HL Tang 鄧漢樂
KH Chu 朱國康
YF Mak 麥婉芬
W Lee 李威廉
A Cheuk 卓　鷗
KF Yim 嚴嘉輝
KS Fung 馮加信
HWH Chan 陳慧嫻
KL Tong 唐國隆

Minimal change disease following exposure to mercury-containing skin lightening cream

因接觸含水銀的美白霜引致微小病變腎病

A 34-year-old woman developed nephrotic syndrome after using a skin lightening cream that contained an extremely high level of mercury. Blood and urine mercury levels were elevated and a renal biopsy revealed minimal change disease. Membranous nephropathy was excluded using immunofluorescence and electron microscopy. Her proteinuria remitted 9 months after she stopped using the cosmetic cream. This is the first reported case in the English literature of proven minimal change disease secondary to mercury exposure. It is important that mercury poisoning due to cosmetic cream is considered in the differential diagnoses for any woman who presents with nephrotic syndrome.

一名34歲女性在使用一種含有極高量水銀的美白霜後，出現腎病綜合症。血液和尿液水銀含量急升，腎活組織檢驗顯示病人患上微小病變腎病，而螢光染色體檢查和電子顯微鏡檢驗排除了膜性腎病變的可能。在停止使用有關美白霜後9個月，病人蛋白尿水平回復正常。這是英文文獻上首宗被證實因接觸過量水銀而患上微小病變腎病的病例。對任何出現腎病綜合症女性，在診斷時須考慮因化妝品引致中毒的可能性。

Key words:
Cosmetics;
Glomerulonephritis;
Mercury;
Nephrotic syndrome;
Skin/drug effects

關鍵詞：
化妝品；
腎小球腎炎；
水銀；
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Princess Margaret Hospital, Laichikok, Hong Kong:
Division of Nephrology, Department of Medicine and Geriatrics
HL Tang, MRCP, FHKAM (Medicine)
KH Chu, MRCP, FHKAM (Medicine)
W Lee, MRCP, FHKAM (Medicine)
A Cheuk, MRCP, FHKAM (Medicine)
KF Yim, MRCP
KS Fung, FRCP, FHKAM (Medicine)
HWH Chan, FRCP, FHKAM (Medicine)
KL Tong, FRCP, FHKAM (Medicine)
Department of Pathology
YF Mak, FRCPA, FHKAM (Pathology)

Correspondence to: Dr HL Tang
(e-mail: tanghl@ha.org.hk)

Introduction

Mercury is a silvery liquid that is volatile at room temperature because of its high vapour pressure and able to enter the human body via ingestion, inhalation, and absorption through the skin. Chronic mercury poisoning commonly affects the kidneys and the central nervous system. Involvement of the kidneys usually causes nephrotic syndrome. As early as 1818, mercury was identified as a cause of proteinuria in humans.[1] The renal pathology seen in most cases of mercury-induced nephrotic syndrome is membranous nephropathy.[1-6] In the past, mercurial diuretics and mercury-containing ointments prescribed for psoriasis were the main sources of exposure.[2,7,8] Skin lightening creams that contain mercury are a more recent source of mercury poisoning.[3,4,6,9] We report the first proven case of minimal change disease caused by exposure to mercury-containing skin lightening cream.

Case report

In November 2002, a 34-year-old Chinese woman was admitted to Princess Margaret Hospital with a 1-month history of bilateral ankle swelling. She had no history of renal disease, hypertension, or diabetes mellitus. Physical examination revealed bilateral pitting ankle oedema up to the knee. Her facial skin was particularly light-coloured. Examination of the abdomen, cardiovascular, respiratory and central nervous systems revealed no abnormalities. Laboratory investigations showed: sodium, 137 mmol/L; potassium, 3.5 mmol/L; urea, 3.9 mmol/L; creatinine, 52 μmol/L; albumin, 15 g/L; globulin, 35 mmol/L; liver enzymes, normal range; random blood glucose, normal range; haemoglobin, white blood cells and platelets, normal range; an increased total cholesterol, 10.4 mmol/L, and triglycerides, 5.88 mmol/L. Her 24-hour urine protein excretion was 8.35 g and creatinine clearance 114 mL/min. Urine microscopy revealed no red blood cells or casts. Investigations for a cause of her nephrotic

