Immunoperoxidase Staining of Collagen Type IV Alpha-Chains in Kidney and Skin of Alport’s Patients in Thailand

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Background: The X-linked Alport’s syndrome (XL-AS) is the majority of AS patients, due to mutation of gene encoding type IV collagen (COL4) α5 in glomerular basement membrane (GBM) and epidermal basement membrane (EBM). Immunoperoxidase technique has been studied to reveal expression of type IV collagen in kidney and skin for diagnosis of AS in Thailand. Methods: Cross-sectional analysis was performed: 23 subjects were included and divided into four groups. First were 8 patients with kidney biopsy-proven AS (7 males/1 female XL-AS). Second were 3 patients with thin basement membrane nephropathy (TBMN). Third were 7 first-degree relatives and the last group, 5 highly suspected cases of AS. Immunoperoxidase staining for COL4 α1, α3, and α5 were performed in 7 renal and 23 skin biopsies with formalin fixed paraffin embedded. Results: Phase1; the immunoperoxidase staining in four kidney specimens of AS patients showed absence of GBM COL4 α3 and α5. Phase 2; EBM of eight AS showed negative immunoperoxidase staining for COL4 α5 corresponding for XL-AS. Phase 3; two TBMN patients showed negative EBM COL4 α5 and GBM COL4 α3 and α5. In the relatives, 5 showed absent/discontinuous staining of COL4 α5. In suspected cases, EBM COL4 α5 was negative in all three males and positive in two females. Conclusions: Immunoperoxidase staining for COL4α chains of skin and kidney in suspected cases of AS is useful and convenient particularly in limited resources areas. Skin biopsy is less invasive than renal biopsy and can detect 80% X-linked AS patients.

Key Words: Nephritis, hereditary; Hematuria, benign familial; Skin biopsy; Collagen type IV; Immunoperoxidase
Extracorporeal Membrane Oxygenation Support

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Extracorporeal membrane oxygenation (ECMO) use is increasing in cadaver donor before the declaration of brain death. Its complications are bleeding, hemolysis, and thrombosis. Because graft thrombosis is one of the important alerting sign of hyperacute rejection, we have to differentiate between antibody mediated rejection and ECMO related complication. We experienced a biopsy proven case of glomerular thrombosis after ECMO support in a sequential renal graft biopsy. A kidney transplantation (KT) was done in a thirty-eight male from a cadaveric donor, who was a thirty-nine-year-old female suffered from subarachnoid hemorrhage with ECMO management. Zerotime biopsy disclosed multiple fibrin thrombi in the glomerular capillaries and aff erent arteriolar lumen without any neutrophilic infiltration or peritubular capillaritis. The second graft biopsy, 3 days after KT, demonstrated much decreased number of thrombi with red blood cell casts. C4d staining was negative. The third graft biopsy, 20 days after KT showed normal appearing kidney without any thrombi.

Key Words: Kidney transplantation; Antibody mediated rejection; Extracorporeal membrane oxygenation; Thrombosis

Morphologic Prognostic Features in Clear Cell Renal Cell Carcinoma: Analysis of 668 Cases

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Background: Clear cell renal cell carcinoma (CCRCC) has poorer prognosis than papillary or chromophobe renal cell carcinoma. CCRCC is mainly composed of clear cells but also shows various histologic features. We evaluated the prognostic significance of several histologic features in CCRCC. Methods: We analyzed 668 CCRCC patients who had undergone partial of radical nephropathy at Seoul National University Hospital (SNUH) between 1995 and 2005. We reviewed certain histological parameters, including eosinophilic cytoplasm, necrosis, sarcomatous change, and rhabdoid feature. The prognostic significance was estimated using the Kaplan-Meier method and the log-rank test. Results: On univariate analysis, variables significantly correlated with shorter survival rate were eosinophilic cytoplasm (p<0.001), necrosis (p<0.001), sarcomatous change (p=0.005), and rhabdoid feature (p<0.001). Tumor necrosis (p=0.001) and rhabdoid feature (p=0.042) were independent prognostic factors for nuclear grade and TNM staging in the multivariate analysis. Conclusions: The histologic features including eosinophilic cytoplasm, necrosis, sarcomatous change, and rhabdoid feature were associated with poor prognosis. Among them, tumor necrosis, and rhabdoid feature proved to be independent prognostic indicators. Therefore, to predict clinical outcome of patients, careful pathologic examination to find out diverse histologic features of renal cell carcinoma is needed.

