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Case Report / Olgu sunumu

The Pediatric Case of a Recently Defined Syndrome: Shrunken Pore Syndrome

Yeni Tanımlanmış Bir Sendrom olan Shrunken Pore Sendromlu Çocuk Hasta

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Abstract

Introduction: Creatinine was started to be used as a marker of glomerular filtration rate (GFR) in 1920's. Later in the 1990s, cystatin C was shown to be superior to creatinine in assessing GFR. In some patients, glomerular filtration of cystatin C was found to be low compared to creatinine, and it was hypothesized that glomerular pores may have been shrunken in these patients. For the group of patients having a cystatin C based estimation of GFR (eGFR cystatin C) to creatinine-based estimation of GFR (eGFR creatinine) ratio of ≤60%, the pathophysiological classification is defined as Shrunken Pore Syndrome.

Case: A 16-month-old female patient was admitted to Ege University Pediatric nephrology clinic with the diagnosis of neurogenic bladder secondary to meningomyelocele. She had a history of antenatal meningomyelocele, and hydrocephalus diagnosed as Arnold Chiari type 2. On postnatal day 1, she had undergone meningomyelocele sac excision and ventriculoperitoneal shunt operation. There was no history of pyelonephritis. Systemic examination revealed a dysmorphic facial appearance, operation scar on her back and syndactyly of the toes, and paraplegia on neurological examination. In laboratory examination; urea: 24 mg/dL, creatinine: 0.3 mg/dL, parathormone: 47 ng/mL, cystatin C: 1.4 mg/L (RR: 0.53-0.95), blood β2 microglobulin: 2716 ng/mL. Patient's eGFRcystatin C: 107 ml/min/1.73m^2 and eGFRcreatinine: 188 ml/min/1.73m^2. Shrunken Pore Syndrome was considered due to the difference between the patient's eGFRcystatin C value and eGFRcreatinine value.

Conclusion: Shrunken Pore Syndrome has no known treatment; however, it is important to diagnose these patients because of accompanying risks such as increased cardiac mortality. With the usage of cystatin C as a marker of GFR, possible mortality risks can be predictable and preventive measures can be taken early on.

Keywords: Shrunken pore syndrome,cystatin C, creatinine, GFR, glomerular filtration rate

Öz

Giriş: Sistatin C bazlı tahmini Glomerüler filtrasyon hızı (GFR) ölçümleri son dönem böbrek yetmezliği, kardiyovasküler bulgular ve mortaliteyi öngörmede kreatinin bazlı ölçümlerden üstün olup; cinsiyet, yaş ve kas kitlesinden bağımsızdır. Bazı olgularda sistatin C'nin filtrasyonunun, kreatinine göre daha az olduğu gözlemlenmiş ve bunun porların daralmasından kaynaklandığı kanıtlanmıştır. Sistatin C bazlı tahmini GFR (eGFRsistatin C), kreatinin bazlı tahmini GFR'nin (eGFRkreatinin) %60'ına eşit veya bunun altında olması patofizyolojik olarak 'Shrunken Pore Sendromu' olarak tanımlanmıştır. Bu yazıda Shrunlen Pore sendromlu bir kız olgudan bahsedildi.

Olgu: 16 aylık kız hastanın meningomiyelosel ve nörojenik mesane ile Ege Üniversitesi Çocuk Nefroloji polikliniğine başvurdu. Özgeçmişinde antenatal meningomyelosel ve hidrosefali nedeniyle Arnold Chiari tip 2 tanısı, postnatal 1. günde meningomyelosel kesesi eksizyonu ve ventrikülöperitoneal şant operasyonu mevcuttu. Piyelonefrit öyküsü yoktu. Fizik bakısında; dismorfik yüz görünümü, parapleji, belde operasyon skarı, ayak parmaklarında sindaktili mevcuttu. Laboratuvar incelemesinde; üre:24 mg/dL, kreatinin: 0,3 mg/dL, parathormon: 47 ng/mL, Sistatin C 1,4 mg/L (RA:0,53-0,95), kan beta 2 mikroglobulin: 2716 ng/mL idi. Hastanın eGFRsistatin C: 107 ml/ dk/1,73m^2 ve eGFRkreatinin: 188 ml/dk/1,73m^2 idi. Hastada eGFR sistatin C değeri ile eGFRkreatinin değeri arasındaki farktan dolayı Shrunken Pore Sendromu düşünüldü.

Sonuç: Shrunken Pore Sendromlu hastalarda artmış kardiyak mortalite riski belirtildiğinden; GFR belirteci olarak sistatin C'nin kullanılması, hem kardiyak riskli hastaları hem de hastalığın gerçek prevalansını belirlemeyi sağlamakta önem taşımaktadır.

