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MEDULLARY SPONGE KIDNEY - THE MYSTERIOUS NAME OF A SIMPLE DISEASE

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ABSTRACT

Medullary sponge kidney (renal spongiosis), (MSK) is a rare developmental anomaly of the kidney of unknown cause. It is presumed, that people with a genetic predisposition (<5% family occurrence) are prone to the disease. The peak of diagnosis is between the ages of 20-50, usually by chance (due to lack of symptoms) during an abdominal X-ray, where the so-called nephrocalcinosis (calcifications in the kidney) can be observed. Another radiologic test, that may suggest the condition in question is abdominal ultrasound, where cysts up to 8 mm in diameter in the medullary part of the kidney and calcifications can be seen. Diagnosis may also be based on the diagnosis of pre-existing stones and urinary tract infections, or hematuria. Urography has the highest sensitivity to sponge kidney. Symptoms, if already present, are characterized by low back pain, hematuria, hematuria, recurrent urinary tract infections, proteinuria, sterile purulence. Ultimately, the aforementioned pathologies can lead to kidney failure. To date, no causal treatment has been developed; only symptomatic treatment of lithiasis foci and urinary tract infections is possible. The purpose of the following paper was to describe the definition, epidemiology and etiology of MSK and to highlight the randomness of diagnosis and the problem in the lack of specific therapy for this renal developmental disorder. Current publications and guidelines from scientific societies around the world were reviewed, using MeSH-compliant keywords.

Key words: kidneys, medullary sponge kidney, calcification, kidney failure

1. INTRODUCTION AND METHODOLOGY

The kidneys are paired internal organs, shaped like beans, located retroperitoneally in the abdominal cavity, whose functions can be divided into excretory, regulatory and endocrine parts [3]. The adrenal glands are adjacent at the top [3]. Their location is estimated at the height of the first three lumbar vertebrae and the last two thoracic vertebrae (the left kidney usually lies 1.5-3 cm higher than the right), under the liver and behind the stomach [3]. The kidney in humans weighs an average of 120-200 g [3]. Microscopically, the functional unit is the nephron, consisting of two functional units - the tubules and the glomerulus [2]. The number of nephrons per kidney varies widely, with an average of 1.5 million [4]. We can divide them into short-loop nephrons (which form the cortex) and long-loop nephrons (which form the medulla) [4]. This organ is supplied with blood through the renal artery, which diverges from the abdominal part of the aorta [2]. This artery divides into five main branches, these in turn give rise to the interlobar arteries [2]. They divide into arch arteries, from which the interlobular arteries originate [2]. Eventually, the supply arterioles diverge from them [2]. They are responsible for the final delivery of blood to the glomeruli, where the process of filtration takes place [2, 4]. In a day, 1,700 liters of blood flow through both kidneys, from which an average of 1.5 liters of urine is produced [2]. Thanks to such a complex structure, the organs in question are responsible not only for the production of urine, known to everyone, but also influence the maintenance of proper blood pressure, produce erythropoietin and active forms of vitamin D3, or regulate acid-base balance [2, 4]. Any abnormalities in the structure and function of the kidneys can therefore make themselves felt throughout the body, so thorough diagnostics for any suspicions or regular preventive examinations for familial burdens are key here [4]. Sometimes, however, even observing one's own health and the basic examinations available at the primary health care allow serious kidney disease entities to be overlooked because of poor or no symptoms, and the diagnosis occurs completely by chance [2, 4]. An example of such pathology is medullary sponge kidney (MSK) [1]. It was first described by Hermann Beitzke in 1908 [8]. Detected most often incidentally on abdominal X-ray due to other pathology [9]. A developmental anomaly of the kidney of unknown etiology, encountered infrequently (1:20000 births), which can give life-threatening complications in the long term [9]. So far, no causal treatment has been developed, there is only treatment of complications and avoidance of urinary tract infections [9].