Key Words: Carcinoma, renal cell; Necrosis; Rhabdoid tumor; Prognosis

Transglutaminase-2 Expression and Its Prognostic Value in Clear Cell Renal Cell Carcinoma

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Background: Recent studies have shown that the up-regulation of transglutaminase-2 (TG2) in some carcinomas is associated with poor prognosis. The aim of the study was to examine clinical outcome of clear cell renal cell carcinoma (CCRCC) according to expression level of TG2. Methods: We analyzed 638 CCRCC patients who had undergone partial of radical nephropathy at Seoul National University Hospital (SNUH) between 1995 and 2005. The expression of TG2 was determined by immunohistochemistry and was analyzed using the H-score. The clinical outcome was estimated using the Kaplan-Meier method and the log-rank test. Results: TG2 high expression was found in 53 cases (8.3%) and it was significantly associated with high Fuhrman nuclear grade (p=0.004). But TG2 expression was not associated with TNM stage and tumor size. The survival analysis showed a significant association between TG2 high expression and worse cancer specific survival (p=0.003) or overall survival (p=0.018). On multivariate analysis, TG2 expression was an independent prognostic indicator for histologic grade and TNM staging (p=0.029). Conclusions: In conclusion, the high expression of TG2 in CCRCC is associated with poor prognosis. Therefore, TG2 expression could be important prognostic factor in CCRCC.

Key Words: Transglutaminases; Carcinoma, renal cell; Prognosis

Membranous Glomerulonephritis in Multiple Myeloma

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Renal involvement in multiple myeloma is mostly cast nephropathy in form. Light chain deposition disease or ischemia by infiltration of myeloma cells are occasionally described. However, glomerulonephritis such as membranoproliferative glomerulonephritis, membranous glomerulonephritis, and minimal change disease, can also occur very uncommonly. Here, we present a case of membranous glomerulonephritis, which was the first presentation of myeloma, and were not accompanied by tubulointerstitial change. A 77-year-old woman was admitted because of both leg edema and proteinuria. The 24-hour protein was 9,453.6 mg/day and the albumin was 2.5 g/dL. Serum immunofluorescence and immunoelctrophoresis exhibited monoclonal peak in the IgG heavy chain and lambda light chain. The nonselective glomeruli appeared normal in appearance without spikes on special stains. The immunofluorescent staining disclosed weak positive granular staining of IgG and lambda light chain along the peripheral capillary wall. Multi ple subepithelial electron dense deposits were identified on ultrastructural examination. The bone marrow core biopsy demonstrated increased immature plasma cell series, which were positive for CD138 and lambda light chain.
**Key Words:** Glomerulonephritis, membranous; Nephrotic syndrome; Multiple myeloma

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**AP20-PP-0008**

**Eosinophilic Tubulointerstitial Nephritis in Churg-Strauss Syndrome with Fatal Clinical Outcome**

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Churg-Strauss syndrome (CSS) is an autoimmune vasculitis of small to medium sized vessel, leading to necrosis, and is clinically associated with asthma and eosinophilia. Renal involvement of CSS may be seen in about 50% of cases, and is generally presenting as glomerulonephritis. We experienced a rare case of severe eosinophilic tubulointerstitial nephritis due to Churg-Strauss syndrome showing fatal clinical outcome. A 64-year-old man with cough and sputum for 2 weeks presented with new-onset fever. Physical examination showed wheezing. Chest computed tomography implied total atelectasis of right middle lobe and pneumonia of right lower lobe. Laboratory data showed leukocytosis, hypereosinophilia (2,590/μL), elevated serum IgE (1,103 IU/mL), elevated blood urea nitrogen (73 mg/dL) and creatinine (3.96 mg/dL) and positivity of myeloperoxidase antineutrophil cytoplasmic antibody. Nasal cavity biopsy showed chronic inflammation with a few eosinophils. At renal biopsy, all glomeruli showed normal looking with no cellular proliferation. Interstitium was markedly expanded with diffuse and severe eosinophil infiltration, which invaded adjacent tubules, and produced tubulitis. Charcot-Leyden crystals were found in eosinophilic rich area. Blood vessels showed necrotizing vasculitis in small sized arteries of interstitium with granuloma. Immunofluorescence demonstrated no immune deposits. The patient was treated with steroids and cytotoxic but expired at 41 days after hospitalization due to myocardial infarction.

