Misty Mesentery in Patients with Ureterolithiasis: Just Coincidence?

Kirli Mezenter ve Üreterolitiazis Birlikteliği Tesadüf mü?

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ABSTRACT

Objective: The purpose of this study is to evaluate the misty mesentery sign on computed tomography in patients with ureterolithiasis.

Methods: This retrospective study enrolled all consecutive patients with ureteral stone diagnosed in abdominal computed tomography in the 3-year study period. Computed tomography scans were reviewed to assess the presence and interrelations between misty mesentery, ureteral diameter, volume and location of stones, presence of periureteral and perinephric stranding, thickening of the perirenal fascia, nephromegaly, and grade of hydronephrosis.

Results: Four hundred thirty-four patients were included in the analysis. Misty mesentery was identified in 62 (14.2%) patients. Patients with misty mesentery were significantly older (mean age=45.2±12.2) than those without (mean age=37.3±10.9) (p=0.022). Perirenal fascial thickening was identified in 101 (23.2%) patients and found to be significantly associated with misty mesentery (χ²=7.74, p=0.005). Two hundred patients (46%) were noted to exhibit periureteral stranding which was noted to be significantly related with misty mesentery (χ²=13.6, p=0.000). The relationship between misty mesentery and pelvicalyceal ectasia, perinephric stranding, ureteral location of the stone, and nephromegaly were not found statistically significant.

Conclusions: Ureterolithiasis can be accompanied by misty mesentery at computed tomography examination. There may be a potential association between ureterolithiasis and misty mesentery.

Keywords: Mesentery, diagnosis, ureterolithiasis, ureteral calculi, multidetector computed tomography

ÖZ

Amaç: Bu çalışmanın amacı, üreterolitiazis hastalarında bilgisayarlı tomografi üzerindeki kirli mezenter bulgusunu değerlendirmektir.

Yöntem: Bu retrospektif çalışma 3 yıllık zaman aralığında abdominal bilgisayarlı tomografi ile üreter taş tanısı konulan tüm hastalar dahil edildi. Bilgisayarlı tomografi görüntüleri, kirli mezenterin varlığı ve ilişkilerini, üreter çapı, taşların hacmini ve yerini, periüreteral ve perinefrik yağlı planlarda çizgilenmenin varlığını, perirenal fasya kalınlaşmasını, nefromegali ve hidronefroz derecesini değerlendirmek için gözden geçirdik.

Bulgular: Çalışmaya 434 hasta dahil edildi. Hastaların 62’sinde (%14,2) kirli mezenter saptandı. Kirli mezenterli olan hastaların yaş (yaş ortalaması, 37,3±10,9) olmayanlara kıyasla anlamlı olarak daha büyük bulundu (yaş ortalaması, 45,2±12,2) (p=0,022). Perirenal fasyal kalınlaşma 101 (%23,2) hastada belirlendi ve kirli mezenter ile anlamlı bir sekilde ilişkilidir (χ²=7,74, p=0,005). İki yüz hastanın (%46) kirli mezenter ile anlamlı bir ilişki olduğunu belirtilen periüreteral yağlı planlarda çizgilenme, perinefrik yağlı planlarda çizgilenme, taşın üretral yerleşimin yerli ve nefromegali arasındaki ilişki istatistiksel olarak anlamlı bulunmadı.

Sonuç: Bilgisayarlı tomografi ile üreterolitiazis ve kirli mezenter birlikte izlenebilir. Üreterolitiazis ve kirli mezenter arasında potansiyel bir ilişki olabilir.

Anahtar kelimeler: Mezenter, taş, üreterolitiazis, üreteral taş, çok kesitli bilgisayarlı tomografi

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INTRODUCTION

“Misty mesentery” (MM) is a term indicating a pathological increase in mesenteric fat attenuation in computed tomography (CT). It is frequently observed on multidetector CT (MDCT) scans performed during routine clinical practice, and can be associated with various pathological conditions such as edema, inflammation, hemorrhage, or neoplastic infiltration. In patients with an acute abdominal disease, an MM sign can be considered as a feature of an underlying disease.

