

CASE REPORT

Visceral Aluminum Deposition In Chronic Renal Insufficiency

(Light Microscopy and X-ray Microanalysis)

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Aluminum is a common element in our environment, but has been proved to be toxic, mainly in chronic renal insufficiency. Most cases of ALU intoxication occur during hemodialysis due to treatment of aluminum-containing drugs. In the present case, we describe visceral manifestations of aluminum deposition in a middle aged, multidialysed, male patient. Light and polarization micro-

copy examinations and X-ray microanalysis revealed amorph, extracellular aluminum deposits in various parenchymal organs causing failure of heart, lung and kidney functions. There were no anamnestic data concerning aluminum-containing drugs or occupational exposure. (Pathology Oncology Research Vol 2, No1-2, 94-97, 1996)

Key words: aluminum, renal insufficiency, myocardium, lung, kidney

Introduction

Aluminum (ALU) is the third most abundant element in the earth crust and it is widely diffused. However, until the early 1970s, the biological interest in ALU was due to iatrogeny and its toxic effects were limited to industrial exposure of ALU dust.⁵ ALU accumulation plays an important role in the pathogenesis of encephalopathy (dialysis dementia characterized by speech disorders, myoclonic jerks and EEG disorders), microcytic anemia, osteomalacia/osteodystrophy, extraskeletal calcification and other severe disorders in the uremic patients undergoing long term hemodialysis treatment.^{1,5,14} ALU is readily transferred from the dialysate to the patient's bloodstream during hemodialysis.¹² Recent studies have emphasized the potential neurotoxicity of ALU in dialysis encephalopathy and it has also been suggested that it may have a role in the pathogenesis of Alzheimer's disease.¹⁰

ALU also has an effect on red blood cells and chromosomes; can depress parathormone secretion either indirectly, through elevated plasma calcium, or directly by an effect on hormone release.¹¹ The heart and lymphocytes are probably damaged by ALU overload.⁶ Accumulation

of ALU in the organs occurs when the gastrointestinal tract is bypassed, therefore it could be a serious problem during haemodialysis or parenteral feeding. Many sources have been recognized to be contaminated with ALU. These include the water used for dialysis, ALU containing medicines such as oral phosphate binding agents, parenteral nutrition solutions, processed human serum albumin, intravenous fluids in infants and environmental and industrial sources.^{1,7,8} In 1991, a dialysis center in Pennsylvania identified an epidemic of ALU intoxication caused by the use of an electric pump with an ALU housing to deliver acid concentrate used in bicarbonate dialysis.⁴ Interestingly, osteal or cerebral accumulation of ALU was reported before but none of those reports mentioned visceral accumulations. However, rare cases of occupational pulmonary fibrosis have been reported where the role of ALU was suspected.¹³

We report the case of a multidialysed man with toxic ALU deposition in the myocardium, lung and kidney. The deposits were analyzed by light and polarized microscopy and verified by electron probe X-ray microanalysis.

Materials and Methods

Light microscopy

Tissue samples were routinely fixed in formaldehyde, and embedded in paraffin. Sections were stained with haematoxylin eosin (HE) and silver to detect CaCO₃.