The aim of the following paper is to present the principles of diagnosis, epidemiology and management of a patient diagnosed with medullary sponge kidney. Current publications and guidelines of internal medicine and endocrinology societies from many countries of the world from 2006-2022, available in the online scientific databases PubMed, Google Scholar and MedRxiv, were reviewed, using MeSH-compliant keywords.

2. DESCRIPTION OF THE STAGE OF KNOWLEDGE

2.1. DEFINITION AND ETIOLOGY

The sponge kidney was the first to be fully consciously encountered by German physician Hermann Beitzke in 1908, with no imaging methods available at the time, of course [8]. It was only after the advent of contrast agents in radiological diagnosis in the 1930s and the development of intravenous urography, that this led to the discovery of many renal pathologies, including medullary sponge kidney [9]. Its full diagnosis and description took place in 1939 by

a multidisciplinary team of specialists: a radiologist (Lenarduzzi), a urologist (Cacchi) and a pathologist (Ricci), and the thing took place at the University Hospital of Padua [5]. The name of the condition itself, however, was introduced in 1949, also by Cacchi and Ricci [9]. According to the definition, it is a developmental disorder of the kidney of unknown etiology, characterized by small calcifications in the collecting ducts and renal tubules in a process known as renal calcification, visible on imaging studies, and usually without symptoms [1]. It can affect one or both kidneys [10]. The diagnosis usually occurs incidentally, when the examination is performed on the patient for other reasons [9]. On a review radiograph, deposits, which are cysts 1 to 8 mm in diameter, can be seen in the pyramidal view [11]. They mainly consist of calcium oxalate and calcium phosphate [9]. On the other hand, hyperechoic pyramids can be seen on ultrasound [12]. The imaging study with the highest sensitivity remains urography at all times [12]. The genesis of this affliction remains undetermined, but a not insignificant contribution of genetic predisposition is suspected [6]. To date, it has not been determined, what gene could be involved in the inheritance of this disease entity, but it is believed, that the inheritance may be autosomal dominant in this case [6]. Familial occurrence is encountered in less than 5% of cases [23]. Recent studies have suggested, that sponge kidney may be related to the occurrence of hyperparathyroidism [7]. Increasingly, patients with both pathologies are being encountered [7]. If suspicions turn out to be correct, the interaction between the glial cell lineage-derived neurotrophic factor (GDNF) gene and the RET protooncogene may play a significant role here [7]. It can also occur as part of the clinical syndrome of other congenital disorders, such as Ehlers-Danlos syndrome, Beckwith-Wiedemann syndrome, Marfan syndrome, ADPKD, Carole syndrome [6, 9, 11]. Medullary sponge kidney can also be associated with the presence of tumors, such as Wilms tumor, or on the occasion of having a horseshoe kidney [9,19]. It cannot be prevented, the process of formation of the disease continues from the fetal life stage [9]. The course is usually mild, rarely leading to fatal cases [10]. However, in 10%, it can lead to kidney failure, most likely through recurrent urinary tract infections and kidney stones [11].

2.2. EPIDEMIOLOGY

Medullary sponge kidney is a rare condition, occurring with a frequency of 1:20000 births [7]. It affects men and women equally, with some sources reporting that it affects women slightly more often [6]. In the United States, it has been determined that the disease occurs in 1 in 1000-5000 people [6]. If recurrent kidney stones are present, it is found in 20% of patients [7]. MSK can occur at any age, but the peak of diagnosis is in children during adolescence and adults between the ages of 20-50 [1]. The incidence among different ethnic and racial groups is at a fairly equal level [6]. However, very rare cases of neonates with the condition have also been described [6]. The epidemiology of MSK is very difficult to assess due to the rarity of symptoms, leaving many patients with undiagnosed sponge kidney [10].