MDCT is a sensitive and reliable imaging modality commonly used to evaluate the presence and location of the ureteral stones. With a rise in the frequency of abdominal MDCT use in the diagnosis of urolithiasis, other coexistent unknown pathologies are also encountered, sometimes complicating the clinical picture. In our daily CT reporting sessions, we encountered cases of ureterolithiasis with coexistent MM. An association of MM with urolithiasis has not been thoroughly investigated so far. The present study is designed to evaluate prevalence and possible association of MM in patients with ureterolithiasis detected on CT.

MATERIAL and METHODS

Patient selection

This study was approved by the local Ethics Committee (Acibadem University Ethics Committee November 22nd, 2018, 2018/18). Abdominal CT examinations of all consecutive patients (n=479) with ureterolithiasis applied between January 2013 and December 2016 were reviewed retrospectively. Medical records of the patients were reviewed for clinical histories, previous abdominal surgery, and laboratory data. A total of 27 patients including cases with coexistent diseases known to be associated with MM such as hypoproteinaemia, heart failure, nephrosis, cirrhosis, inflammatory diseases of the gastrointestinal tract such as cholecystitis, pancreatitis, diverticulitis, and inflammatory bowel disease, malignancy, ischemia, autoimmune diseases, vasculitis, previous abdominal surgery, or trauma, were excluded from the study. Central mesenteric density could not be evaluated in 18 patients due to paucity of intra-abdominal fat. The remaining 434 patients (334 men, 100 women) were included in the analysis.

CT imaging

All patients had undergone CT performed using a 64-detector CT scanner (Definition, Siemens, Forchheim, Germany) without IV and oral contrast medium. Unenhanced MDCT parameters dedicated for the imaging evaluation of urinary stone disease in our institution are: acquisition 24x1.2 mm, slice collimation 1.2 mm, slice width 3 mm, pitch 1.2, effective mAs 210; kVp, 100-120. Scanning was performed with the patient laid in supine position and images were obtained from the top of the kidneys through the base of the urinary bladder in a single breath hold. Imaging data were postprocessed (Leonardo workstation, Siemens Medical Solutions, Germany) and multiplanar reconstructions were performed. In 19 patients documents of follow-up abdominal CT examinations were present and they were evaluated for the changes of the MM.

Image analysis

Two radiologists with a 10-year experience in abdominal radiology separately reviewed the CT scans to assess the presence and distribution of MM. There were discrepancies in interpretations of two radiologists on detection of MM in only four patients’ (0.9%). Other variables were evaluated by two radiologists jointly and the conclusion was achieved by consensus.

Diagnostic criteria of MM were well-defined mass with fatty or soft tissue density at the root of the small bowel mesentery with an attenuation value higher than the retroperitoneal and subcutaneous fat tissue; encircled but not displaced mesenteric vessels by this mass; well-defined soft tissue
nodules within the mass; hypodense fatty halo enclosing vessels or nodules and a hyperdense stripe partially surrounding the fatty mass. Density values in Hounsfield unit (HU) of the retroperitoneal and subcutaneous fat and misty mesentery avoiding vessels, bowel loops and if any, soft tissue nodules were obtained by circular standard ROIs including at least 20 pixels. Density measurements were obtained from the three separate areas of subcutaneous fat, retroperitoneal fat and involved mesentery in the same 3-mm-thickness noncontrast unenhanced axial CT image.

We have evaluated the distribution of the MM in three separate categories: jejunal mesentery, ileal mesentery, sigmoid mesentery. Presence of hypodense fatty halo enclosing vessels or nodules (fat ring sign) and a hyperdense stripe partially surrounding the fatty mass were evaluated. Maximum thickness of the involved mesentery, short diameter of the soft tissue nodules and maximum diameter of mesenteric vessels in the MM were also evaluated.