Anahtar Kelimeler: Shrunken pore sendromu, glomerüler filtrasyon hızı, GFR, sistatin C, sistatin C GFR

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INTRODUCTION

Creatinine was started to be used as a marker of glomerular filtration rate (GFR) in 1920's. Later in the 1990s, cystatin C was shown to be superior to creatinine in assessing GFR. Cystatin C-based estimated GFR (eGFR cystatin C) calculations give us the most realistic results regardless of race, sex, age and muscle mass. However, the most accurate results are gathered with both cystatin C and creatinine calculations. In addition, it is reported that cystatin C-based predictive measurements are superior to creatinine-based measurements in predicting end-stage renal disease, cardiovascular findings, hospitalization and mortality.[1] Creatinine with a molecular weight of 113 Da and cystatin C of 13343 Da is normally filtered freely through the glomerular membrane. In some patients, glomerular filtration of cystatin C was found to be low compared to creatinine, and it was hypothesized that glomerular pores may have been shrunken in these patients. For the group of patients having a cystatin C based estimation of GFR (eGFR cystatin C) to creatinine-based estimation of GFR (eGFR creatinine) ratio of ≤60%, the pathophysiological classification is defined as Shrunken Pore Syndrome.[2] Shrunken pore syndrome is defined thoroughly in adult patients, however there is only one literature on Shrunken pore syndrome in children and no case reports. In this paper, we report and discuss, in accordance with the literature, a pediatric patient with newly defined Shrunken pore syndrome.

CASE

A 16-month-old female patient admitted to Ege University Pediatric nephrology clinic with the diagnosis of neurogenic bladder secondary to meningomyelocele. She was hospitalized because of high cystatin C levels detected in routine check-ups. She had a history of antenatal meningomyelocele, and hydrocephalus diagnosed as Arnold Chiari type 2. On postnatal day 1, she had undergone meningomyelocele sac excision and ventriculoperitoneal shunt operation. The patient then underwent repeated shunt revision operations. There was no history of pyelonephritis. In the family history, the mother had type 2 diabetes mellitus and hypothyroidism. On physical examination; her weight was 11 kg (50-75p), height was 71 cm (<3p), blood pressure was 100/65 mmHg (90-97p). Systemic examination revealed a dysmorphic facial appearance (deeply located eyes, bitemporal stenosis), operation scar on her back and syndactyly of the toes, 1/6 systolic murmur on cardiologic examination, and paraplegia on neurological examination. In laboratory examination; hemoglobin:11.3 g/dL (RR: 11-13), hematocrit: 34.31% (RR: 37-53.7) leukocyte: 11.6 103/µL (RR:6-17) neutrophils: 6.27 103/µL (RR: 2-6.9), platelet: 387 103/µL (RR: 142-424), urea: 24 mg/dL (RR: 10.7-57.7), creatinine: 0.3 mg/dL (RR: 0.3-1.0), uric acid: 4.5 mg/dL (RR: 1.9-5.4), total protein: 6.6 g/dL (RR: 5.2-7.4) albumin: 4.1 g/dL (RR: 3.1-4.8), AST: 30 U/L (RR: 18-63), ALT: 18 U/L (RR: 10-32), Na : 134 mmol/L (RR: 132-143), K: 4.7 mmol/L (RR: 3.2-5.7), Cl: 103 mmol/L (RR: 98-116), CRP: 0.2 mg/dL (RR: 0-0.5), cystatin c: 1.4 mg/L (RR: 0.53-0.95), blood β2 microglobulin: 2716 ng/mL (RR: 651-2295) In routine urine examination: density: 1015 g/mL, pH: 6.5, leukocyte: 1/hpf (RR:0-5), erythrocyte: 1/hpf (RR:0-5), spot urine protein/creatinine: 0.39 g/g creatinine (RR: <0.40), spot urine beta 2 microglobulin: 84.8 mg/g creatinine (RR: <300), FENa: 1.3%, FEK: 15.9%, TPR: 83 mmHg (RR:65-110). Urine culture was negative. Patient's eGFRcystatin C value: 107 ml/min/1.73m^2 (RR: 93-207) and eGFRcreatinine value: 188 ml/min/1.73m^2 (RR: 87.9-122.5). On ultrasound examination; the right kidney was 57 mm (3-10p) and the left kidney was 58 mm (3-10p) in length, with an average parenchymal thickness of 8 mm on the right and 7 mm on the left. Renal parenchyma scintigraphy with Technetium 99m revealed, kidneys were of normal shape and size and radiopharmaceutical involvement was within normal limits. The contours were also appeared regular. The contribution of the right kidney to the total renal function was 48% and of the left kidney was 52%. The patient had post voiding residues and was diagnosed with neurogenic bladder and a combined treatment of clean intermittent catheterization, amoxicillin and oxybutynin was prescribed. Shrunken Pore syndrome was considered due to the difference between the patient's eGFRcystatin C value and eGFRcreatinine value. Electrocardiogram results: ASD sekundum 7-8 mm, at the pulmonary arteries maximum 17 mmHg gradient was found. Ejection fraction was 69%.