**Key Words:** Eosinophilic tubulointerstitial nephritis; Churg-Strauss syndrome; Kidney

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**AP20-PP-0009**

**C4d Expression in the Lupus Nephritis Is Higher in the Class V Lupus Nephritis and Not Correlated with Activity or Renal Function**

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**Background:** Systemic lupus erythematosus (SLE) is immune complex mediated disease and lupus nephritis (LN) is found in 60% of SLE patients. The glomerular expression of C4d in LN can be correlated with microthrombosis or disease activity. However, these results are controversial. Our aim is to evaluate that the glomerular C4d expression can be a marker of activity or renal dysfunction of LN.

**Methods:** Biopsy-proven 87 LN were evaluated with following factors: age, amount of proteinuria, estimated glomerular filtration rate (eGFR), serum C3 and C4, serum antinuclear antibody (ANA) level, World Health Organization (WHO) class, activity and chronicity. Immunohistochemistry of the C4d was performed and scored with semi-quantitive method. **Results:** The score of glomerular C4d (GC4d) is the highest in the WHO class V (class II, 0.56 ± 0.56; class III, 0.56 ± 0.60; class IV, 0.75 ± 0.74; class V, 1.15 ± 0.89; p < 0.05). The GC4d scores showed positive correlation with proteinuria, serum C3 and C4 level and negative correlation with ANA titer (p < 0.05). Serum creatinine level, eGFR, activity, and chronicity revealed no correlation with GC4d scores (p > 0.05). **Conclusions:** Class V LN showed higher GC4d scores than other WHO group. Proteinuria, serum C3 and C4 levels had positive correlation with GC4d scores. Class V LN is the membranous LN and revealed large amount of proteinuria like membranous nephropathy (MN) which shows glomerular C4d deposition in almost 100% cases. Our results suggest that the pathogenesis of class V LN is similar to MN and in situ classic complement activation can be involved in the pathogenetic mechanisms. There was no correlation between GC4d expression and activity or renal function.

**Key Words:** Complement C4d; Lupus nephritis; Class V; Activity; Renal function

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**AP20-PP-0011**

**The Status of Anaplastic Lymphoma Kinase Gene Rearrangement in Renal Cell Carcinoma of Korean**

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**Background:** Recently, the studies of target therapy on advanced renal cell carcinoma (RCC) patients are performed actively. The clinical trial of target therapy on anaplastic lymphoma kinase (ALK) inhibitor in several tumors is ongoing, according to the early reports; it shows excellent interim result in non-small cell lung cancer. Several studies reported cases of RCC with ALK gene fusion, and the fusion partners of these genes were diverse. The subtypes of these RCCs were non-clear cell type such as papillary, medullary and unclassified. In this study, we investigated the status of ALK gene rearrangement in RCC of Korean by large-scale study.

**Methods:** We used tissue microarray slides of Korean RCC patients diagnosed at the Seoul National University Hospital by nephrectomy between 1995 and 2005. Total 850 cases (689 clear cell RCC cases and 161 non-clear cell RCC cases) were available. We used ALK immunohistochemistry for screening test and confirmed using fluorescence in situ hybridization (FISH) analysis. **Results:** ALK immunohistochemical staining showed membranous positivity in one case (0.12% of total 850 RCC cases and 0.62% of 161 non-clear cell type RCC cases) only. And we also observed break apart signals by FISH in that case. The patient was 44-year-old male and the initial pathologic diagnosis was papillary type 2.

**Conclusions:** In spite of the rarity, this study showed the presence of ALK gene rearrangement in Korean RCC patients. This result will provide a scientific basis of another new target therapy on advanced RCC patients.

**Key Words:** Carcinoma, renal cell; Anaplastic lymphoma kinase; Immunohistochemistry; In situ hybridization, fluorescence
**Urokinase, Urokinase Receptor, and Plasminogen Activator Inhibitor-1 Expression on Podocytes in IgA Glomerulonephritis**

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**Background:** The purpose of this study was to observe the expression of urokinase (uPA), urokinase receptor (uPAR), and plasminogen activator inhibitor-1 (PAI-1) on podocytes in IgA glomerulonephritis (GN).

**Methods:** Fifty-two renal biopsy specimens of IgA GN were deparaffinized and subjected to immunohistochemical staining for uPA, PAI-1, and uPAR. According to the expression of uPA and uPAR on podocytes, the subjects were classified into three groups: uPA, uPAR, and the “negative” group. The prevalence of the variables of “Oxford classification for IgA GN” was compared among the groups.