Ureteral diameter, volume and location of stones, presence of perinephric and/or periureteral stranding, thickening of the perirenal fascia, nephromegaly, and grade of hydronephrosis were also evaluated. The ureteral diameter was determined as the largest transverse dimension 1 cm below the ureteropelvic junction at the effected side. The severity of hydronephrosis was assigned to one of the groups as Grade 1 (mild), Grade 2 (moderate), and Grade 3 (severe). The stone volume (SV) is calculated by multiplying length (l), width (w), and depth (d) of the stone in millimetres with a constant of 0.52 according to the formula: $SV = lwxdxm \times 0.52^9$. The locations of the stones were classified as proximal, mid, and distal ureter. The presence of perinephric or periureteral stranding was determined based on the heterogeneity of the adjacent adipose tissue and its comparison with the opposite side. If perinephric changes were noted in both kidneys, perinephric spaces were evaluated for symmetry and the presence of more extensive changes on the symptomatic side were considered as positive findings. Thickness of the renal fascia was also evaluated in comparison with that of the contralateral side. Nephromegaly was assessed by measuring the length and parenchymal thickness of both kidneys and asymmetrical increases were stated.\cite{12}

Statistical analysis
Categorical variables were compared via chi-square test and means of numeric variables were compared with t-test in SPSS software (version 17.0; SPSS; Chicago, Illinois, USA). Statistical significance was considered when p values were below 0.05. Pearson’s correlation coefficient was measured to demonstrate the correlation (if any) between the interpretations of the images for the presence of MM by the two radiologists.

RESULTS
Four hundred and thirty-four consecutive patients [334 men (77%), 100 women (23%)] with ureterolithiasis admitted to the emergency department and urology outpatient clinic were recruited for the study. Mean age of the patients was 38.4±11.5 years [range, 18-85]. MM was present in 62 (14.2%) patients. Pearson’s correlation coefficient (r) was calculated as 0.964 (p<0.001).

Fourteen women (22.6%), and 48 (77.4%) men had MM in CT images ($x^2=1.26$, p<0.001). Patients with MM were significantly older (mean age, 45.2±12.2 years) than those without (mean age, 37.3±10.9 years) (t-test, p=0.022).

The mean mesenteric density was -79.4±9.1 Hounsfield Units (HU) (range=-50-96) in patients with MM, which was significantly higher than those of retroperitoneal (mean, -102.9±5.2 HU) and subcutaneous fatty tissue (mean -105.7±6.2 HU) (paired t-test, p<0.001). The thickness of the affected mesenteric fat tissue was 42.9±13.1 mm. MM was localized on the jejunal mesentery in 55 (88.7%), and on both jejunal and ileal mesenteries.
in 6 (9.7%) patients. In one patient (1.6%) sigmoid mesentery was also involved in addition to jejunal and ileal mesenteries. A hyperdense stripe partly surrounding involved mesentery was present in 32 (51.6%) patients. A hypodense fatty halo was present in 17 (27.4%) patients. Well-defined nodules of soft tissue density was present in all patients with a mean short diameter of 5.4±1.6 mm (range, 2-9.3 mm). The mean diameter of the involved mesenteric veins was 3.2±0.6 mm (range, 2-4.3 mm).

Perirenal fascial thickening was identified in 101 (23.2%) patients, including 23 (23%) cases with misty mesentery. Fascial thickening was found to be significantly correlated with MM ($x^2=7.74$, $p=0.005$) (Table 1).

Table I. The relationship between misty mesentery and age, perirenal fascial thickening, periureteral stranding, pelvicalyceal ectasia, nephromegaly, perinephric stranding.

<table>
<thead>
<tr>
<th></th>
<th>Misty Mesentery (+)</th>
<th>Misty Mesentery (-)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr) (n=62)</td>
<td>45.2±12.2</td>
<td>37.3±10.9</td>
<td>0.022</td>
</tr>
<tr>
<td>Perirenal fascial thickening (n=101)</td>
<td>23</td>
<td>78</td>
<td>0.005</td>
</tr>
<tr>
<td>Periureteral stranding (n=200)</td>
<td>42</td>
<td>158</td>
<td>0.000</td>
</tr>
<tr>
<td>Pelvicalyceal ectasia (n=335)</td>
<td>55</td>
<td>280</td>
<td>0.64</td>
</tr>
<tr>
<td>Nephromegaly (n=144)</td>
<td>23</td>
<td>121</td>
<td>0.47</td>
</tr>
<tr>
<td>Perinephric stranding (n=190)</td>
<td>34</td>
<td>156</td>
<td>0.058</td>
</tr>
</tbody>
</table>

Two hundred patients (46%) exhibited periureteral stranding, and 42 (21%) of them were found to be associated with MM. Periureteral stranding was found to be significantly correlated with the presence of MM ($x^2=3.59$, $p=0.058$).

