



Multilocular Cystic Nephroma—A Brief Review

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Abstract

Cystic renal neoplasms can be classified as benign and malignant, consisting of multilocular cystic renal cell cancer, cystic renal cell cancer, multilocular cystic nephroma and benign multilocular cysts. The objective of this article is to summarize the clinical aspects of multilocular cystic nephroma and discuss the major similarities that provoke difficulties in proper diagnosis and treatment.

Subject Areas

Urology, Nephrology

Keywords

Cystic Nephroma, MCN, Renal Neoplasms, Urology, Kidneys

1. Introduction

Multilocular Cystic Nephroma (MCN) is a controversial, rare, non-genetic type of benign kidney tumor. It's usually a mixed mesenchymal and epithelial [1] [2] [3], slow growing, unilateral mass of the lower pole of the kidney composed of numerous cysts, without solid elements. It has an excellent prognosis [4]. While the clinical, radiologic, and histologic features of cystic nephroma are well described, the immunohistochemical features are not [5].

More than 200 cases have been reported in literature [3] [6]. They were previously known as multilocular cystic renal cell carcinomas. In literature you may also stumble upon the terms multicystic nephroma (MCN), polycystic nephroblastoma, cystic nephroma, cystic renal hamartoma, cystadenoma, mixed epithelial stromal tumor (MEST) and renal epithelial and stromal tumor (REST) [1] [2] [6]. REST can be used to beset MCN and MEST.

This tumor is most common upon female patients around 40 to 60 years of age with a male to female ratio of 1:8 [1] [2] [3] but it is also described in infants

around the ages of 2 to 4 years old of which 73% are males [2] [3], with a male to female ratio of 3:1. Thus, it can be classified as congenital, affecting infant males, or acquired affecting mostly postmenopausal females with a male to female ratio of 1:9. The congenital form is usually observed in infants under the age of two, with male to female ratio 2:1 [6].

2. Discussion

It was initially marked out in 1892 by Edmunds as a cystic adenoma of the kidney [2] [6]. The definition multicystic nephroma was first proposed in 1951 and later modified and further redivided into cystic nephroma and cystic partially differentiated nephroma depending on the absence and presence of blastemal elements [2].

It must be noted that they are considered to be a separate type of nephroma in comparison with pediatric cystic nephroma according to the 2016 WHO classification [1]. They differ on both immunohistochemical and genetic bases. They were also renamed as multilocular cystic renal neoplasms of low malignant potential due to the fact that they have no recurrence or metastasis in patients.

According to the World Health Organization (WHO) they are classified under the mixed epithelial-stromal tumors of the kidneys [6].

This tumor appears to be influenced by hormones since it mostly affects females, especially if they have a history of oral intake of estrogens. Cases have also been reported consisting of male patients with a history of hormone manipulations for prostate cancer [6].

Even though MCN is not considered a premalignant condition, there are cases reporting co-existing foci of renal cell carcinoma in the lining of the cyst wall [2].

In the past they were considered to be developmental defects of neoplastic origin probably raised from the ureteral bud with malignant potential [2] [7]. Bahubeshi *et al.* reported that mutation of germline DICER1 is associated with familial cystic nephroma [4].

In 1956, Boggs and Kimmelstiel first proposed the true neoplastic nature of the lesions in a case report, suggesting the term benign multilocular cystic nephroma for this condition [7].

3. Diagnosis

3.1. Clinical Presentation

These types of nephroma are often accidentally discovered while patients undergo imaging for other reasons of medical assessment do to the fact that they are mainly asymptomatic by nature. Clinical presentation though nonspecific may consist of abdominal pain, loin pain and a palpable and painless abdominal mass [1] [8], along with urinary tract infection and hematuria (due to extension of the tumor to the renal pelvis) [2] and hypertension (in adults) [6]. Pleuropulmonary blastoma can be seen in these patients and in their families [9].

3.2. Imaging

a. On X-ray imaging they may be identified as large masses displacing and effacing the bowel loops. Calcifications are sparsely seen (**Figure 1**).

b. On ultrasonography the radiographer observes an irregular cystic mass coming from the kidney and may recognize the claw sign which can play a decisive role in the diagnosis (**Figure 2**). The cysts show up as hypoechoic lesions delineated by hyperechoic septae [2]. Sonographic findings relate to the size of the locules. When locules are small, a non-specific complex intra-renal mass is demonstrated. In contrast, when locules are large the sonogram will demonstrate a renal mass with multilocular configuration, discrete septa and sono-lucent spaces [6]. Calcifications are rarely seen [6].

c. On computed tomography pyelography (CTIVP) the cystic mass is easier to identify along with variable septal enhancement, with well-defined margins and herniation in the renal pelvis. No contrast excretion is seen in the cystic components [1] [3]. Delayed excretion with hydro-calycosis or no visualization occurs in cases with obstruction by pelvic herniation of the tumor [6] (**Figure 3**).

It usually falls in the Bosniak III classification of renal cystic masses with a potential of malignant risk of 60% [3]. In addition, according to Ian M. Silver, visualization of an ectopic ureterocele also suggests a diagnosis of multicystic



Figure 1. Excretory urography X-ray showing a mass on the left kidney [10].

