Imaging Evidence for Renomegaly in Patients with POEMS Syndrome

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Rationale and Objectives: Organomegaly in POEMS syndrome generally refers to the liver, spleen, and lymph nodes. This study investigates whether there is a significant difference in kidney sizes in patients with POEMS compared to normal controls.

Materials and Methods: Calculated kidney volumes from 77 patients with POEMS syndrome who had undergone imaging by computed tomography or magnetic resonance imaging were compared to frequency-matched controls. For the POEMS patients and the controls, the volume of each kidney was obtained from a three-dimensional segmentation algorithm. Univariate and multiple variable linear regression models were used to identify any differences in kidney size between normal and POEMS patients.

Results: There was a univariate statistically significant association between disease state and the difference in kidney volume; having POEMS was associated with 16.3 cm^3 greater kidney volume difference compared to control patients, $P < .001$. Using a multiple variable model and after adjusting for age, sex, and the smaller kidney size, there was a statistically significant association between disease state and the difference in kidney volume; having POEMS was associated with 16.8 cm^3 greater kidney volume compared to control patients, $P < .001$. There was not an independent statistically significant association between age, sex, or volume of the smaller kidney and the difference in kidney volume.

Conclusion: This confirms what is known or suspected clinically, that organomegaly in POEMS includes renomegaly.

Key Words: POEMS syndrome; kidney; renal volume; kidney volume; organomegaly.

POEMS syndrome, sometimes referred to as Crow-Fukase syndrome and Takatsuki syndrome, is a rare multisystem disorder with the dominant clinical feature of chronic progressive sensorimotor polyneuropathy. Bardwick et al first used the acronym, POEMS, in 1980 to describe important features of the syndrome: polyneuropathy (P), organomegaly (O), endocrinopathy (E), M-protein (M), and skin changes (S) (1). Other characteristics of this disorder, not included in the acronym, include sclerotic bone lesions, Castleman disease, edema, papilledema, pleural effusion, ascites, thrombocytosis, polycythemia, fatigue, clubbing, peripheral neuropathy, monoclonal plasma cell dyscrasia, and elevated vascular endothelial growth factor levels (2–4). The peak incidence of POEMS occurs in the fifth and sixth decades (median age, 51 years) (2,3).

Organomegaly typically characterized by hepatomegaly, splenomegaly, and lymphadenopathy or Castleman disease is a common feature of POEMS syndrome with an incidence of 50% in one large case series (3). Results of our exhaustive literature search of variations in renal size associated with POEMS yielded two reports of bilateral renal enlargement (5–7), four cases of bilateral renal contraction in a case series of 52 patients, and two cases of unilateral renal contraction from the same series (8).

The purpose of this investigation is to further characterize the features and significance of unilateral kidney contraction on kidney size in POEMS patients as compared to normal controls.

MATERIALS AND METHODS

A retrospective review was performed following approval by the Institutional Review Board maintaining Health Insurance Portability and Accountability Act compliance. The POEMS syndrome database at our institution identified 207 patients with the diagnosis of POEMS syndrome between October 1, 1974, and February 29, 2008. The diagnosis of POEMS syndrome was based on the Mayo Clinic criteria that require the presence of a monoclonal plasma cell disorder and polyneuropathy along with one other major criteria (osteosclerotic myeloma, Castleman disease or elevated vascular serum, or plasma endothelial growth factor) and one minor criteria (organomegaly, volume overload, endocrinopathy, skin changes, papilledema, or thrombocytosis/polycythemia) (2). For each of the POEMS patients, the most recent cross-sectional imaging study including ultrasonography (US), computed tomography (CT), and magnetic resonance

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TABLE 1. Calculated Kidney Volumes and Volume Differences

Variable	POEMS / Controls Min	Max	Median	Mean	Std. Dev.
Age (years)	**28** / 19	**78** / 67	**51** / 49	**53** / 48	**12** / 10
Larger Kidney Volume (cm^3)	**100** / 116	**497** / 306	**196** / 167	**202** / 174	**64** / 35
Smaller Kidney Volume (cm^3)	**29** / 112	**385** / 266	**166** / 157	**174** / 162	**59** / 31
Volume Difference (cm^3)	**0** / 0	**191** / 40	**20** / 10	**28** / 12	**32** / 10