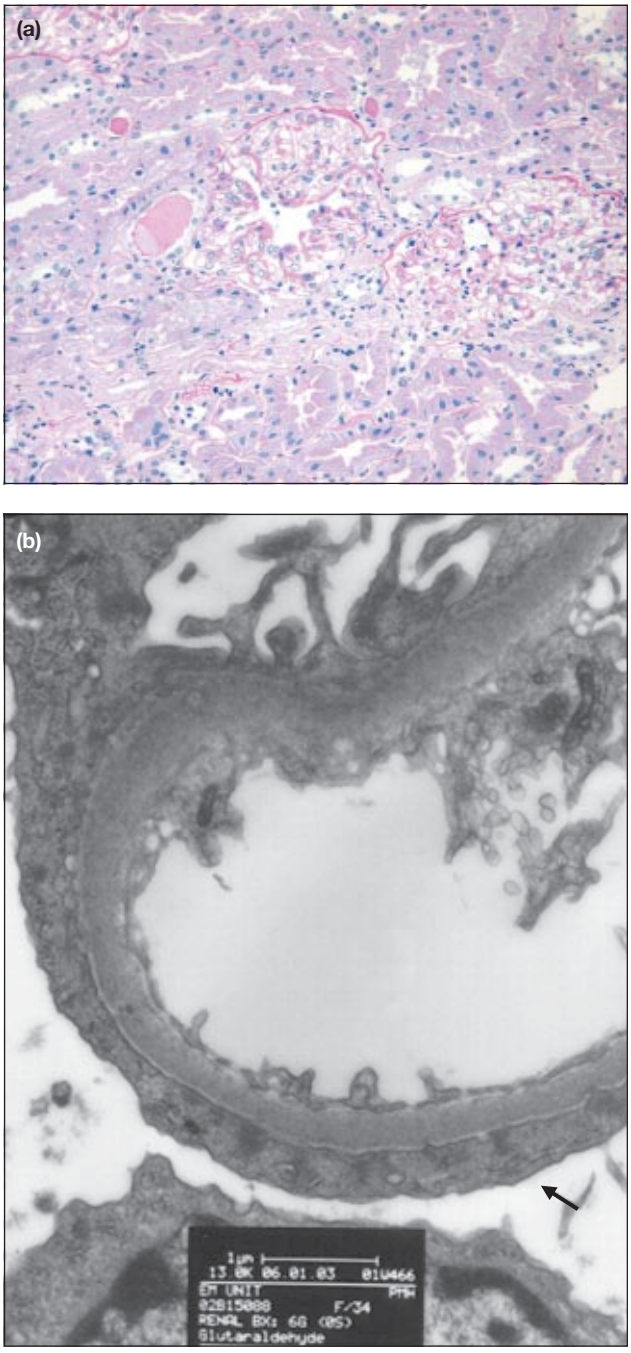

Fig 1. (a) Light microscopy with periodic acid-Schiff stain: glomeruli show no proliferation or spike formation. (b) Electron microscopy: podocyte shows fusion of the foot processes (arrow)

syndrome were negative: anti-nuclear antibody titre, 1/80; anti-dsDNA, negative; anti-neutrophil cytoplasmic antibody, negative; and C3, 1.28 g/L (normal). A review of her history revealed that she was a beautician who had been applying a skin lightening facial cream purchased from Mainland China once daily for the past 4 months. In view of this history, her blood mercury level was checked and found to be elevated, 124 nmol/L (reference level, <50 nmol/L), as was her urine mercury (287 nmol/L, reference level, <50 nmol/L). A renal biopsy was performed and light microscopy revealed 41 glomeruli with no significant proliferation or spike formation (Fig 1a). Immunofluorescence microscopy revealed only scanty granular deposits of immunoglobulin M and C3 in the mesangium. No immune deposits were found in the capillary loops. On electron microscopy, the podocytes showed moderate fusion of the foot processes (Fig 1b) and microvilli formation. No electron dense deposits were detected in the capillary loops and mesangium. Minimal change disease was diagnosed.