**Results:** On podocytes, uPA was positive in 11 cases and uPAR was positive in 38 cases; however, PAI-1 was negative in all cases. Expression of both uPA and uPAR on the podocyte was less frequently accompanied by tubulointerstitial fibrosis.

**Conclusions:** Our results suggest a possible protective effect of uPA/uPAR expression on the podocyte against interstitial fibrosis.

**Key Words:** Glomerulonephritis, IGA; Plasminogen activator inhibitor 1; Urokinase-type plasminogen activator; Receptors, urokinase plasminogen activator

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**C4d Immunoreactivity of Intraoperative “Zero-Hour” Biopsy in Renal Allograft**

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**Background:** It has been known that C4d deposition in peritubular capillaries (PTCs) have correlation with antibody mediated rejection (AMR) in renal allograft. The identification of C4d deposition in PTCs is useful to diagnose AMR, a number of related studies are currently underway. Moreover several studies reported C4d immunoreactivity in some glomerular diseases, and we occasionally met C4d immunoreactive post-transplantation biopsies in not PTCs such as glomeruli, arterioles, unrelated to AMR. In this study, we investigated relationship between C4d immunoreactivity of intraoperative “zero-hour” biopsy in renal allograft, thought to be due to donor condition, and rejection episode during follow-up.

**Methods:** We collected renal transplantation cases examining initial C4d immunohistochemical status, operated at the Seoul National University Hospital between 2010 and 2011. A total 147 cases were available. **Results:** Of 147 cases, twenty four cases (16.3%) showed strong C4d staining in glomeruli, 38 cases (25.9%) weak and the rest cases (57.8%) negative. Nine cases (6.1%) showed positive C4d staining in at least some of the arterioles and the rest cases (93.9%) negative. There were no significant differences statistically in rejection episode of renal allograft specimen according to the glomerular or arteriolar C4d immunoreactivity of intraoperative “zero-hour” biopsy specimen. Especially seven patients (6.4%) experienced antibody-mediated rejection during follow-up, their donors were all living, and there was no significant relationship with other parameters statistically.

**Conclusions:** It is concluded that there were no significant differences in rejection episode of renal allograft specimen according to the C4d immunostaining intensity of intraoperative “zero-hour” biopsy specimen.

**Key Words:** Complement C4d; Kidney transplantation; Graft rejection; Immunohistochemistry

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**Thrombotic Microangiopathy of the Kidney after Hematopoietic Stem Cell Transplantation**

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Transplantation-associated thrombotic microangiopathy (TA-TMA) is a severe and multifactorial complication of hematopoietic stem cell transplantation (HSCT). Here we report a case of TMA confirmed by renal biopsy after HSCT. A 38-year-old male visited our hospital because of ecchymosis that lasted for three months. He had received allogeneic HSCT 10 months ago because of acute lymphocytic leukemia. He continued on prednisolone due to chronic graft-versus-host disease.

**Results:** Immunofluorescence analysis showed thrombi in glomeruli for fibrinogen. Electron microscopy showed subendothelial expansion. Despite treatment, the patient died of respiratory failure. Endothelial injury is common after HSCT and results from exposure to conditioning regimens, calcineurin inhibitors, GVHD and infections. These factors contribute to the development of TA-TMA. Only rarely is renal biopsy performed for assessment probable to unsatisfactory general condition of patients, thrombocytopenia and bleeding tendency.

**Key Words:** Complement C4d; Kidney transplantation; Graft rejection; Immunohistochemistry
Usefulness of Oxford Classification in Assessing Immunoglobulin A Nephropathy Following Transplantation

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Background: We explored the efficacy of the Oxford classification for assessing native immunoglobulin A nephropathy (IgAN) in post-transplant patients compared with the glomerular injury score (GIS) and Haas classification. Methods: A total of 125 renal allograft biopsies obtained from 114 patients diagnosed with IgAN were assessed. The average time to biopsy was 70.5 ± 45.3 months after transplantation. Mesangial hypercellularity (M1), endocapillary hypercellularity (E1), segmental glomerulosclerosis (S1), and tubulointerstitial fibrosis (T1-2) were present in 12.8%, 6.4%, 45.6%, and 20.8% of the samples, respectively. Results: There was a significant correlation between Oxford-MEST scores and GIS or Haas subclass. S1 and T1-2 were correlated with elevated serum creatinine level, proteinuria, and decreased estimated glomerular filtration rate (eGFR), and E1 correlated with decreased eGFR at the time of biopsy. The 10- and 15-year graft survival rates were 62.9% and 34.3%, respectively. The graft survival rate was significantly lower in the presence of S1 and T1-2, E, S, and T scores predicted graft survival and E and T scores also predicted serum creatinine doubling. Conclusions: In conclusion, the Oxford classification scheme is useful for evaluating chronic graft dysfunction in patients with post-transplant IgAN. The presence of endocapillary hypercellularity and segmental sclerosis should be included in the renal allograft biopsy report.

