The aging kidney – a review

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Abstract

In the near future the number of elderly patients will rise considerably. Because of their peculiar characteristics and needs, management of these patients requires specific knowledge in various fields of medicine. In the past, many efforts have been made to investigate the renal changes that take place with aging. However, because of interfering factors such as hypertension and/or atherosclerosis, genuine age-related alterations are difficult to evaluate. In this article the changes in renal morphology and physiology that are inherent to the aging process are reviewed.

Introduction

The rising number of elderly people forces us to direct our attention more and more to ailments that are characteristic for the aged and this includes concern about renal function. The kidney is involved not only in the control of the "internal environment" but also in the regulation of blood pressure and hemodynamics. In addition, the kidney is of great importance with respect to the excretion of drugs. Exploration of the effects of aging on renal morphology and function is difficult because of problems in defining normality, the frequent occurrence of multiple pathological processes and the limited accrual of adequate material to investigate. In humans, it is virtually impossible to exclude subclinical disease states during investigations of the impact of "normal" aging, especially in elderly people. Animal models in the past have suffered from the same problems. However, Dodane et al. have developed an animal model that is nearly free of any kind of renal disease [1]. They demonstrated, in rats fed at libitum, that the sole significant morphological change occurring in that species was thickening of the glomerular basement membrane without any increase in mesangial matrix or mesangial cellularity. Functional changes comprised increased urinary volume, reduced urinary osmolality, renal loss of calcium, and discrete glucosuria.

In another study, in rats almost free of glomerulosclerosis, individual filtration and reabsorption of sodium, potassium, calcium and magnesium appeared to be independent of age. Only reabsorption of phosphate decreased with age [2]. In the following we will describe some changes, occurring in the kidneys during the aging process, that are believed to be due to senescence rather than to specific disease.

Morphological changes

Between the age of 40 and 80 renal mass falls from 250–270 gram to 180–200 gram [3]. This reduction in mass correlates with the degree of sclerosis of intrarenal arteries, suggesting that the age-related changes are intermingled with atherosclerotic changes. The loss of tissue mass is greater in the cortical than in the medullary area.

In patients without apparent renal disease macroscopic changes in the kidney at necropsy vary from only a fine granularity at the surface to coarse scars. In more than 50% of patients only slight or even no abnormalities are found. Scarring is evenly distributed over the surface of the kidney.

Senescence of the kidney is associated with loss of functional nephrons which leads to a progressive
decrease in glomerular filtration rate (GFR). However, it is still a matter of debate whether this loss of nephrons really is a phenomenon of aging or whether it ought to be attributed to concomitant pathologic conditions such as hypertension, (asymptomatic) bacteriuria, hyperlipidemia or atherosclerosis. In an autopsy study, Kasiskes showed that glomerulosclerosis correlates with the extent of atherosclerotic vascular changes [4]. Both age and the extent of intrarenal vascular abnormalities correlated independently with the number of hyalinized glomeruli, both in the cortex and in the medulla. In contrast, hypertension in this study, was not independently associated with glomerulosclerosis, when age and vascular abnormalities were taken into account. However, even in the absence of apparent atherosclerotic lesions some glomerular sclerosis leading to glomerular loss may be found [5].

Whatever the cause, after the third decade glomerular sclerosis begins and at the age of 80 years some 10–30% of the glomeruli are hyalinized or sclerotic. The number of glomeruli has been measured by various methods (histologic, angiographic). All results show a decline in glomerular number but with a wide variation in absolute figures. Simultaneous with the reduction in the number of glomeruli hyperperfusion and hyperfiltration of remaining glomeruli develop [6]. Hyperfiltration, in turn, leads to disruption of the capillary membranes. This results in the development of mesangial deposits and initiation or acceleration of glomerular sclerosis. Another factor to take into consideration is the presence of hyperlipidemia. Hyperlipidemic conditions produce glomerular injury and sclerosis although the exact mechanism is not fully understood [7]. A synergistic interaction between hypertension and hyperlipidemia is likely in the development of vascular injury. Hyperlipidemia is, however, an independent risk factor for the development of focal glomerular sclerosis [8]. The development of glomerular sclerosis is further enhanced by several cytokines and other hormonal factors, although the exact pathophysiologic processes involved still have to be elucidated [9].

Histologic changes in the aging kidney are most apparent at the capillary level, in the renal arterial tree and the glomerular and tubular basal membrane.

Vascular tree. With age interlobular tortuosity increases, the caliber of large vessels becomes irregular, patchy sclerosis develops and the number of agglomerular arterioles rises [10]. In preglomerular vessels the spiralling is most pronounced; it is attributed to the redistribution of intrarenal flow. In interlobular arteries a progressive thickening of the intima due to deposition of elastic tissue is found. This is associated with atrophy of the media. In arteries smaller than 100 \( \mu \)m hypertrophy of the media, proliferation of the intima and deposition of hyalin material are the predominant features [11]. Changes in small arteries appear from the second decade onwards and are aggravated by hypertension.

Glomerulus. In a review, Goldstein et al. described the age-related changes taking place in the rat kidney [12]. In rats the earliest indications of altered renal morphology are thickening of the mesangium and the glomerular basement membrane. Mesangial cellularity increases, potentially leading to obliteration of the urinary space. Glomerular epithelial cells exhibit various ultrastructural changes the significance of which is not yet fully known. Nuclear indentation is present and an increase in number and size of vesicles and myelin bodies can be seen [13]. The changes in the glomerular basement membrane, mesangial matrix and glomerular epithelial cells lead to adhesion of capillary loops, hyalinization and eventually sclerosis of the capillary tuft. In an autopsy study, Darmady et al. showed that the basement membrane of Bowman’s capsule progressively thickens during life and that reduplication of both glomerular and tubular basement membranes occurs [11]. Electron microscopic investigations reveal that the glomerular basement membrane thickens only until the fourth decade [14]. After the age of 60, however, the surface area of the glomerular basement membrane decreases. The glomerular tuft progressively collapses and the basement membrane wrinkles. Hyaline material is deposited in the residual glomerular tuft and in the space of Bowman’s capsule. In cortical glomeruli hyalinization and collapse of the glomerulus is accompanied by obliteration of the vas afferens. In juxta-medullary glomeruli, however, the afferent arteriole directly passes into the efferent arteriole, thereby forming arteriolae rectae verae. This has been confirmed by microangiographic investigations [5].

Tubule. The basement membrane of the proximal tubule thickens and tubular epithelial cells undergo fatty degeneration and gradual atrophy. Especially in the proximal parts of the tubule ultrastructural changes occur. The pars convoluta of the proximal tubule is affected by focal cellular necrosis with focal brush border loss, irregular cell height, bulbous projections, an increased number of apical vesicles, heterophagic