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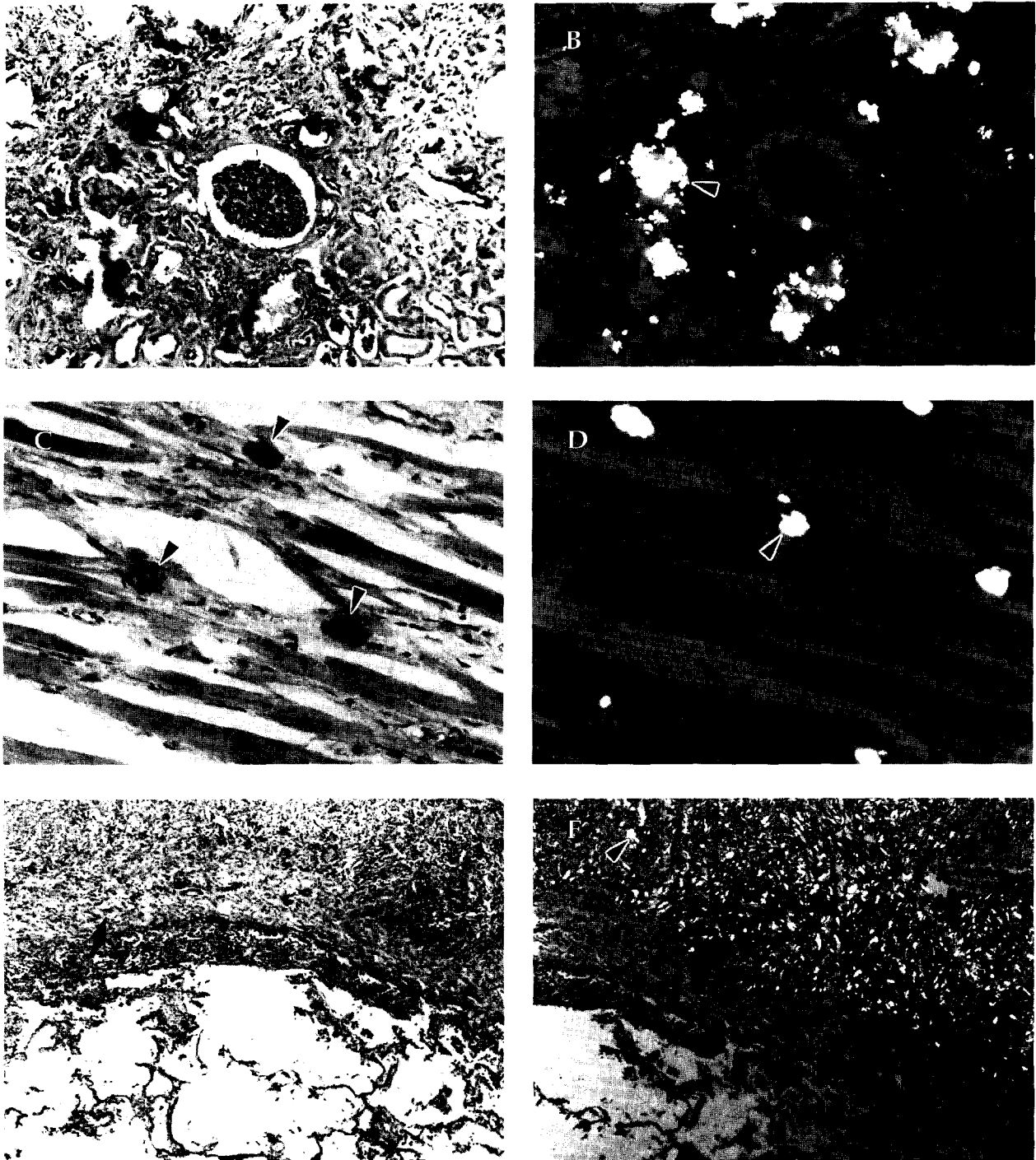


Figure 1. Aluminum containing deposits. (HE staining). Amorphous material is surrounded by fibrotic tissue and lymphocytes in the kidney (a); deposits in the myocardium, surrounded by connective tissue (c); deposit is surrounded by fibrosis in the lung (e). Polarization microscopy of ALU containing deposits. Anisotropic deposits in the kidney (b); in the myocardium (d) and in the lung (f).

X-ray microanalytical techniques

Thick paraffin sections were dewaxed by xylene and embedded in Epon 812. Ultrathin sections were mounted on copper grids, and examined without counterstaining.

Microanalysis was performed using a JEM 100C electron microscope, attached to an ORTEC 6230 energy disperse X-ray microanalyser, in STEM mode at 80 KV where specimen angle was 30° and collection time was 100 sec.

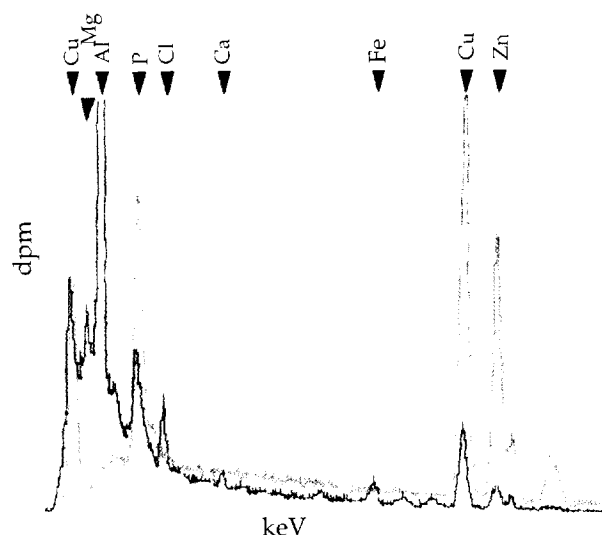


Figure 2. X-ray microanalysis of the amorphous, anisotropic material in STEM mode. (U 80 kV; $\alpha = 30^\circ$ and $T = 100$ sec). Note the presence of Cu, P and Zn from the copper grid (control = black line). The x-ray microanalysis of the tissue samples detected Al, Mg and Cl (red line).