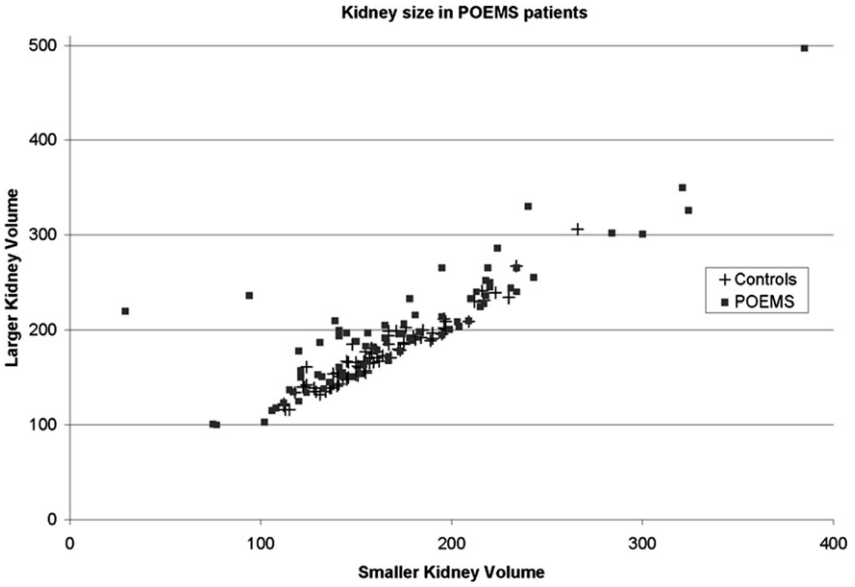

Figure 1. Scatterplot of data from Table 1. Overall, POEMS patients tended to have a larger difference in kidney volume when compared to controls.

imaging (MRI) performed at our institution was obtained. Patients were excluded from the study if no cross-sectional imaging study was performed, or if the kidneys were not entirely visualized on the study. Given the non–three-dimensional nature of US and its known unreliability in estimating renal volume, CT or MRI performed within 3 months of the US, if available, was used in the analysis; otherwise, US data alone were excluded from the analysis.

Control patients were obtained from the living kidney donor database at our institution; 221 patients who had undergone protocol imaging were identified. To qualify as kidney donors, they must have normal kidney function and be free of any significant chronic medical conditions. The controls and POEMS patients were 1:1 frequency matched by age (<45 years and ≥45 years) and gender, with the selection of age cutoff based on the peak incidence of POEMS. All control subjects had CT exams performed at our institution.

For the 77 frequency-matched POEMS patients and controls with CT or MRI data, the kidneys were segmented using a standard three-dimensional segmentation algorithm on a GE AW Workstation (GE Healthcare, Waukesha, WI). From the voxel dimensions, kidney volumes were then obtained from the segmented kidneys. The segmentations were performed by a senior radiology resident (A.C.) who performed 84% of the segmentations, and a board-certified radiologist (C.L.) who performed 13% of the segmentations. Five patients (3%) were segmented in blinded fashion by both radiologists on separate occasions to assess interrater reliability.

Data were described by group using mean ± standard deviation, range, or count (percent) as appropriate. Within the control patients, and similarly within the POEMS patients, the volume of the smaller kidney was compared to the volume of the larger kidney using a paired t-test. Then univariate linear regression models were constructed using all 154 patients for the outcome of the difference (larger-smaller) in kidney size. Covariates considered included age (continuous), age group, sex, height, weight, body surface area, body mass index, POEMS status, and the size of the smaller kidney. A multiple variable model was constructed using continuous age, sex, POEMS status, and size of the smaller kidney, based on univariate statistical significance and previous clinical experience. An intraclass correlation coefficient and 95% confidence interval was constructed to investigate interrater reliability of kidney volumes. All statistical analyses were performed using SAS v9.1 (SAS Institute Inc., Cary, NC). A significance level of $\alpha = 0.05$ was used, and all tests were two-sided.