The Kidney in Congenital Cyanotic Heart Disease

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Glomerulomegaly, or glomerular enlargement, was first reported in patients with congenital cyanotic heart disease in 1953.[1] This finding was initially noted on visual inspection and subsequently confirmed via morphometric measurements.[2-4] Beyond cyanotic heart disease, several other conditions are also associated with glomerulomegaly, including cor pulmonale, pulmonary hypertension, polycythemia vera, sickle cell disease, obesity, alcoholism, fatty liver, and cystic fibrosis.[5] More broadly speaking, glomerular hypertrophy is generally observed in both congenital (oligomeganephronia, congenital solitary kidney) and acquired (chronic kidney disease, post-nephrectomy) conditions associated with reduced nephron mass and is thought to be due to compensatory glomerular hyperfiltration that is required to maintain overall renal clearance.[6] The following are 10 points to remember about glomerulomegaly and the kidney in congenital cyanotic heart disease.

- Although glomerulomegaly used to be thought of as a benign condition, glomerular enlargement is now known to be associated with increased risk of glomerulosclerosis, progressive decline in kidney function, and poorer prognosis.[7]
- In kidney transplant recipients, increasing glomerular size in the donor kidney is associated with a higher risk of late allograft dysfunction.[8]
- A threshold glomerular size that predisposes to glomerulosclerosis has not yet been established.[7]
- The putative mechanisms for the development of glomerulomegaly vary according to underlying physiologic abnormalities; these include increased right ventricular pressure causing congestion, increased blood volume, hypoxemia, hyperviscosity, and lipid abnormalities.[5]
- In congenital heart disease, the term “cyanotic nephropathy” was coined because glomerulomegaly was thought to lead to a decline in kidney function.[9] Proteinuria is the most frequently observed clinical abnormality.[4]
- Glomerulomegaly in minimal change disease predicts subsequent progression to focal segmental glomerular sclerosis (FSGS).[10]
- Glomerulomegaly in proliferative (class III or IV) lupus nephritis has been reported to be associated with lower probability of disease remission at 3 years post-induction therapy.[11]
- Obesity-related glomerulopathy, defined as proteinuric renal disease in patients with a body mass index > 30 kg/m^2, is associated with glomerulomegaly and secondary FSGS.[12,13] The classic presentation is moderate-to-massive proteinuria with a normal serum albumin level (in contrast to hypoalbuminemia seen in primary FSGS).[14]
- Obesity is an independent risk factor for the development and progression of chronic kidney disease.[15] Even in obese patients who have normal kidney function, body mass index positively correlates with glomerulomegaly.[16] Interventions to reduce weight—including lifestyle modifications and, when unsuccessful, bariatric surgery—should be considered early for these patients.
- Blockade of the renin-angiotensin system is the mainstay of therapy to reduce glomerular hyperfiltration. The Eighth Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-8) guidelines recommend angiotensin-converting enzyme inhibitors or angiotensin receptor blockers as first-line therapy for hypertensive patients with chronic kidney disease.[17]

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