The cosmetic cream was found to contain mercury levels of 30 000 parts per million (reference level, <1 part per million). The patient was advised to stop using the cream and chelation therapy with D-penicillamine was given for 10 days. Her proteinuria gradually returned to a normal level of less than 0.01 g per day over a period of 9 months (Fig 2). Blood and urine mercury levels also decreased with time and this reduction coincided with the decrease in proteinuria (Fig 2). Her blood and urine mercury levels returned to normal 1 month and 9 months respectively after cessation of facial cream usage. No steroid therapy was prescribed and the patient had no history of taking any drugs such as non-steroidal anti-inflammatory drugs before presentation.

Discussion

The pathological diagnosis of minimal change disease in our patient was confirmed by light microscopy, immunofluorescence, and electron microscopy findings. Membranous nephropathy was excluded by the absence of immune deposits in the capillary loops on immunofluorescence microscopy and the absence of subepithelial electron dense deposits on electron microscopy. No steroid therapy or other immunosuppressive agents were prescribed to treat her nephrotic syndrome. Resolution of proteinuria coincided with normalisation of blood and urine mercury levels. Of Chinese patients with minimal change disease, in the 18 to 50 age-group, only around 5% will achieve spontaneous remission.[10] This led us to conclude that mercury poisoning was the cause of minimal change disease in our patient.

There have been a few reports of minimal change lesions in renal histology following exposure to mercury.[7,9,11] In one report, 50% of young African women in Kenya who used mercury-containing skin lightening creams developed 'minimal change' glomerular lesions.[9] In other patients, minimal glomerular structural lesions have developed after use of mercurial diuretics and occupational contact with mercury.[7,11] Neither immunofluorescence nor electron microscopy were performed in any of these series so the diagnosis of membranous nephropathy could have been missed. Our patient is the first reported case in the English literature of proven minimal change disease secondary to mercury poisoning.