Case Report

The 66 year old male patient had a thyroidectomy due to multiplex nodular struma and nephrolithiasis some time ago (stone analysis was not performed). In 1994, the patient was admitted to the hospital due to polydipsia and weight loss. *Physical examination* revealed cachexia, generalized edema, pale mucus membranes, organic psychosyndrome and grade III cardiac failure. *Laboratory tests* proved azotemia with markedly elevated serum creatinin and blood urea nitrogen; as well as markedly elevated TSH level corresponding to severe primary hypothyreosis. The iron level in the serum was low but total and ionized se-Ca, se-P, se-Na, se-uric acid, transaminase and protein levels were within the normal range. Myocardium-specific enzyme activities were also normal. *ECG* showed low voltage, left bundle branch block. *Echocardiography* detected dilated ventricles and atria and an akinetic septum, left ventricular anterior wall and apex. There was also restrictive functional defect. These findings corresponded to a severe dilatative cardiomyopathy. Blood pressure was in the range of 115/70-85/60 Hgmm. *Ultrasonography* revealed several stones in the renal pelvis of both kidneys and increased echogenicity of the renal parenchyma. *EEG* showed diffuse activity. *Brain CT* revealed atrophy and a hypodense area in the region of the right arteria media cerebri.

Regular hemodialysis was started on a 3x4 hours weekly schedule and the patient remained on hemodialysis during the following 5 months. The parameters of the dialysis were: blood flow: 200 ml/min, acetate buffer, 2 mM K and 1.75 mM Ca, polysulfon dialyser. Repeated pleurocentesis was performed due to a left side hydrothorax. A pleuro-

desis was done to prevent the recurrence of the hydrothorax. The *drugs* which were given regularly contained no ALU. The patient died due to ventricular arrhythmia five month after his first admission.

The *autopsy* revealed enlarged heart (weight 600 gr) with dilated chambers, without signs of myocardial infarction. Kidneys showed atrophy, nephrosclerosis and contained several small and one coral stone. The lung was edematous, with several small fibrotic granulomas. Other organs suffered mainly from the consequences of generalized atherosclerosis. *Light microscopic* examination of the kidney showed chronic pyelonephritis. Additionally, amorphous, crystallized foreign material was deposited in the glomerular wall, along the tubular structures and in the interstitium (Fig. 1 a). All the deposits were surrounded by histiocytes and few lymphocytes. In the myocardium, fibrosis and foreign material deposits were found in and between the myofibrils (Fig. 1 c). The lung exhibited edema, emphysema and large, extracellular foreign body deposits (Fig. 1 e). *Polarization microscopy* showed bright, anisotropic, amorphous deposits in all lesions (Fig. 1 b, d, f).

For X-ray microanalysis, sections were re-embedded from paraffin into Epon. Ultrathin sections were placed onto copper grids. Control analysis indicated the predominant presence of Cu and trace elements of the grid material. X-ray analysis of the patients samples proved that the deposited material in the lung had Al, Cl and trace amount of Mg suggesting the presence of $AlCl_3$ (Fig. 2).

Discussion

The potential source of ALU in our case is hemodialysis, but we can not rule out the role of ALU containing cooking utensils or foils which may increase the ALU content of food.³ Results from many studies suggest monitoring serum ALU level in patients with renal insufficiency.⁹ In order to prevent an accumulation of ALU when performing dialysis, it has to be used dialysates poor in ALU or to avoid phosphate binders containing ALU. They may be replaced by other phosphate binders, such as calcium carbonate or calcium acetate and with a diet poor in phosphates.¹⁵

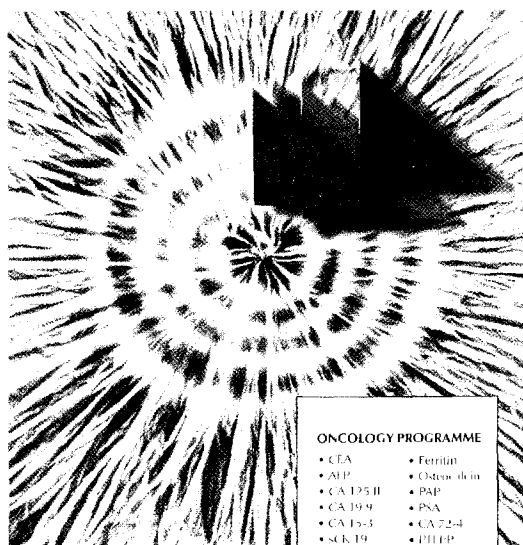
This case raises the possibility that chronic exposure to aluminum may be more common than thought previously. Furthermore, our case is unique, since it is the first report of *visceral* deposition of ALU in man.

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TUMOUR MARKERS



ONCOLOGY PROGRAMME

- CEA
- AFP
- CA 125 II
- CA 19-9
- CA 15-3
- S-CB 19
- HCG
- Calcitonin
- Ferritin
- Osteocalcin
- PAP
- PSA
- CA 72-4
- PHLIP
- T-IG

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