Perinephric stranding was present in 190 patients (43.8%), in 34 of which (17.8%) MM was present ($x^2=0.50$, $p=0.47$).

The relationship between MM and pelvicalyceal ectasia, perinephric stranding, ureteral location of the stone, and nephromegaly was not found to be statistically significant.

The mean diameter of the calculi was 8.33±3.16 mm (range, 3-28). Stone volume ranged between 2 and 7900 mm$^3$ and median stone volume was 114.2 mm$^3$. The median stone diameters in patients with and without MM were comparable (8.19 and 8.36 mm, respectively, t-test, $p=0.70$). The median stone volumes in patients with, and without MM were 69.6 mm$^3$, and 121.7 mm$^3$, respectively (t-test, $p=0.49$).

Nineteen patients underwent one follow-up CT examination with an interval of 1 month to 3 years from the initial examination. The density and size of the MM was slightly increased in two, and
decreased in 3 patients with MM in follow-up CT examinations. CT findings were stable in the remaining 14 patients. In one patient, we found images of CT examination in our digital archive which was performed one year before due to another indication and did not reveal the presence of MM.

DISCUSSION

In CT, normal mesenteric fat appears homogenous with an attenuation similar to that of the retroperitoneal and subcutaneous fat tissues. Although the disease has had alternative terminology including retractile mesenteritis in 1924, mesenteric lipodystrophy’’ in 1955 and “mesenteric panniculitis” (MP) finally recognized by Ogden et al., with technological advancement and better disease definition the term “misty mesentery” (MM) used by Mindelzun et al. indicates a pathological increase in mesenteric fat attenuation in CT (Figs. 1 and 2). Furthermore, all of these subdivisions can be defined as “sclerosing mesenteritis” (SM) totally and have many names according to underlying predominant inflammatory pattern.

MM may be an incidental finding in an asymptomatic patient imaged for other clinical reasons. However, it may also be caused by various pathological conditions including mesenteric edema, lymphedema, inflammation, hemorrhage, trauma and neoplasm. Additionally Unlu et al. revealed that prevalence of idiopathic incidental misty mesentery appearance was 7% in obese patients based on the high body mass indices of these patients, chronic low grade inflammatory changes induced by adipose tissue deposition which are suggestive of an association between obesity and appearance of MM on CT.

To our knowledge, an association between urolithiasis and MM has not been thoroughly investigated previously. In a study investigating prevalence of SM and associated diseases, Canyigit et al. evaluated 2100 patients and detected 51 (2.4%) patients with MM findings. Urolithiasis has been detected as an associated factor in 10 (19.6%) of 51 patients with MM on that study. However, it was not stated whether nephrolithiasis or urolithiasis was associated with SM.

Normal mesenteric fat has a density between -100 and -160 HU, and the mean mesenteric...
density increases with infiltration by fluid or cells. The density of MM may have different values depending on the severity and cause of the disease. It is lowest in lymphedema and increases progressively in edema, inflammatory and neoplastic cell infiltration, hemorrhage, and fibrosis. Mindelzun et al, Canyigit et al, Daskalogiannaki et al. also measured the mean mesenteric density value as -40 (-60), -62±18.6, -54±2, respectively in their heterogenous patient groups. In our homogenous patient population with ureterolithiasis, the mean mesenteric density was distinctively found to be lower (-79.4 ±9.1 HU). In other studies, inclusion of other causes of MM, such as severe forms of inflammatory processes and neoplasms, may be the cause of their higher mean mesenteric density values. Lower mean mesenteric density values in our study may be representation of mesenteric lymphedema, edema, or less severe forms of inflammatory infiltration as a cause of increased mesenteric density.