Key Words: IgA; Oxford classification; Transplantation; MEST scores

Light Chain Proximal Tubulopathy Containing Cytoplasmic Needle-like Crystalloids without Fanconi Syndrome: A Case Report

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Light chain proximal tubulopathy (LCPT) is a rare form of renal involvement in the plasma cell dyscrasia, mostly associated with Fanconi syndrome. LCPT without clinical features of Fanconi syndrome is very rare and only 2 cases have been reported to our knowledge. Here, we report a case of LCPT in multiple myeloma patient without clinical Fanconi syndrome. A 57-year-old Korean woman presented with asymptomatic persistent proteinuria. She had no significant past medical or family history. Serum creatinine and blood urea nitrogen were 0.89 and 11.9 mg/dL, respectively. Urine analysis showed 1+ proteinuria and 24-hour urine protein was 449 mg/day. Urine Bence Jonce protein, kappa type, was detected. Multiple myeloma was diagnosed by subsequent bone marrow biopsy, which revealed 30% plasmacytosis with kappa light chain restriction. The patient had normal level of venous pH, bicarbonate and other electrolytes. There was no evidence of proximal tubular dysfunction or type II renal tubular acidosis. Renal biopsy was performed and all glomeruli appeared histologically unremarkable. Some proximal tubules showed abundant intracytoplasmic filibrillary or cleft-like spaces, which appeared pale on hematoxylin and eosin and periodic acid-Schiff stains. On immunofluorescence, these inclusions stained strongly for kappa light chain. Congo red staining was negative. On electron microscopy, abundant intracellular and focal intraluminal crystalline inclusions were prominent. They were electron dense or isodense, needle like rectangular and pyramidal shaped structures. After 6 months, mild proteinuria still remains but there were no signs of disease progression.

Key Words: Light chain proximal tubulopathy; Fanconi syndrome; Light chain tubulopathy

The Heterogeneous Entity of Transplant Glomerulopathy: A Clinicopathologic Analysis of Transplant Glomerulopathy in Renal Allograft

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Background: Transplant glomerulopathy (TG) is characterized by the duplication of glomerular basement membrane resulted by chronic endothelial injury. Recently, it is suggested that various conditions can cause TG, such as antibody-mediated rejection (AMR), T-cell mediated rejection (TCMR), calcineurin inhibitor (CNI) toxicity and thrombotic microangiopathy (TMA). Methods: To identify the pathologic entity of TG, a total of 60 biopsies in 47 patients diagnosed as TG from 1994 to 2013 were analyzed by clinicopathologic criteria, comparing with 60 control patients of chronic renal injury without TG and rejection. Results: The mean age was 47.9 years (range, 22 to 71 years) and male to female ratio was 32:15. We classified TG into 4 groups: 27 AMR (45%), 3 TCMR (5%), 3 AMR + TCMR (5%), 13 CNI toxicity (21.6%), and 14 others (23.3%). The glomerular thrombi reminiscent of TMA (19%) were found only in 5 AMR and 6 CNI toxicity cases (11%). The hepatitis C virus infection was increasingly detected in TG patients (14/58, 24%) in contrast to non-TG (0/59, p = 0.000). The mean graft survival of TG is 11.5 years (range, 5 to 273 months), which is not significantly different from control group. Conclusions: TG is a spectrum of various diseases, and most associated with AMR and related to hepatitis C virus infection.

