時參與並携回最新資料，將來可鼓勵各專業領域的醫師一起參加以平衡加强各移植領域的發展。 (3) 鑑於大數據時代的來臨，病理標本及診斷統計均可進行高通性大數據分析。此為擴展移植醫学研究的視野與研發能力以及追求一流尖端醫療必備的核心概念，推得推廣。這次會議展示的許多成果强調跨領域合作及生物資訊應用的重要性。本院移植病患的臨床資料及各類檢体繁多，須有計劃及系統性收集。目前本院已進行所謂〝移植結前捐贈器官生檢(time zero donor biopsy)〞以及〝移植後定期生檢(protocol recipient biopsy)〞的計劃。此為國內首先倡導施行，在此合作下，將可收集完整豐的移植標本，而本部也已配合使用最新的〝班夫移植病理診斷分類〞作系統性及報列性報告。計劃朝向整合臨床及病理醫師以及基礎免疫學者，組成研究團隊的方向進行。以創新的構想结合本院豐富臨床資料及病理檢体來爭取大型研究經費，將來才有機會將成果育成為有經濟價值的診斷或治療產品。同時也要鼓勵年輕優秀醫師科學家，投身於新穎生物技術的學習及應用發展，以接軌下一世代的移植病理診斷技術及治療的提昇。 (4) 此次大會新穎議題如移植器官老化，移植相關生物標誌的進展，組織再生及修復，移植組織工程病理等均為具經濟性的發展項目。可做為移植醫學研發培育的目標

四、 建議及改進事項：

(1). 建立移植病理診斷專業團隊。此次參展最大的感想是除了

在研究議題及成果上也要附合應用及主流趨勢並且要能受到國際同儕的重視。最重要的是要確立我們的移植病理診斷在各器官系統上能維持在國際尖端水平，成為全國或國際移植醫療学習及諮詢的對象。為達成此目的應鼓勵各領域移植專家多參與此類專業科學會議，吸取新知之外，也可建立合作管道。

(2). 發展有效率及前瞻的移植病理研究專業團隊。此次大會提出許多新穎移植病理診斷相關的生物標誌，其中許多分子生物標誌已開發為診斷產品。如能成立有效率及前瞻的研究專業團隊將來可歸劃朝向研發具經濟性的產品來進行。

(3). 建立移植病理組織庫以提供移植研究專業團隊充足的研究材料。移植病理組織庫除一般病理切片臘塊包埋材料外，應收集充足的冷凍組織以進行基因及其表現的分析。臨床上也要能配收集合血液、尿液及分泌物。此次會議中，許多成果發表的背後均有龐大組織庫網絡的支援。

(4). 建立動物移植平台及其組織庫以提供移植研究專業團隊充足的研究材料，以進行產品測試。動物模式為發展前瞻性移植臨床及病理研究不可缺少的工具。此次會議中，許多動物前瞻性移植研究的成果發表均有完善動物移植平台的支援。尤其利用小動物做移植研究須有顯微手術設備及專技人員的培養支援，技術門檻較高，應整合規化。

(5). 建立移植病人之臨床及病理資料庫。此次大會提出許多新穎生物標誌及藥物的人體實驗，均須有充足及詳細的臨床及病理資料作分析的基礎。在目前大數據應用為大型研究必要的條件下，此平台的建立將有助本院團隊具有完整的研究資訊，取得領先的地位。

五. 附錄

2017 BANFF-SCT Joint Scientific Meeting

BARCEL
27-31 Marc

Barcelona, January 14th, 2017

Dear Prof. Yang,

On behalf of the Scientific Committee we have the pleasure of informing you that your paper, with submission reference **2,** titled:

ISOLATED CRYSTALLOID PODOCYTOPATHY WITH FOCAL SEGMENTAL GLOMERULOSCLEROSIS IN RENAL ALLOGRAFT: AN UNUSUAL PRESENTATION OF POST-TRANSPLANT MONOCLONAL GAMMOPATHY OF RENAL SIGNIFICANCE

has been **ACCEPTED** for **POSTER PRESENTATION** to the 2017 Banff-SCT Joint Scientific Meeting to be held in Barcelona from 27th to 31st of March, 2017.

The final number assigned to your **POSTER** presentation is **P-1.**

This number will identify your poster in the final program and book of abstracts.

The first author will have to present its communication during the Joint POSTER SESSION which will take place on **29/03/2017**, at **18:30.**

Your poster must be display from Wednesday 29th at 9.00 hours to Friday 31st March at 13.00 hours. However, poster boards will be available to start displaying your poster from Monday 27th March 2017 at 9.00 hours.

Isolated Crystalloid Podocytopathy in Renal Allograft: An Unusual Presentation of Post-transplant Monoclonal Gammopathy of Renal Significance

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Introduction

Monoclonal gammopathy of renal significance (MGRS) denotes a spectrum of hematological disorders which cause direct renal damage by deposing monoclonal immunoglobulin and/or indirect renal injury triggered by secreted factors or autoantibody activity. These hematological disorders are often clinically obscure due to low tumor burden, indolent neoplastic cells, and/or lack of overt end-organ damage. The patterns of renal injury vary widely and glomerulopathies are more common than tubular disorders. As in native kidney, MGRS, if not properly treated, may cause severe consequences in allograft kidney resulting in morbidity or even graft loss.