MM might be the result of renal urine leaks caused by urinary tract obstruction as reported to be associated with SM. Renal urine leaks result from disruption of the calices, infundibula, or renal pelvis. Most common cause is renal trauma, but it may also be the result of transmitted back pressure caused by obstruction of the genitourinary system due to a ureteral stone or pelvic mass, pregnancy, retroperitoneal fibrosis, posterior urethral valves, or bladder outlet obstruction. Although the root of the small bowel mesentery is contiguous posterolaterally to the anterior pararenal space, there is no communication between the pararenal space and the intraperitoneal compartment to allow passage of urine leaks from perinephric and pararenal spaces into intraperitoneal compartment. There is also no known interconnection between retroperitoneal lymphatics draining renal and perirenal areas in urinary tract obstruction and intraperitoneal lymphatics to account for increased mesenteric density in ureterolithiasis. Therefore other mechanisms might be responsible for the development of MM in patients with ureterolithiasis other than direct passage of urine leaks from retroperitoneal into intraperitoneal compartments.

In their study, Canyigit et al. suggested that nonspecific chronic inflammatory reaction in SM is triggered by independent factors that cause disturbances of proinflammatory and anti-inflammatory cytokines in mesenteric fat. We suggest that urine in perinephric and pararenal spaces may incite an inflammatory response by adipocytes causing SM-like changes in intraabdominal adipose tissue as defined in the previous study regarding obesity and MM. We believe this might be pathogenetic mechanism for the cause of MM in patients with ureterolithiasis.

The predilection for SM in the segmental involvement of the jejunal mesentery is striking which was present in our 55 (88.7%) patients. Although prior studies have described a very strong association between MP and malignancy because of inclusion of patients with a known history of cancer, Ehrenpreis et al. showed that only 1.4% of patients had a CT finding of mesenteric panniculitis. In addition to representing the occurrence of a new cancer, this study indicated that follow up abdominal CTs in patients with known malignancies did not demonstrate a worsening in disease state or worsening of MP.

Autoimmune response to unknown sources and ischemia of the mesentery have been proposed as pathogenetic mechanisms. Although CT findings may be suggestive, histologic confirmation is necessary for definite diagnosis. On CT scans, mesenteric panniculitis and mesenteric lipodystrophy stages of SM are manifested as a well-circumscribed inhomogeneous fatty mass at the root of the mesentery. The two CT findings which were considered specific for this disorder include: a fat ring sign that reflects preservation of fat around the mesenteric vessels, and presence of a hyperdense stripe which is a tumoral pseudocapsule partially or completely surrounding the
fatty tissue. On CT a hyperdense stripe partly surrounding involved mesentery was present in 32 (51.6%) patients, whereas fat ring sign was present in 17 (27.4%) patients in our study.

In a study by Daskalogiannaki, comprising a selected group of patients that had undergone CT examination for various indications, the prevalence of SM was found to be 0.6% in over 7000 abdominal CT examinations. In the study by Canyigit, prevalence was higher in Turkish population (2.4%). MM was present in 62 (14.2%) of 434 patients with ureterolithiasis in our study, a high prevalence for a change coexistence. By carefully reviewing patients’ medical records for clinical histories, previous abdominal surgery, and laboratory data, we have tried to rule out other coexistent diseases and factors that might cause SM in a homogenous patient group that was presented with acute flank pain and evaluated for ureterolithiasis in an emergency setting. However, there are such a large number of possible associated diseases and factors that, it seems to be very difficult to completely exclude all the factors that may be involved in to determine a causal relationship between urolithiasis and MM.

We evaluated not only the prevalence but also the relationship between MM and secondary CT findings of obstruction, such as perinephric and periureteral stranding, thickening of the perirenal fascia, nephromegaly, and grade of hydronephrosis in ureterolithiasis. The kidney responds to the increased pressure in the ureter with resorption of urine through pyelosinus, pyelotubular, pyelolymphatic, and pyelovenous backflow mechanisms in acute obstruction. As our data suggest, there is a significant relation between coexisting perirenal fascial thickening, periureteral stranding, and MM. Although all the secondary signs of urinary obstruction have the same etiologies including backward pressure, and peaks at approximately 6-8 hr of pain duration pelvicalyceal ectasia, perinephric stranding, and nephromegaly, were not found to be significantly associated with MM contrary to the expectation. Perirenal fascial thickening and periureteral stranding might be developing at different time points compared to other secondary findings during the period of urinary obstruction. But, we did not evaluate the duration of pain due to unavailable data in the medical records in most of the patients so as to estimate the duration of obstruction, which might be important for the development of MM.