Key Words: Kidney transplantation; Glomerulopathy; Hepatitis; Antibody
**Microscopic Polyangiitis**

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Kidney is involved as a part of systemic vasculitis. Although the American College of Rheumatology (ACR) criteria and Chapel Hill Consensus Conference (CHCC) definitions for classification of systemic vasculitis have been used, there are still some degree of overlap, especially between microscopical polyangiitis and polyarteritis nodosa. We report a case of antineutrophil cytoplasmatic antibody (ANCA) associated vasculitis revealing fibrinoid necrosis in arcuate artery and fibrocellular crescentic glomerulopathy in renal biopsy. A 76-year-old woman presented with fever for a week and the temperature was up to 39°C once or twice a day. She had weight loss of 10 kg recently. On admission, blood and urine culture were performed and antibiotics were given. She had no arthralgia, headache and abdominal pain nor skin rash, lymphadenopathy, cardiac murmur and abnormal lung sounds on physical examination. Initial laboratory findings are as follows: white blood cell (WBC) count 15.510/mm$^3$ (neutrophil 81%, lymphocyte 10.3%, eosinophil 3.1%), hemoglobin 9.8 g/dL, platelet 551,000/mm$^3$, aspartate aminotransferase/alanine aminotransferase 111/69 IU/L, total protein/albumin 5.8/2.8 g/dL, blood urea nitrogen/creatinine 19/1.1 mg/dL, and urine protein 1+, blood 3+, red blood cell 1-4/HPF, WBC 10-29/HPF, erythrocyte sedimentation rate 75 mm/hr and C-reactive protein 16.1 mg/dL. Chest X-ray was normal. Despite of antibiotics, fever persisted. Antibiotics were discontinued and work-up for hidden malignancy was performed. Additional tests showed antinuclear antibody 1:40, speckled pattern, C3/C4 111/24 mg/dL, cryoglobulin negative, and RA factor 23.5 IU/mL. She was discharged with no-steroidal anti-inflammatory drug. One week later, her symptoms were getting worse with persistent mild fever. Myeloperoxidase-ANCA (enzyme-linked immunosorbent assay) was reported as positive. At this time, serum creatinine level was elevated up to 2.6 mg/dL. She was admitted again and underwent kidney biopsy.

**Key Words:** Vasculitis; Antibodies, antineutrophil cytoplasmic; Polyarteritis nodosa; Microscopic polyangiitis

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**Impacted Renal Stone Associated Clear Cell Adenocarcinoma Arising from the Renal Pelvis: A Case Report**

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Clear cell adenocarcinoma (CCA) occurs most often in the vagina, uterine cervix, endometrium, and ovary. In the urinary system, it has been rarely reported in the lower urinary tract with a female predominance. CCA arising in the upper urinary tract including renal pelvis and ureter is extremely rare and only few cases are reported. This is the first reported case in Korea. The association of renal stone with various kinds of carcinomas, such as squamous cell carcinoma, renal cell carcinoma and CCA has been known but it is rarely reported. Here we present a case of CCA arising from renal pelvis occurring in a 76-year-old male patient. He admitted for gross hematuria during the last month, and previously diagnosed as chronic kidney disease with renal stones for 6 years. Imaging study demonstrated two staghorn calculi in the left kidney. Surgical specimens showed hydronephrosis with irregularly shaped impacted stones in renal pelvis and calyces. There was a 2.3 cm-sized exophytic mass located in the renal pelvis. It showed tubulo-papillary growth pattern and consisted of cells having eosinophilic or clear cytoplasm with hobnail features, consistent with characteristic features of CCA. The tumor cells were positive for cytokeratin (CK)-7, CK-903, monoclonal carcinoembryonic antigen, alpha-methylacyl-CoA racemase, and Ki-67, but negative for CK-20, CD10, and PAX-2. The patient has been well with no signs of recurrence or metastasis during a year after surgery. It is important to meticulously evaluate the kidney with long-standing impacted stones. Because coexisting carcinomas can be developed.

**Key Words:** Adenocarcinoma, clear cell; Kidney pelvis; Kidney calculi

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**Ossifying Renal Tumor of Infancy: A Case Report**

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Ossifying renal tumor of infancy (ORTI) is a very rare benign pediatric renal neoplasm with few cases having been published. ORTI is diagnosed in the first 2 years of life, predominantly boys. ORTI is usually presented with painless gross hematuria, as it involves and protrudes into pelvocalyceal system. Histologically ORTI is partially calcified solid tumor with 3 major components—an osteoid core, osteoblast—likes cells, and spindle cells. The histogenesis of ORTI remains unclear. We report a case of ORTI occurring Korean infant. A one-month-old infant was admitted to hospital for the intermittent gross hematuria, which started 2 weeks after his normal birth. Abdominal computed tomography scan showed a well-defined heterogeneous partially calcified soft-tissue mass at mid portion of left kidney which extended into pelvocalyceal system. Left total nephrectomy was done. The kidney revealed a well-defined, roughly ovoid, yellow-tan, soft, solid mass, measuring 2.5×2×1.8 cm in size. The mass showed partially gray white hard areas. Microscopically, the tumor basically consisted of fairly uniform small primitive mesenchymal cell-like cells with round to oval vesicular nuclei, which had indistinct nucleoli, and of scant, ill-defined cytoplasm. Frequent mitosis is noted. These neoplastic cells proliferated in a solid dense sheet with no epithelial differentiation. There were entrapped dilated collecting ducts. Multiple osteoid islands were noted with scattered larger polygonal osteoblast-like cells with light amply cytoplasm. Dystrophic calcification was present focally. The patient’s postoperative course was excellent. He has had neither recurrence nor metastasis and is presently doing well for more than 16 years.