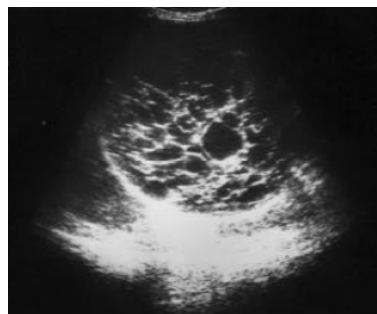


Figure 2. Abdominal ultrasound showing a left MCN [11].

dysplastic kidney [8].

The Bosniak classification for computed tomography is helpful in determining the risk of malignancy. However, multilocular cystic nephroma is usually assigned to Category III and above, and the malignant potential is greater than 54% [4].

Bosniak is a classification system of renal cystic masses and divides them into five categories. It was named after Morton A. Bosniak, a professor in radiology at New York University Langone School of Medicine. It supports the process of predicting the risk of malignancy and implying treatment and follow ups. Bosniak I classification refers to benign, simple cysts with no potential of malignancy; Bosniak II to reliably benign cysts that are minimally complex with no risk of being malignant; Bosniak III to cysts that are intermediately complex with 55% risk of being malignant; and Bosniak IV consists of cysts that are approximately 90% likely of being malignant [12] [13].

d. MRI imaging is sparsely indicated. It reveals images with variable signals and hyperintense cysts. Septa are usually hypointense on all sequences due to fibrous content [1] [2] (Figure 4).

e. Angiography would not help with the diagnosis because MCN may be hypovascular, hypervascular or even avascular [2] (Figure 5).

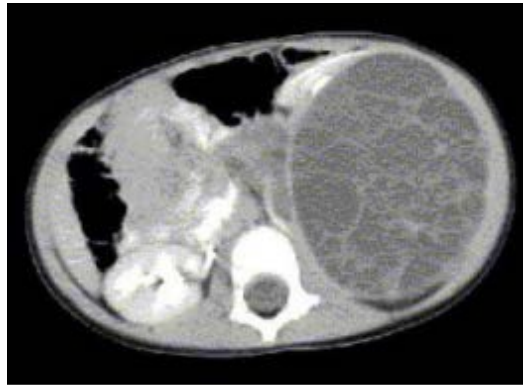


Figure 3. Computed tomography scan showing a left MCN [7].

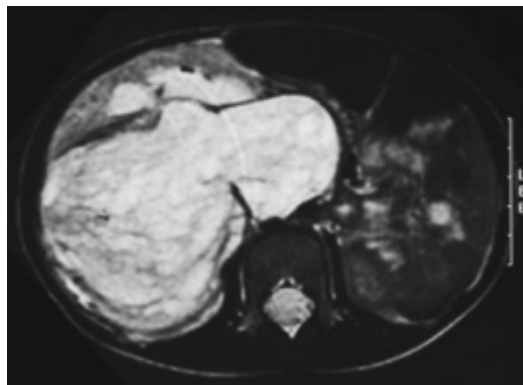


Figure 4. Axial MRI showing a large right MCN [7].

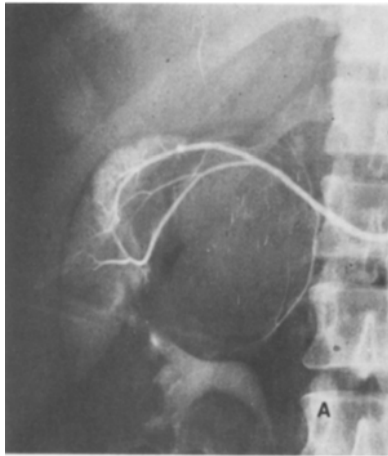


Figure 5. Angiogram showing a poorly vascularized space-occupying process (MCN) [14].

As of the 1990s, CT became the primary imaging examination for the evaluation of MCN [1] [7]. The cross-sectional imaging techniques of CT, ultrasound, and MRI show the multilocular cystic features of MCN but unfortunately cannot be used to accurately differentiate MCN from other complex cystic renal masses, particularly a subset of cystic renal cell carcinomas [3].

f. Finally, scintigraphy of the kidneys can be performed. Scintigrams demonstrate a defect corresponding to the renal mass.

Nuclear medicine studies have a low degree of confidence in the diagnosis of multilocular cystic nephroma specifically. Although a general nonspecific renal mass can be identified, details cannot be differentiated. The lack of precision results in high false-positive and false-negative rates because of the inaccuracy of the method [7].

Patients are usually led to partial or radical nephrectomies due to difficulties on proper diagnosis solely on imaging which generally has suspicious and malignant features.

3.3. Percutaneous Renal Biopsy

An alternative approach favors the use of percutaneous renal biopsy for indefinite masses in an effort to reduce the number of surgical interventions and related complications [4]. This is risky though due to the potential for tumor seeding of the needle track and morbidity of the procedure. However, the risk of seeding is considered rare and the morbidity of the procedure in comparison with surgical intervention is, in general, less pernicious [2] [6] [15]. Other problems are that biopsy results may not be representative of the entire mass and that there are limitations immanent to this procedure compared with the biopsy of solid masses [3].