Results

The patient was a 51-year-old man who had received living-donor kidney transplant from his wife in 2008. His postransplantation course was uneventful until 4 years ago, when he was found to have gradual increased urine protein-creatinine ratio to 1.56. A renal biopsy was performed. The light microscopic examination revealed only mild focal interstitial fibrosis and hyaline arteriolosclerosis (fig 1a and 1b). Immunofluorescent examination using frozen tissue showed negative staining for IgG, IgM, IgA, C1q, C3, C4, C4d, kappa-light chain (κ-LC) and lambda-light chain (λ-LC) on both glomerular and tubular components (figure 1c and 1e). However, ultrastructural examination revealed cytoplasmic inclusions with crystalloid structures in the podocytes (figure 1g and 1h). No crystalloid inclusion was found in other renal cells. The repeated stains of κ-LC and λ-LC by immunoperoxidase method following antigen retrieval on formalin-fixed paraffin-embedded tissue sections demonstrated restrictive staining of podocytes for κ-LC (figure 1d and 1f). Based on the implication of renal biopsy, a workup for paraproteinemic disease was initiated. The patient had mild elevated free κ-LC (20.84 mg/L) and the serum free κ-LC to λ-LC ratio was 2.4. Serum immunoelectrophoresis revealed a monoclonal IgGκ. Bone marrow biopsy showed interstitial infiltration of plasma cells about 10% by CD138 with a κ to λ ratio about 4:1. Bone marrow karyotype analysis revealed no clonal chromosomal abnormalities. Skeketal survey showed no osteolytic lesion. Four years after initial presentation of monoclonal gammopathy, the patient's serum creatine level remained stable in a range of 1.09-1.16 mg/dL and the urine protein-creatinine ratios varied between 0.5 to 1.8. Serum free κ-LC was slightly increased to 24.4 mg/L. A follow-up renal biopsy was performed in 2016. Light microscopy showed focal segmental glomerulosclerosis (fig 2a and 2b, white arrows). The podocytes remained positive for κ-LC (figure 2d). Similar to previous biopsy, cytoplasmic inclusions were found only in podocytes without involving other renal cells (figure 2g). The crystalloid inclusions showed lamellated structure with a regular periodicity of 4.4 nm (figure 2i). Occasionally, the crystalloid inclusions protruded to form cilia-like membrane spikes on cell surface (fig 2h, black arrow).

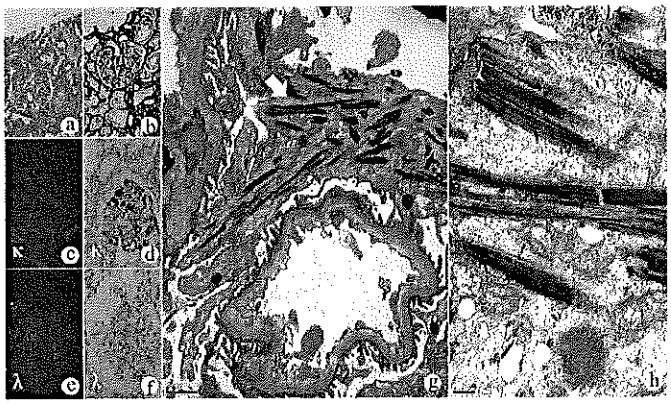

Figure 1.

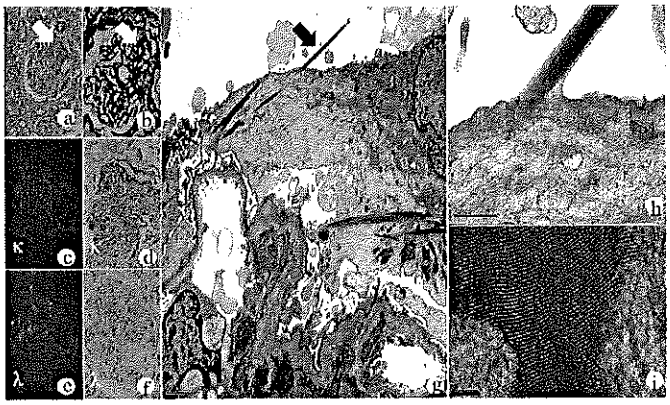

Figure 2.

Conclusions

Crystalloid podocytopathy is one of the rarest glomerulopathies related to MGRS. As far as our knowledge, this is the first report of MGRS presents as isolated crystalloid podocytopathy in the allograft kidney. The crystalloid deposits are mainly kappa-light chains, of which the variable κ1 domain accounts for resistance to proteolysis and promote self reactivity and crystallization (Nephrol Dial Transplant 25: 2982–2990, 2010). However, the mechanism of preferential podocytic deposition of crystalloid immunoglobulin remains unclear. Two inherent features of crystalloid podocytopathy may mislead the pathological diagnosis. Firstly, the crystallization of kappa-light chains frequently causes locking antigenicity and false-negative staining using conventional immunofluorescent method on frozen tissue. Antigen retrieve is required to demonstrate the kappa-light chain crystalloid deposits. Secondly, the dominant morphology of focal segmental glomerulosclerosis may obscure the recognition of underlyin crystalloid deposits and bias the pathological diagnosis as recurrent or de novo FSGS. Aware of these pitfalls helps to avoid misdiagnosing the crystalloid podocytopathy.

Acknowledgements

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