2.3. DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

A medullary sponge kidney is usually an incidental finding during routine, or otherwise performed imaging studies [13]. Despite having very sparse symptoms, or none at all, this disease entity can lead a patient to very dangerous complications, such as renal failure [9]. A person with this condition can suffer from chronic low back pain for years before the cause is discovered [13]. A fairly significant reason for the difficult diagnosis, including imaging, is the infrequent use of contrast agents in the diagnosis of UTI [14]. The method, that gives the most

certainty about the diagnosis, remains all the time biopsy and other endoscopic methods, which, as is well known, are examinations, that are a burden to the patient and are not performed without a specific reason [14]. However, despite the rare appearance of symptoms, careful diagnostic management should be initiated in a patient with suspected MSK, as untreated disease can significantly impede life and, in extreme cases, lead to dangerous renal failure [14].

CLINICAL EXAMINATION. The basic element here is the nephrological history, with special inquiry of the patient about blood in the urine, since this is usually the only symptom of this disease entity (it occurs in 10-20% of patients) [9]. Diagnosing patients with medullary sponge kidney is difficult due to the lack of any symptoms in most cases [6]. Other, rarer signs that can guide the doctor are chronic perennial low back pain, sterile pus and proteinuria [9]. Fever, nausea and vomiting are symptoms that can occur with URI, against which there is a higher risk of disease, having a sponge kidney [9]. Another common (70%) complication of this group of patients is nephrolithiasis (can cause attacks of renal colic), due to concomitant hypercalciuria, urinary stasis and acidosis of the distal renal tubules [6]. Stones are recurrent, on average every 2 years, but usually do not require urologic intervention [19]. In 12-20% of patients with kidney stones, sponge kidney was diagnosed [6]. The doctor must pay attention to whether the patient is in the risk group due to his age (peak diagnosis 20-50 years) [6]. The risk group also applies to patients with other renal malformations, patients with hyperparathyroidism and patients on a sodium-rich diet [14]. In addition, hemifacial hypertrophy was found in 25% of those suffering from MSK [6]. Family history is also worth noting, as familial occurrence hits 5% of cases [9]. In urinalysis, hypercalciuria, hypocyuria and high pH [19]. Reduced eGFR affects only 10% of patients [19]. It is also suspected that MSK may cause hypertension in patients in this group, through activation of the renin-angiotensin-aldosterone system, thereby causing secondary hypertension [20].

RADIOLOGICAL EXAMINATION. Ultrasound is the first imaging study to detect MSK [9]. This is due to the asymptomatic progression of the disease, or very faint symptoms, so that the diagnosis is usually made incidentally, when an examination is performed for another reason [9]. In most cases, the probe shows bilateral cysts (in 80%), small in diameter, usually not exceeding 30 mm [15]. Their location was usually in the medullary and papillary parts of the kidneys [15]. In about 30% of patients, there are cases of larger cysts (25-65 mm in diameter) with cortical localization [15]. They are almost always accompanied by microcalcifications, referred to by radiologists as "hyperechoic spots" or "hyperechoic lines", with a medullary location or renal stones 3-10 mm in diameter [12, 15]. Another examination that can just as often incidentally show MSK is an X-ray [15]. To better show the lesions, an intravenous pyelogram is used, showing the cysts as clusters of light, with the entire kidney giving the image of a "bouquet of flowers," a "bunch of grapes," or a "paintbrush," due to the distally present microcalcifications in the collecting ducts [16]. This method all the time remains the gold standard for diagnosing MSK with the highest sensitivity [17]. As for computed tomography, more and more centers are moving away from the idea of using contrast in genitourinary imaging diagnosis, which carries over to the increasingly rare diagnosis of the condition by this method [14]. The radiologist may then encounter a pitfall in the form of "white pyramiding," which manifests as hyperdense renal pyramids that have the appearance of triangular structures with a high degree of attenuation [16]. If, on the other hand, the patient is given a contrast agent, which is useful in this case, the image shows dilated renal tubules and a "brushy appearance," just like an X-ray [16].