Shannon *et al.* reported that among 235 biopsies for less than 5 cm incidental renal masses, 184 (78%) were diagnostic and 51 (22%) were nondiagnostic due to insufficient material. Diagnostic biopsies revealed 138 malignant (75%) and

46 benign (25%) lesions. For a small renal mass (<4 cm), preoperative renal biopsy can be considered and has the potential to avoid a significant number of major surgical procedures [4].

3.4. Differential Diagnosis

Differential diagnosis may vary as they may appear to be malignant on imaging, posing as cystic renal cell carcinomas, cystic partially differentiated nephroblastomas, lymphangiomas, cystic standard nephroblastomas (cystic Wilms tumor), cystic mesoblastic nephroma and other renal cysts, multicystic dysplastic kidney, medullary sponge kidney, tubulocystic carcinoma [4]. It is not easily differentiated from multilocular cystic renal neoplasm of low malignant potential. The overall final diagnosis is made after excision of the tumor.

3.5. Histopathology

Macroscopically, MCN is an encapsulated, well-demarcated tumor, composed entirely of numerous cysts and septa without solid areas. The cysts consist of serosanguineous fluid and the tumor may be focal or replace the whole kidney, being 5 - 20 cm in diameter [9] [15].

Microscopically on histopathology, micrographs reveal cysts lined by a simple flat, cuboidal or hobnail epithelium and seta variably lined by fibrous and or ovarian-like stroma. They appear as unifocal multiloculated cystic masses surrounded by a thick fibrous and compressed parenchyma. These features have great similarities with other cystic tumors and cause confusion in the diagnosis [1] [5] [6] [9] [15].

These tumors are also positive to estrogen receptor immunostaining patterns, and progesterone receptors in ovarian type stroma, vimentin and desmin in stromal cells, keratin in epithelium as well as CD10, calretinin and inhibin probably due to the ontogenic similarity to the ovarian stroma and smooth muscle differentiation [6] [9] [10].

Boggs and Kimmelstiel defined certain criteria in order to enable the differentiation from polycystic disease, multicystic kidneys, simple renal cysts and cystic renal cell carcinoma. These criteria include: multilocular lesion, cysts lined with epithelium, cysts that do not communicate with the pelvis and normal residual renal tissue. While the histologic features of CN are well described [1], final pathologic diagnosis is almost exclusively based on immunohistochemistry [6].

3.6. Treatment Options

Because neither the clinical nor the imaging features of MCN can predict its histologic characteristics, radical or nephron sparing nephrectomy, with or without lymph node excision, depending on the site and size of the lesion, is required for both diagnosis and treatment [1] [2] [8]. Although surgical resection remains the standard of care for small renal masses, cryoablation and radiofrequency ablation have emerged as minimally invasive treatment alternatives [4].

It is generally perceived that Imaging-guided RFA and cryoablation are effective and safe treatments of Bosniak III and IV cystic renal neoplasms with outcomes comparable to those of surgical therapies and long term follow ups have demonstrated low recurrence rates [16] [17].

There is currently no data referring to the outcomes of these techniques in this particular kidney tumor.

Therefore, the Bosniak classification is not an absolute criterion for determining the need for surgical intervention in renal mass treatment. Tumor size and the potential impact on renal function if the tumor is removed should be strongly considered when deciding on surgical intervention [2] [8]. Elective partial nephrectomy is acceptable if the tumor is 40 mm or smaller and if the contralateral kidney function is preserved. In our literature review, the most common presentation of MCNs was as a unilateral single mass, with a median size of 100 mm in patients 10 years old or younger and 73 mm for those 11 years old or older. More recent studies in the literature have stated that tumors within the kidney between 40 and 70 mm may also be candidates for a more conservative surgical approach [3].

4. Conclusions

MCN is a rare lesion and is not a premalignant condition in children and adults. Nonspecific clinical presentations and confusing radiological features create difficult preoperative differentiation from other cystic renal neoplasia's [2] [6].

Despite the advances in pathology and radiology, MCN still remains a surgically treated lesion. With no definitive features that allow confident pre-operative diagnosis [2].

Imaging evaluation is important for suggesting the diagnosis of MLCN but has several limitations, and it is not enough to distinguish between malignant and benign complex cysts [3].

Overall, cystic kidney tumors are still prone to confusion and dilemma in preoperative diagnosis because they have a diffuse cystic growth development and are similar in their macroscopic appearances [15].

Surgical excision is curative for multilocular cystic nephroma. Although the prognosis is excellent, long-term follow-up for local recurrence is still recommended because three cases of local recurrence have been reported [4].

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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Abbreviations

MCN: multilocular cystic nephroma
MEST: mixed epithelial stromal tumor
REST: renal epithelial and stromal tumor
WHO: World Health Organization
CTIVP: computed tomography pyelography
MRI: magnetic resonance imaging
CT: computed tomography