KSN 2017 Abstract

Role of inflammation and the uremic milieu in premature vascular aging

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Patients with end-stage renal disease (ESRD) display a progeric vascular phenotype linked to apoptosis, cellular senescence and osteogenic transformation. Systemic inflammation is another common feature of ESRD that has proven to be an established risk factor and a catalyst for complications related to a premature aging phenotype, including muscle wasting, vascular calcification and other forms of premature vascular disease, depression, osteoporosis and frailty. Uremic inflammation is mechanistically related to mechanisms involved in the aging process, such as telomere shortening, mitochondrial dysfunction, senescence and deranged nutrient sensing, which can have direct effect on cellular and tissue function. There are remarkable similarities between the pathophysiology of uremic inflammation and the "inflammaging" process in the general population. Potentially relevant are abnormal or misplaced protein structures as well as abnormalities in tissue homeostasis, evoking danger signals through damage associated molecular patters as well as the senescence associated secretory phenotype (SASP). Systemic inflammation, in combination with the loss of kidney function, can impair the resilience of the body to external and internal stressors by reduced functional and structural tissue reserve, and by impairing normal organ crosstalk. In this presentation the links between uremic inflammation and the prematurely aged phenotype, as well as potential causes and consequences, are discussed.