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Togavirus-Like Particles in Renal Epithelium of Patients With Systemic Lupus Erythematosus

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Summary. Virus-like particles, about 45 nm in diameter, were present in renal epithelium (tubules and podocytes) of 12 patients with confirmed systemic lupus erythematosus (SLE) and in 2 patients with probable SLE. They were not detected in renal biopsies from non-SLE patients. Morphologically, they suggest togavirus-like particles.

Key words: Systemic lupus erythematosus – Renal epithelium – Togavirus-like particles.

Introduction

An autoimmune mechanism is involved in the pathogenesis of systemic lupus erythematosus (SLE) but the precise cause remains unknown. Chronic viral infection appears to be the most likely possibility (see Christian and Phillips, 1973). An endogenous murine type C virus is involved in the pathogenesis of New Zealand black mouse disease, which ressembles human SLE (Yoshiki et al., 1976) and the expression of type C virus antigen appears enhanced in SLE patients (Lewis et al., 1974; Strand and August, 1974; Mellors and Mellors, 1976; Ordonez et al., 1977). However, this could apply to other virus antigens; for exemple, SLE might be connected with measles virus or a related paramyxovirus infection (Lucas et al., 1972; Alekberova et al., 1975). Tubulo-reticular or glomiform inclusions considered to be paramyxovirus-like formations (Györkey et al., 1969) have been reported in various cell-types (mainly in endothelial cells) in SLE patients. These inclusions, derived from the rough endoplasmic reticulum, are not specific to SLE (Pincus et al., 1970) and their signification is as yet undetermined (see Hruban et al., 1976). C-virus-like particles have also been reported in placentas from patients with SLE (Imamura et al., 1976). Another type of virus-like particle of about 45 nm in diameter has been observed in renal epithelium from 2 SLE patients presenting with a glomerulo-nephrotic

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syndrome (Fonck-Cussac et al., 1972). Our electron microscopic searches for such particles in renal biopsies showed that they were invariably present in renal epithelium from 12 confimred cases of SLE and from 2 patients with probable SLE.

Material and Methods

The diagnosis of SLE was made according to the criteria of Dubois (1974). All the patients (10 women and 4 men) had a more or less marked renal deficiency, with a nephrotic syndrome in 3 cases. Renal biopsies have been studied with conventional techniques under both light and electron microscopes.

Results

The glomerular lesions were polymorphic, as is generally the case in lupus nephritis, and were not correlated with the gravity of the clinical condition. Glomiform inclusions in endothelial cells were sometimes observed. Intra-epithelial virus-like particles were detected in all cases.

Spherical and enveloped particles, about 45 nm in diameter (with 25–30 nm cores), were found in podocytes and cells of the tubules without any preference for a particular segment. They were either enclosed in relatively large clear vacuoles or concentrated within tubular or vesicular formations in areas generally surrounded by a membrane (Fig. 1). The vacuoles usually contained scattered particles, often against their walls, intermingled with tubules and vesicles (Figs. 1, 3, 4, 7) and often contained myeloid bodies (Fig. 1). Enveloped particles were frequently seen budding from vacuolar walls (Fig. 7). Budding of particles were rare at the epithelial cell surface. Cylinders consisting of finely fibrillar material with little cell débris, were always associated with abundant extracellular virus-like particles (Figs. 2, 4–6). In several cases, intact particles were found in urinary residues.

Systematic searches on numerous thin sections were usually necessary to detect these particles in the kidney. This may explain why they have not been reported in earlier ultrastructural observations on kidney biopsies from SLE patients.