In our study, age was found to be another significant factor associated with the presence of MM. It has been reported that the incidence of SM increases with age, being more frequent between the 6th and 7th decades of life. Although the patients with MM were significantly older than those without in our study, mean age was 45.2±12.2 years, younger than age group of SM. Our data and study of Unlu et al. are alike regarding mean age of these patients. Since SM is associated with many diseases and risk factors, different diseases might effect different age groups in SM.

One of the limitation of this study was that follow-up CT examinations were performed in only 19 patients so as to evaluate temporal changes in the mesenteric density as the obstruction is relieved. Because, in our center, follow up of patients with known ureterolithiasis are preferably performed with direct urinary system radiograms and ultrasonography due to radiation-exposure concerns. Follow-up MDCTs of the 19 patients were performed 1 month-3 years after the first examination, either due to another attack of urolithiasis (12 patients), or to confirm the passage of the stone (7 patients). The density and size of the MM was slightly increased in two patients as detected in follow-up CT examinations (Figs. 3a and 3b). In one patient, ureteral stone did not pass and MM has become more prominent with the increased duration of obstruction in follow-up CTs (Figs. 4a and 4b). The density and size of the MM was slightly decreased in three patients. The CT findings were stable in remaining 14 patients. The
previous event does not exclude the possibility of an association. Only in one patient with MM and ureterolithiasis, we found images of CT examination in our digital archive performed one year before diagnosis of ureterolithiasis due to another reason, in which MM was not present (Figs. 5a and 5b).

Another limitation is that histopathologic confirmation was not made in patients with MM. In the study by Daskalogiannaki et al, the diagnosis was pathologically confirmed in only 4 of 49 patients...
with CT findings of MP\textsuperscript{2}. This finding suggests that many other conditions might be mistaken as MP without histopathologic confirmation. The histopathological confirmation of the diagnosis is a controversial issue, some advocates it while some suggests that if CT findings are characteristic, surgery could be avoided\textsuperscript{18,31}. But it is obvious that it is very exceptional to think of a histopathological examination for a definite diagnosis in these patients with MM who are completely normal other than ureterolithiasis. In a review by Taffel et al.\textsuperscript{7} various mesenteric pathologies ranging from MM to solid masses were identified and an algorithm was formulated. Accordingly, MM associated with lymph nodes less than 5 mm and without any coexistent disease does not require further workup in asymptomatic patients. On the contrary, patients with lymph nodes larger than 5 mm should undergo clinical evaluation and a 6\textsuperscript{th} month follow-up CT should be performed. When soft tissue nodules are larger than 10 mm in short diameter biopsy is recommended in cases with misty mesentery with suspicion of malignancy\textsuperscript{5,7}. The mean short diameter of the soft tissue nodular densities within the involved mesentery was of 5.4±1.6 mm, and ranged from 2 to 9.3 mm in our study, obviating necessity of tissue biopsy. Examining the clinical and laboratory findings of all patients with MM, we tried to rule out the possibility of other well-known causes of misty mesentery.

**CONCLUSION**

The current study has shown that there may be a potential association between ureterolithiasis and misty mesentery. Although there is a high prevalence of MM in patients with ureterolithiasis, this finding is merely coincidental, and it is not possible to make a definite causal relationship. Our study revealed that MM is not an occult disease like malign processes when associated with acute or previous attack of ureterolithiasis. In patients with ureterolithiasis or a history of ureteral calculi on CT, differentiating definitively MM from malign processes is challenging and thanks to satisfactory results of our study unnecessary operative interventions and follow-up CTs were obviated in our patient group. Nevertheless, further studies with controlled follow-up CT examinations and if possible histological diagnosis are needed to support our observation.
REFERENCES