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Teaching Point
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Maltese cross-like crystals in the urinary sediment of a diabetic patient

Christoph Etter[1], Ruth Russi[1], Giovanni B. Fogazzi[2], Rudolf P. Wüthrich[1] and Andreas L. Serra[1]

[1]Division of Nephrology, University Hospital, Zürich, Switzerland and [2]Divisione di Nefrologia e Dialisi, Ospedale Maggiore, IRCCS, Milano, Italy

Correspondence and offprint requests to: Andreas L. Serra; E-mail: andreas.serra@usz.ch

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Introduction

The urinalysis is an important step in the diagnostic work-up of patients with kidney diseases. The assessment of the urine includes evaluation of its physical characteristics (colour, clarity and volume), the measurement of biochemical parameters using dipstick tests (urine pH, blood, glucose, ketones, bilirubin, urobilinogen and protein) and importantly the evaluation of the sediment by phase contrast microscopy that has filters to polarize light for the identification of lipids and crystals. The results of the urine analysis are greatly influenced by the pre-analysis sample handling. In particular, improper urine collection methods interfere with test accuracy that may prompt clinicians to further unneeded tests or lead to false diagnosis [1].

Case

A 73-year-old diabetic patient with arterial hypertension was referred to our renal outpatient clinic for evaluation of chronic kidney disease (CKD) with increasing proteinuria. He was suffering from an insulin-dependent diabetes mellitus type 2 for 20 years and had known retinopathy, obliterating peripheral arteriopathy and polyneuropathy. The left kidney was removed in 1973 because of hydronephrosis. He was treated with an angiotensin receptor antagonist (irbesartan) and an aldosterone receptor antagonist (spironolactone) as well as with aspirin and pravastatin. His body weight was 107 kg, body mass index was 37 kg/m^2, blood pressure was 150/80 mmHg and physical examination revealed pitting oedema of both legs. The estimated glomerular filtration rate (GFR) was 44 ml/min/1.73 m^2 (MDRD formula) and the urinary albumin-to-creatinine ratio was 0.076 g/mmol corresponding to an albuminuria of ∼0.8 g/day. Other routine blood chemistry parameters were in the normal range, in particular serum albumin and lipid levels. A renal ultrasound showed a large right kidney (interpole distance 14 cm) with the absence of the left kidney. A dipstick analysis of a random spot urine showed ++ albumin, no leucocytes or erythrocytes, and no glucose. Analysis of the urine sediment with phase contrast microscopy showed abundant roundish particles (Figure 1A) with a structure of birefringent 'Maltese crosses' under polarized light (Figure 1B). The impaired kidney function (CKD stage 3) with proteinuria was interpreted on the basis of long-standing diabetes in a patient with a single kidney, whereas the nature of the mysterious particles in the urine sediment remained unexplained.

Resolution of the mystery

Round particles producing birefringent Maltese crosses under polarized light are commonly seen in the urinary sediment of patients with a nephrotic syndrome. The appearance of the Maltese crosses is due to the birefringence of lipid droplets, which consist mainly of cholesterol esters. The arms of the Maltese crosses seen in these patients with gross proteinuria are symmetrical (Figure 2). Notably, our patient had only moderate proteinuria, no clinical signs of a nephrotic syndrome and the arms of the Maltese crosses were asymmetric and irregular. Lipid droplets associated with gross proteinuria are round and translucent without internal structure, whereas the particles in our patient were of roundish to polygonal shape, colourless and had a nucleus-like centre, a pattern which is typical for cornstarch granules. By comparing the microscopic finding of starch dissolved in water and the urinary sediment of our patient, we presumed to a diagnosis of starch particle contamination. However, the source of the contamination remained unknown.

Cornstarch powder, commonly used as 'lubricant' in latex gloves, has already been identified as a source of contamination of urine specimens. Furthermore, starch has

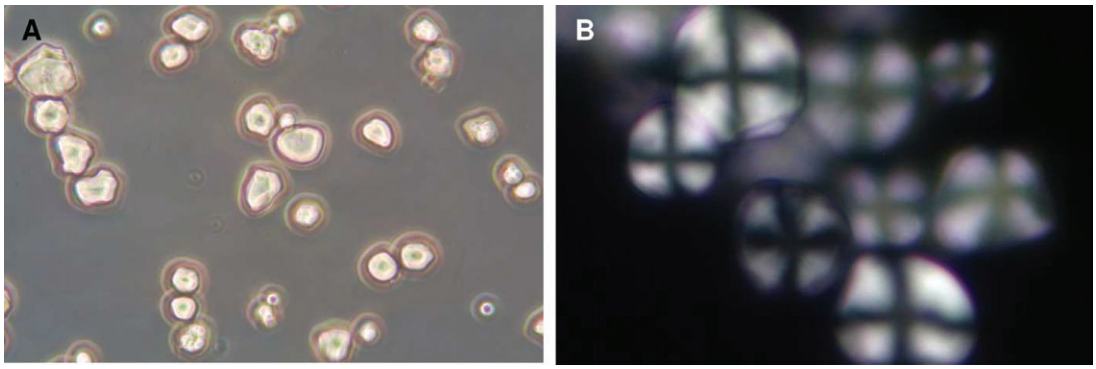

Fig. 1. Examination of urinary sediment by (**A**) phase contrast microscopy showing abundant, roundish and variable-sized particles with a nucleus-like centre (**B**) with a structure of birefringent 'Maltese crosses-like' under polarized light. Original magnification ×400.