HISTOPATHOLOGICAL EXAMINATION. Tests that interfere directly with the patient's body, such as endoscopy or kidney biopsy, can give the doctor 100 percent confirmation of the disease, but because of their invasiveness, there must be factually supported arguments to refer the patient for such testing [14]. A pathomorphologist seeing the specimen will notice dilated papillary collecting ducts lined with cubic epithelium [18]. Within the cyst, there may be severe inflammation and interstitial scarring [14, 18]. The renal cortex usually remains intact [14]. On macroscopic evaluation, cysts not exceeding 1 cm in diameter in the pyramidal part of the medulla [14].

2.4. TREATMENT

Once all the diagnostics have been performed and the severity of the condition has been determined, various therapeutic methods are available, both invasive and non-invasive, depending on the patient's condition and how the disease manifests itself, or how severely it affects the patient's life [13]. If MSK does not produce any bothersome symptoms, periodic urinalysis (such patients have a greater tendency for hypercalciuria and hypocitraturia) and abdominal review x-ray are recommended [1]. Currently, there is no causal treatment for the condition in question, patients can only focus on preventing or treating complications [6]. To prevent URI and the formation of kidney stones, it is recommended to drink plenty of fluids to produce 2-2.5 liters of urine per day, which will give a more dilute urine and reduce the risk of stone accumulation and flush out lingering bacteria in the urinary tract [9]. The patient should also modify his diet, limiting animal protein, which is rich in meat, fish and eggs and promotes the formation of stones consisting of uric acid and calcium [21]. It is also necessary to stop dishes containing large amounts of sodium, which causes greater excretion of calcium in the urine [21]. When the patient is over the age of 50, specialists recommend consuming more calcium (about 1,200 mg per day) [22]. The mechanism in which it is involved involves the binding of calcium oxalate in the digestive tract, which prevents it from passing into the urinary tract and forming stones [22]. In addition, it is recommended to undergo ongoing care from a dietitian, who will modify the diet on an ongoing basis depending on the patient's condition and needs [21]. Oral preparations that will reduce urinary calcium, such as sodium citrate and thiazides, are also available [14]. The patient should also pay more attention to personal hygiene [6]. Those prone to frequent and recurrent urinary tract infections should take low doses of antibiotic regularly as a prophylaxis [23]. If the formation of URI is confirmed, antibiotic therapy appropriate to the culture result should be implemented [6]. Small stones usually do not produce major symptoms or resolve spontaneously, but in situations of larger diameter or more intractable symptoms, it is necessary to implement surgical intervention or use shock wave lithotripsy [6]. Examples of the first method include ureteroscopy, which breaks up the stone using a laser, and percutaneous nephrolithotomy, in which the stone is removed using a nephroscope inserted through an incision in the back [21, 22, 24]. The second method, on the other hand, involves breaking the stone into smaller ones, as small as a grain of sand, which will be passed in the urine up to several weeks after the procedure [21]. The equipment used for this procedure, called a lithotripter, generates sound waves that destroy the stone in the form of a shock wave [21]. Although the procedure is performed extracorporeally and is completely non-invasive, there is sometimes a need for local or general anesthesia [21].

3. CONCLUSIONS

Medullary sponge kidney is a rare condition that is still poorly understood and extremely difficult to diagnose. Through its nonspecific symptoms, lack of symptoms or poor presentation, it is sometimes a disease that takes years to develop in an unsuspecting patient. Although the condition is asymptomatic in most cases, possible complications such as kidney stones and URI can bring considerable discomfort to life. It also doesn't help that the exact genesis of MSK has yet to be investigated and the causal treatment undeveloped. Patients are left with the constant care of a specialist and the prevention of possible complications. It is important here that the public is aware of how much preventive abdominal imaging can give, not only in relation to the pathology in question. However, due to the problems associated with an uneasy diagnosis, not only radiologists, but also urologists, pathomorphologists or at least primary care physicians should have the appropriate skills and patience.

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