SR-FTIR : A new hope for patients waiting for kidney transplantation

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Urinary stone disease, which is as old as mankind, constitutes a major health problem and is affecting an increasing number of people (1). Calcium oxalate, calcium phosphate, uric acid, ammonium hydrogen urate and magnesium ammonium phosphate are the main components of stones (2). Such chemical diversity explains why modern research on such concretions complete the classical techniques used at the hospital such as Fourier Transform Infrared spectroscopy and optical microscopy with physical techniques. We have already shown the opportunities offered by scanning electron microscopy to complete a diagnostic in the case of a severe genetic disorder namely primary hyperoxaluria (3) or to understand the efficiency of lithotripsy (4).

In this lecture, through different examples, we will show that infrared spectroscopy implanted on a synchrotron radiation centre brings major information regarding either the diagnosis or the understanding of the pathology. More precisely, the case of a patient with a rapid worsening of her renal fonction (serum creatinine above 500 µmol/l) is presented. At the hospital, a kidney biopsy shows extensive tubulo-interstitial fibrosis scattered with multiple small crystals. Von Kossa staining was negative, thus excluding presence of calcium salts in the crystals. On polarized light, the crystal birefringence and morphology suggested a possible 2,8-dihydroxyadenine (2,8-DHA) composition, but they were to small in size to allow morphologic identification at simple microscopic examination. For comparison, typical 2,8-DHA crystals are shown at same magnification. We therefore attempted to determine crystal composition by means of Fourier transform infrared (FTIR) microscopy of 5µm biopsy slides. Unfortunately, crystals were under the physic size limit of the method to allow FTIR identification.

In view of the suspicion of (2,8-DHA) composition, with relevant therapeutic implications, we attempted to identify the crystals in the kidney biopsy sample through the SOLEIL synchrotron-generated infrared beamline (SR-FTIR microscope), which is able to analyse very small cristals (5). Indeed, typical vibrations of 2,8-DHA were identified. Adenine phosphoribosyltransferase (APRT) activity measured in erythrocytes was null, giving unequivocal diagnosis of APRT deficiency. Genotype study identified a homozygote frameshift mutation in the *aprt* gene (c.287_288delCT) predicting a truncated APRT protein (Thr96fsX13) (6). Allopurinol therapy (100mg/d) and hyperhydratation were immediately started. Remarkably, renal function rapidly improved, however without recover of normal values (serum creatinine 253 µmol/l), thus avoiding the need of dialysis. In another patient who benefit a kidney graft, a cytomegalovirus infection required an antiviral therapy based on foscavir administration. Few weeks later, a decrease in kidney function was observed. A biopsy of the transplant revealed the presence of crystals in glomeruli and tubules. A SR-FTIR microscope analysis revealed the crystals were made of foscavir while crystals in the tubules were composed of apatite, which corresponds to a metabolized drug.

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