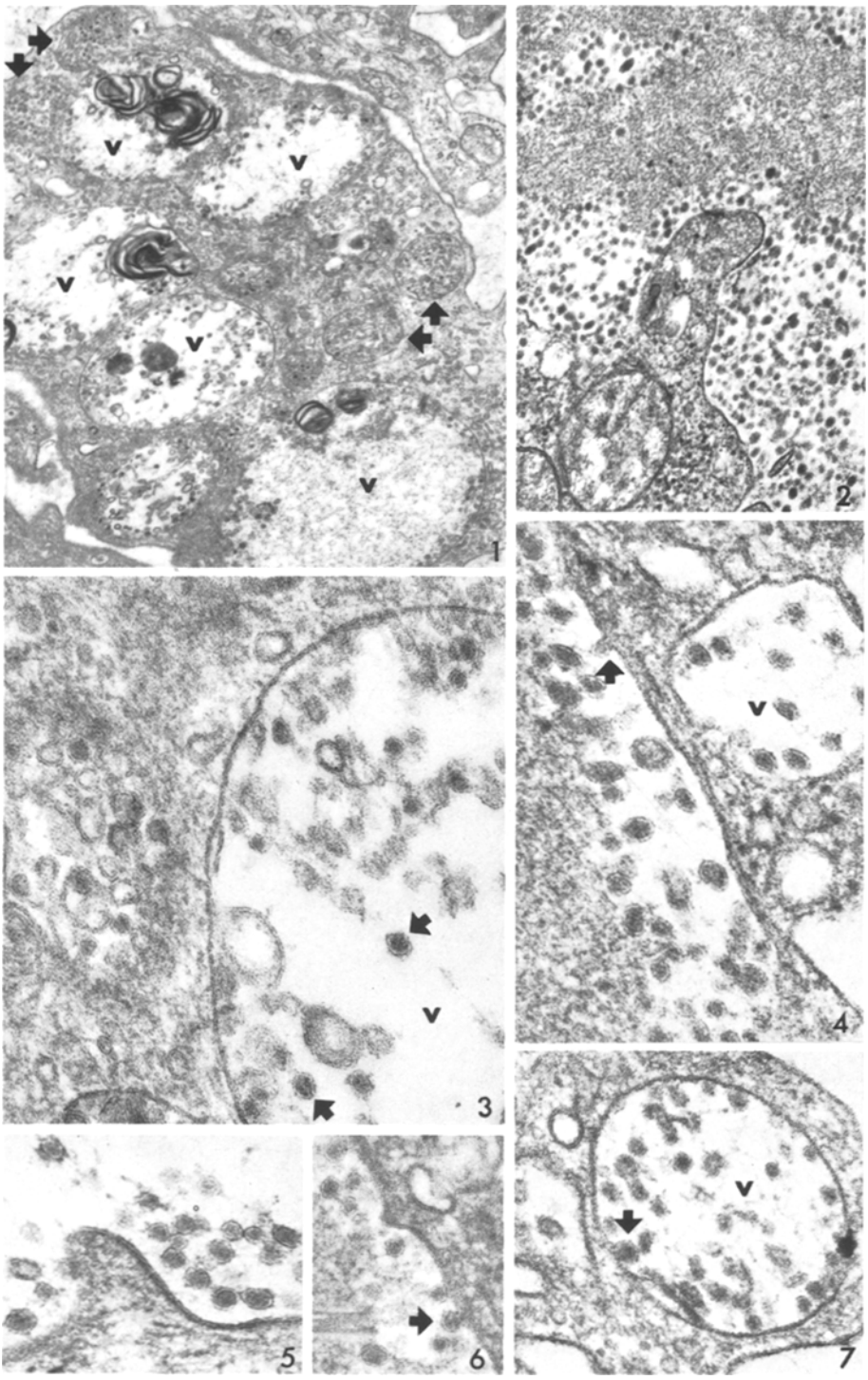
Fig. 1. Podocyte with numerous vacuoles (*V*) containing dispersed particles and vesicles, and numerous clusters of particles and vesicles surrounded by a membrane *(arrows)*. Note intravacuolar myelinic bodies. × 15,000

Fig. 2. Extracellular particles in a tubular lumen. × 34,000

Fig. 3. Podocyte (detail of Fig. 1). Enveloped particles *(arrows)* in a vacuole. × 83,000

Figs. 4–6. Enveloped particles in tubular lumen. Note probable budding of particles at the cellular surface *(arrows)* and intravacuolar enveloped particles in an epithelial cell *(V)*. 4 × 86,000; 5 × 90,000; 6 × 65,000

Fig. 7. Podocyte with intravacuolar enveloped particles in close contact with vacuole *(V)* membrane. Arrow shows probable budding of particle. × 55,000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Discussion

The intraepithelial particles observed in our SLE cases bear no morphological relationships to C virus-like particles or paramyxovirus-like formations. Their diameter (45 nm) and their relation with membranes suggest viral particles of the togavirus family (see Higashi, 1973). Confirmation both of the viral nature and the pathogenic role of these virus-like particles obviously requires more specific techniques, but we emphasize that we have not found evidence of such particles in the kidney of patients with diseases other than SLE. Their association with cylinders should allow their isolation from urinary residues, where intact particles have been found in several cases.

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