**Key Words:** Kidney; Neoplasms; Infancy; Ossifying; Benign
Primary Sjögren syndrome (PSS) is a progressive autoimmune disease involving exocrine glands. Renal involvement in PSS is well known but membranous glomerulonephritis (MGN) occurs very rarely as a complication. Herein, we report two cases of PSS-associated MGN. To our best knowledge, there are about 20 reported cases worldwide, and this is the first case in Korea. A 59-year-old woman was admitted to the hospital with generalized edema. She was diagnosed as PSS 8 years ago confirmed with positive reactions in anti SS-A/Ro, anti SS-B/La, and antinuclear antibody 1:1,200. Nephrotic syndrome was found and renal biopsy was performed. Microscopic findings were consistent with MGN, stage 2 showing 5.5% glomerulosclerosis, immunoreactivity for IgG, IgM, C3, C1q, light chains, and diffuse subepithelial deposits. A 56-year-old woman was admitted to the hospital with aggravating generalized edema and foamy urine occurred 3 months ago. Serologic tests for autoantibodies showed positive reactions in anti SS-A/Ro, anti SS-B/La, and anti PR3, but she didn’t have obvious sicca syndrome. Subsequently performed sialogram revealed markedly reduced uptake of bilateral submandibular glands, and Schirmer’s test was also positive. Nephrotic syndrome was diagnosed and renal biopsy was performed. Microscopic findings were consistent with MGN, stage 2 with immunoreactivity for IgG, IgM, C3, and diffuse subepithelial deposits. PSS may be underestimated as a cause of MGN, and it should be considered even in the absence of obvious sicca syndrome.

Key Words: Sjögren syndrome; Glomerulonephritis, membranous; Nephrotic syndrome

A Case of Heterochronic Renal Cell Carcinoma and the Metastatic Liver Tumor with Distinctive Phenotypes

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We report a case of heterochronic renal cell carcinoma (RCC) with unusual morphologies and the metastasis to the liver. A 73-year-old Japanese male was referred to our hospital for the treatment of RCC in the right kidney. He had undergone left nephrectomy when he was 59 years old. The main lesion was composed of solid carcinoma that resembled chromophobe RCC in morphology. However, these tumor cells were negatively stained for CD117 and E-cadherin, and positively stained for cytokeratin (CK) 7 and CK34 beta E12. In addition, there was another lesion separately localized in the resected kidney. The lesion was composed of cystic RCC with different immunoprofiles from those of solid tumor. Five years later, when he was 64 years old, a tumor was found in the left lobe of the liver. The morphology of resected liver tumor was tubulopapillary or restiform, and was denied because the tumor cells were negatively stained for hepatic markers (Hep Par 1, GPC3-MM), and positively stained for genital tract markers (PAX2, PAX8). Eight years after left hepatic lobectomy, a cystic tumor was found in the right kidney. The tumor demonstrated tubulocystic appearance. Immunohistochemical staining revealed that it was immunoreactive for CD117 and negative for CK7, CD10, and E-cadherin. We investigated immunostaining patterns and molecular characteristics, and discuss possible relationships among these heterochronic carcinomas.