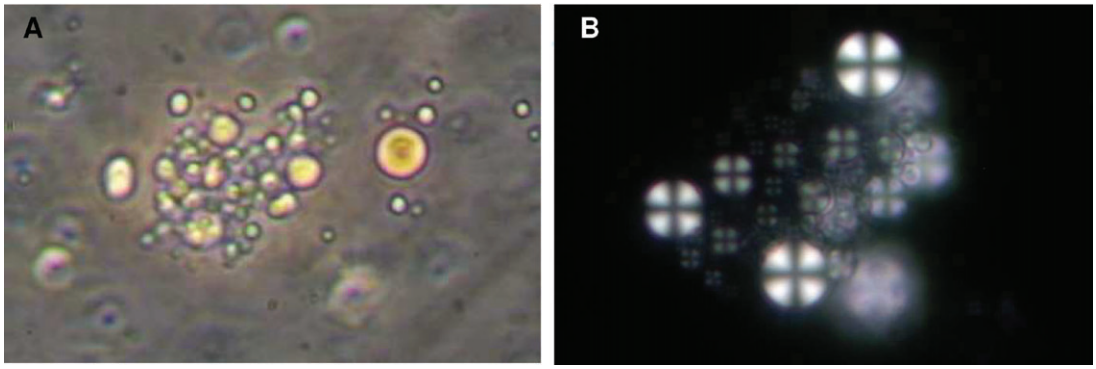

Fig. 2. Urinary sediment analysis of patient with a nephrotic syndrome by (**A**) phase contrast microscopy showing lipid droplets as round translucent particles without internal structures and (**B**) under polarized light, the arms of Maltese crosses are perfectly symmetrical. Original magnification ×400.

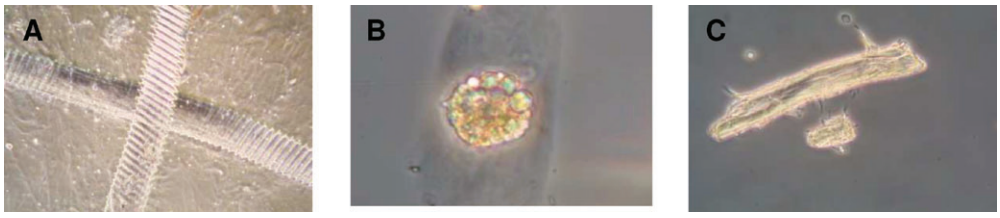

Fig. 3. Contaminants of urinary sediments regularly identified in our laboratory: (**A**) elastic fibre (from underwear), (**B**) globules of fat (from body lotion and creams) and (**C**) piece of toilet paper. Original magnification ×400.

been associated with inhalation lung injury and starch-powdered latex gloves with skin sensitization. Thus, starch powder has therefore been abandoned in many medical centres, including our institution. However, starch continues to be used as carrier in some medical powders. Indeed, our patient admitted to use a disinfectant powder (Merfen® powder) as treatment for his inflamed glans penis. Cornstarch is the principal ingredient of this powder, and after dissolving Merfen® powder in water, we found microscopically the identical particles as seen in the patients' urinary sediment.

Discussion

Our case clearly demonstrates the importance of polarized light, which is mandatory for the correct identification of some lipids, crystals and contaminants. Unfortunately, this simple device is currently used only by a minority of laboratories.

Birefringent Maltese crosses as seen under polarized light represent either lipid particles [2], 2,8-dihydroxyadenine crystals [3] (in patients with the rare congenital adenine phosphoribosyltransferase deficiency) or starch [4]. However, they differ under phase contrast microscopy, and the arms of the Maltese cross in starch are irregular and asymmetric compared to the other two forms (Table 1). Different particles can contaminate the urine, and in most instances the patient is the cause of the contamination. In our laboratory, we regularly identify obvious contaminants such as hair, pieces of toilet paper, elastic fibres (from underwear) or globules of fat (resulting from use of body lotions or creams) (Figure 3). Rarely the laboratory itself is the source of contamination. For

Table 1. Particles producing Maltese cross and Maltese cross-like birefringence in the urinary sediment and their findings under phase contrast microscopy and polarizing light

	Lipid droplets	2,8-di-hydroxyadenine-crystals	Starch
Phase contrast microscopy			
Colour	Translucent	Reddish-brown	Colourless
Form	Round	Round	Round to polygonal
Internal structure	None	Central spicules	Nucleus-like centre
Filter for polarized light			
Arms of Maltese cross	Symmetrical	Symmetrical	Asymmetric, Irregular

example, occasionally a sunflower that is close to the microscope in a urine laboratory may release seeds that can contaminate urine specimens and may then be mistaken for strange microbes. Fortunately, this is quite rare.

Teaching point

- Use correct methods for urine collection and pre-analysis sample handling.
- Have the capability to identify the most important particles in the urinary sediment.
- The use of polarized light is of key importance for the identification of selected particles.
- Use phase contrast microscopy equipped with polarizing filters.
- Interpret urinary sediment findings on the background of the clinical context.

Conflict of interest statement. None declared.

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