DISCUSSION

Shrunken pore syndrome is defined by a difference of 60% or less in eGFRcreatinine/ eGFR cystatin c ratio. In this paper, we reported a child with shrunken pore syndrome who had no other renal abnormalities. In patients with Shrunken Pore Syndrome, creatinine ratios of other low molecular weight proteins such as beta 2 microglobulin, parathyroid hormone, brain natriuretic peptide, amylase, lipase, prealbumin, albumin, alpha 1 acid glycoprotein and retinol binding protein, were also high.[3] The clearance of each of these proteins is done by glomerular filtration and this clearance decreases proportionally with the shrinkage of glomerular pores. The mechanism that gives the syndrome its name, explains this simultaneous increase of all these proteins in the blood panel.[4] In our case our patient had an eGFRcystatin c of 107, which is 57% of the eGFRcreatinine value of 188. Our patient also has a such high blood beta 2 microglobulin level as 2716 ng/mL. The patient underwent renal ultrasonography, urodynamic testing and DMSA testing to rule out other renal abnormalities.

Since shrunken pore syndrome is very recently defined in pediatric patients, there is only one study[5] that shows the prevalence levels in the pediatric group, and it states the prevalence in children as 4.8%. With a regular use of cystatin c as a marker of GFR, shrunken pore syndrome can be diagnosed more frequently, and more data can be collected. Moreover; literature on adult patients also show a link

between high cardiac mortality and shrunken pore syndrome. [2] Our patient also underwent ECO testing to determine an abnormality of the heart due to a suspicion on physical examination, but the results were normal. Tests such as carotid intima media thickness (CIMT), pulse wave velocity (PWV) and augmentation index (AIx) are considered to be the cursor of the clinical or subclinical atherosclerotic vascular diseases [6]. We tried to assess AIx and PWV but the patient being too small did not allow measurements. It can be suggested that when a child is diagnosed with shrunken pore syndrome, these tests can also be checked to assess the cardiovascular health of the child and moreover, these tests can be useful in follow-ups to prevent future cardiac problems.

CONCLUSION

Shrunken pore syndrome has no known treatment; however, it is important to diagnose these patients because of accompanying risks such as increased cardiac mortality. Use of cystatin c as a marker of GFR and a regular control of eGFRcystatin C will help determine possible shrunken pore patients. Thus, possible mortality risks can be predictable and preventive measures can be taken early on.

ETHICAL DECLARATIONS

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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REFERENCES

1. Kyhse-Andersen J, Schmidt C, Nordin G, Andersson B, Nilsson-Ehle P, Lindström V, Grubb A. Serum cystatin C, determined by a rapid, automated particle-enhanced turbidimetric method, is a better marker than serum creatinine for glomerular filtration rate. Clin Chem 1994;40:1921–6.
2. Christensson A, Grubb A, Molvin J, Holm H, Gransbo K, Tasevska-Dinevska G, Bachus E, Jujic A, Magnusson M. The shrunken pore syndrome is associated with declined right ventricular systolic function in a heart failure population - the HARVEST study. Scand J Clin Lab Invest. 2016; 76:568-74.
3. Purde MT, Nock S, Risch L, Medina Escobar P, Grebhardt C, Nydegger UE, Stanga Z, Risch M. The cystatin C/creatinine ratio, a marker of glomerular filtration quality: associated factors, reference intervals, and prediction of morbidity and mortality in healthy seniors. Transl Res 2016;169:80–90.
4. Grubb A, Lindström V, Jonsson M, Bäck SE, Åhlund T, Rippe B, Christensson A. Reduction in glomerular pore size is not restricted to pregnant women. Evidence for a new syndrome: "Shrunken pore syndrome". Scand J Clin Lab Invest 2015;75:333–40.
5. Emil den Bakker, Reinoud Jbj Gemke, Joanna Ae van Wijk, Isabelle Hubeek, Birgit Stoffel-Wagner & Arend Bökenkamp (2019): Evidence for shrunken pore syndrome in children, Scandinavian Journal of Clinical and Laboratory Investigation, DOI: 10.1080/00365513.2019.1692231
6. Kasliwal RR, Bansal M, Desai D, Sharma M. Carotid intima-media thickness: Current evidence, practices, and Indian experience. Indian J Endocrinol Metab. 2014;18(1):13–22. doi:10.4103/2230-8210.126522
7. Ayub S, Khan S, Ozair U, Zafar MN. Cystatin C levels in healthy kidney donors and its correlation with GFR by creatinine clearance J Pak Med Assoc. 201