Key Words: Carcinoma, renal cell; Metastasis; Immunohistochemistry

Klotho Expression in Clear Cell Renal Cell Carcinoma and Its Prognostic Significance

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Background: Klotho has been known to be an aging-suppressor gene and is expressed predominantly in renal tubules. It is closely related to chronic kidney disease progression by deranged phosphate metabolism. A few studies revealed that Klotho expression was related to favorable behavior of melanoma, breast and lung cancers. Clear cell renal cell carcinoma (CCRCC) is the most common kidney cancer and has been known to originate from renal tubules, which are the source of Klotho. Therefore, we examined Klotho expression in CCRCC and investigated its potential prognostic significance. Methods: One hundred twenty six cases of paraffin embedded tissue and 18 cases of fresh tissue of CCRCC were used. Immunohistochemical stain, polymerase chain reaction and western blot analysis for Klotho were performed, and the results were compared with generally well-established prognostic factors in CCRCC and patients’ survival. Results: Immunohistochemically, Klotho was expressed in the cytoplasm of 107 cases (84.9%) of CCRCCs. Klotho expression was significantly enhanced in cases with a lower Fuhrman nuclear grade, lower pathologic T stage, and lower TNM stage; however it was not significantly associated with patients’ survival. Polymerase chain reaction results revealed lower Klotho gene expression in CCRCC than normal kidney tissue. The results of western blot analysis show an increased expression of Klotho in CCRCC than normal kidney tissue, although there is no difference among the cases of low and high Fuhrman nuclear grades of CCRCC. Conclusions: Higher Klotho expression may be associated with favorable prognostic factors of CCRCC.

Key Words: Klotho protein; Carcinoma, renal cell; Immunohistochemistry; Polymerase chain reaction; Blotting, Western
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ORAI1 Expression in Clear Cell Renal Cell Carcinoma

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Background: It has been known that store operated calcium entry (SOCE) mechanisms has a major role in cell proliferation, adhesion, migration, and apoptosis in several types of human cancers, including breast, prostate, lung, and glioblastoma. ORAI1 protein is a critical molecular component of SOCE. The prognostic role of ORAI1 has not been studied in clear cell renal cell carcinoma. Clear cell renal cell carcinoma (CC-RCC) is the most common and lethal tumor in kidney. This study is aimed to investigate the expression of ORAI1, a critical molecular component of SOCE in CC-RCC and demonstrate its correlation with the clinicopathologic parameters and survival of CC-RCC patients.

Methods: We evaluated ORAI1 expression in 126 formalin fixed paraffin embedded tissue specimens of CC-RCC by immunohistochemistry and 18 fresh frozen tissue of CC-RCC by western blot analysis. The correlation between ORAI1 expression in CC-RCC and clinicopathologic parameters and patients’ survival was analyzed. Results: Immunohistochemical staining for ORAI1 reveals nuclear positivity in 63 cases (50.0%) of CC-RCC. ORAI1 immunohistochemical expression was significantly associated with lower Fuhrman nuclear grade, lower pathologic T stage, and lower TNM stage; however it was not correlated with patients’ survival. ORAI1 expression by western blot was increased in CC-RCC than corresponding normal tissue. Conclusions: Expression of ORAI1 may be associated with favorable prognostic factors in CC-RCC.

Key Words: ORAI-1; Carcinoma, renal cell; Immunohistochemistry; Blotting, Western

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Clear Cell Renal Cell Carcinoma Containing Intratumoral Mature Adipose Tissue

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The presence of adipose tissue within renal tumor has been considered as a useful diagnostic feature not in renal cell carcinoma (RCC) but in angiomylipoma (AML). Intratumoral adipose tissue has been reported in RCC even though it is rare. To our knowledge, there are about 20 reported cases worldwide, and this is the first case in Korea. Here we report a case of clear cell RCC containing intratumoral adipose tissue in a 58-year-old Korean man. A 2.5 cm-sized renal mass was incidentally found in the mid-pole of right kidney during abdominal magnetic resonance imaging scan. It showed inhomogeneous low signal intensity with cystic areas in T2 weighted image. Axial T1-weighted in-phase and opposed-phase gradient echo images showed decrease in signal intensity in the mass when compared each other, indicative of intratumoral fat component. The patient underwent the laparoscopic partial nephrectomy, 5.5 × 4.0 × 1.7 cm, and there was a yellow to brown well-demarcated ovoid mass, 2.4 × 1.6 cm, showing areas of hemorrhage and cystic change. Microscopically, it was a clear cell RCC. Foci of adipose tissue, containing 10-100 mature fat cells, were present throughout the center and periphery of the mass. Fat cells were positive for S100 protein, and negative for human melanoma black-45, Melan-A, and smooth muscle actin. Fat containing renal tumor should be examined thoroughly because it can be mistaken for AML or tumor invasion into the surrounding fat tissues. Awareness of the fact that intratumoral fat can be found in RCC is important to prevent misdiagnosis and potential erroneous staging.

Key Words: Carcinoma, renal cell; Adipose tissue; Kidney