It has been suggested that when nephrotic syndrome

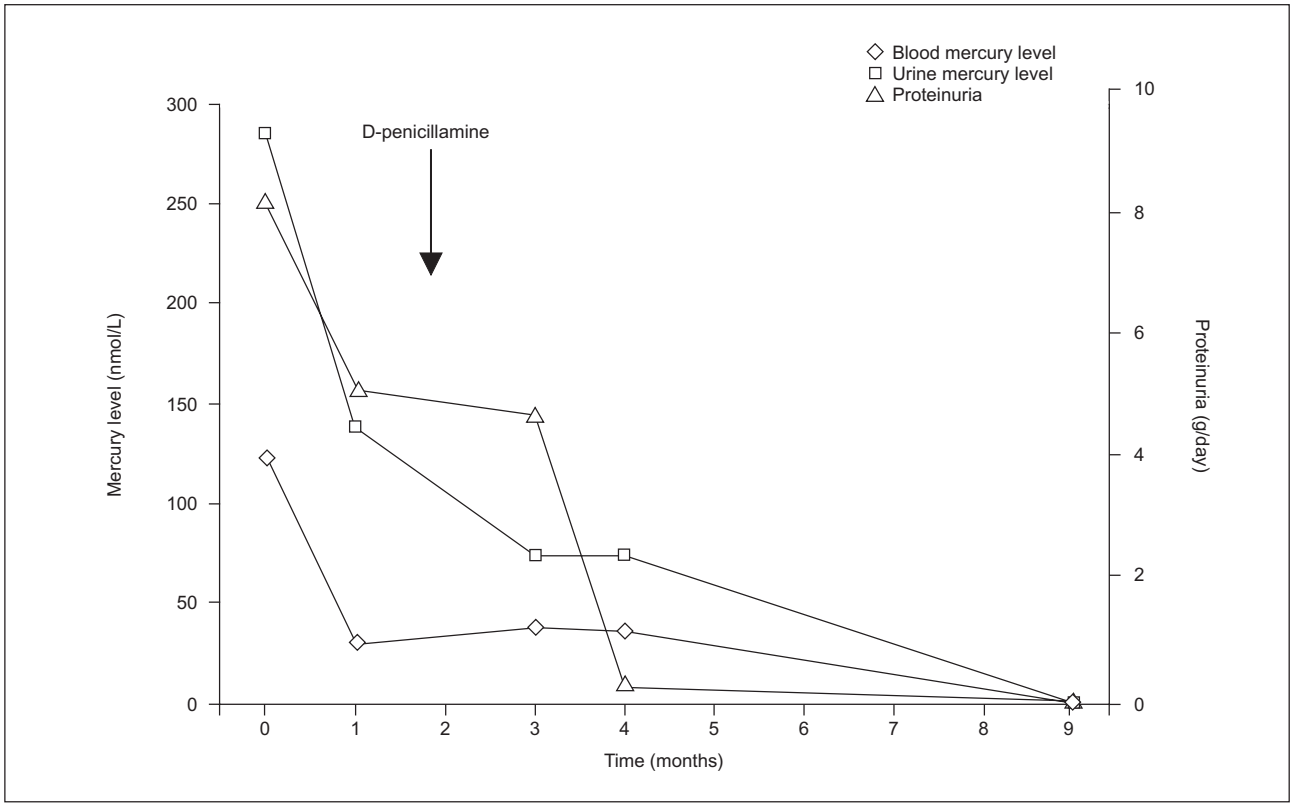

Fig 2. The patient's proteinuria, blood, and urine mercury levels
The reduction of proteinuria coincided with the decrease in blood and urine mercury levels

develops following mercury exposure, it is due to idiosyncratic reactions[11] or an abnormal immune response to the heavy metal.[1] The mechanism by which mercury caused minimal change disease was not evident in our patient. Further case studies of the pathogenesis of minimal change disease following exposure to this heavy metal are needed. More importantly, mercury poisoning due to cosmetic creams should be considered one of the differential diagnoses in any woman, irrespective of age, who presents with proteinuria or nephrotic syndrome, as it has been shown by Sin and Tsang[12] that the age range of people using cosmetic creams is very wide: 15 to 76 years.

References

1. Cameron JS, Trounce JR. Membranous glomerulonephritis and the nephrotic syndrome appearing during mersalyl therapy. Guys Hosp Rep 1965;114:101-7.
2. Becker CG, Becker EL, Maher JF, Schreiner GE. Nephrotic syndrome after contact with mercury. A report of five cases, three after the use of ammoniated mercury ointment. Arch Intern Med 1962;110:178-86.
3. Kibukamusoke JW, Davies DR, Hutt MS. Membranous nephropathy due to skin-lightening cream. Br Med J 1974;2:646-7.
4. Oliveira DB, Foster G, Savill J, Syme PD, Taylor A. Membranous nephropathy caused by mercury-containing skin lightening cream. Postgrad Med J 1987;63:303-4.
5. Aymaz S, Gross O, Krakamp B, Ortmann M, Dienes HP, Weber M. Membranous nephropathy from exposure to mercury in the fluorescent-tube-recycling industry. Nephrol Dial Transplant 2001;16:2253-5.
6. Soo YO, Chow KM, Lam CW, et al. A whitened face woman with nephrotic syndrome. Am J Kidney Dis 2003;41:250-3.
7. Munck O, Nissen NI. Development of nephrotic syndrome during treatment with mercurial diuretics. Acta Med Scand 1956;153:307-13.
8. Burston J, Darmady EM, Stranack F. Nephrosis due to mercurial diuretics. Br Med J 1958;14:1277-9.
9. Barr RD, Rees PH, Cordy PE, Kungu A, Woodger BA, Cameron HM. Nephrotic syndrome in adult Africans in Nairobi. Br Med J 1972;2:131-4.
10. Tse KC, Lam MF, Yip PS, et al. Idiopathic minimal change nephrotic syndrome in older adults: steroid responsiveness and pattern of relapses. Nephrol Dial Transplant 2003;18:1316-20.
11. Kazantzis G, Schiller KF, Asscher AW, Drew RG. Albuminuria and the nephrotic syndrome following exposure to mercury and its compounds. Q J Med 1962;31:403-18.
12. Sin KW, Tsang HF. Large-scale mercury exposure due to a cream cosmetic: community-wide case series. Hong Kong Med J 2003;9:329-34.