

Diagnostic and Therapeutic Approach in Intestinal Tuberculosis

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ABSTRACT

Tuberculosis was still a global health problem. Beside lung, tuberculosis also manifest in other organs, one among them is in abdominal organs. Abdominal tuberculosis was a complex disease with unspecific sign and symptoms so that its diagnostic procedure was not rarely inconclusive. We reported a 24 years old woman with chief complain of worsening abdominal pain in all region, accompanied by nausea, vomiting, bloating, and absent bowel movement. She also had a fresh bloody stool. She had an active pulmonary tuberculosis on initiation phase treatment. Physical examination suggest a bowel obstruction sign with distended abdomen and increase bowel sound. Colonoscopy procedure findings was a mass that obstruct bowel lumen in ileocaecal region, suggest for malignancy similar to computerized tomography (CT) scan result, but pathologic result showed an active colitis without any sign of malignancy. Because of its contradiction, the second colonoscopy was performed and concluded as intestinal tuberculosis, matched with second pathologic examination. Although polymerase chain reaction (PCR) tuberculosis (TB) showed a negative result, a further clinical judgement concluded this as an intestinal tuberculosis case. Patient was finally treated as intestinal tuberculosis with first-line antituberculosis drugs and planned to have colonoscopy evaluation. After general condition was good and obstructive ileus sign was relieved, patient planned for outpatient care.

Keywords: *intestinal tuberculosis, colonoscopy, abdominal pain, diagnosis, therapy*

ABSTRAK

Tuberkulosis (TB) masih merupakan masalah kesehatan global. Selain pada paru, TB juga bermanifestasi pada organ lain, salah satunya organ abdomen. Tuberkulosis abdomen merupakan penyakit kompleks dengan tanda dan gejala non-spesifik sehingga prosedur diagnostiknya tidak jarang akan menghasilkan data yang inkonklusif. Pada laporan kasus ini, dilaporkan seorang perempuan berusia 24 tahun dengan keluhan nyeri perut yang memberat di semua bagian, disertai mual, muntah, kembung, dan tidak bisa buang air besar. Pasien juga mengeluarkan tinja bercampur darah segar. Dia menderita TB paru aktif pada pengobatan fase inisiasi. Pemeriksaan fisik menunjukkan obstruksi usus dengan abdomen buncit dan peningkatan bising usus. Pada temuan prosedur kolonoskopi, terdapat massa yang menghambat lumen usus di daerah ileosekal, diduga adanya keganasan, mirip dengan hasil computerized tomography (CT) scan, namun hasil pemeriksaan patologi

menunjukkan kolitis aktif tanpa tanda-tanda keganasan. Karena kontradiksi ini, maka dilakukan kolonoskopi kedua dan disimpulkan sebagai tuberkulosis usus, sesuai dengan pemeriksaan patologi yang kedua. Walaupun reaksi berantai polimerase TB menunjukkan hasil negatif, penilaian klinis lebih lanjut menyimpulkannya sebagai kasus tuberkulosis usus. Pasien akhirnya diterapi sebagai pasien tuberkulosis usus dengan obat anti tuberkulosis kategori satu dan direncanakan untuk menjalani evaluasi kolonskopi. Setelah kondisi umum baik dan gejala ileus obstruktif tidak ada, pasien direncanakan untuk rawat jalan.

Kata kunci: TB usus, kolonoskopi, nyeri perut, diagnosis, terapi

INTRODUCTION

Tuberculosis (TB) was a worldwide emergency with high mortality and morbidity. TB remained one of the top 10 cause of death, with mortality was as high as 1.4 million TB deaths case in 2015. Indonesia with other five countries (China, Nigeria, Pakistan, India and South Africa) accounted for 60% of the new cases for TB. Based on WHO 2016 report, total best estimated TB incidence among Indonesian was 1,020,000 cases each year with estimated mortality was still high, more than 126,000 death every year.^{1,2}

Extrapulmonary TB was a *Mycobacterium tuberculosis* infection in organs other than lung, such as pleura, lymph nodes, urinary tract, skin, joint, bone, meningens, and also abdominal organs, indeed intestinal TB. The disease site of the largest proportion of extrapulmonary TB was pleural (41,1%), lymphatic (30,6%), genitourinary (7%), bone/joint (5,8%), cutaneous (4,5%), meningeal (4,1%), peritoneal (2,6%), gastrointestinal (2%) and others (2,3%).³

Diagnostic approach for extrapulmonary TB consist of clinical examination with other examination such as bacteriological and pathological examination, and also bacteriological examination to make sure wether pulmonary TB was also present or not.¹ Abdominal tuberculosis was a complex disease with unspecific sign and symptoms. Most of its diagnostic procedure was invasive, expensive, and not rarely inconclusive.⁴ This report will present an intestinal tuberculosis case with partial obstruction ileus as its main symptoms. As intestinal TB diagnostic was difficult with many possible differential diagnosis, especially colon tumor, this case was an interesting case to learn about diagnostic and therapeutic approach in patietns with intestinal TB problems.

CASE ILLUSTRATION

A female patient aged 24 years old come with worsening abdominal pain since three days before admission as a chief complaint. The abdominal pain felt as cramp in all abdominal region, followed by nausea

and vomiting. The pain actually was present since three months ago but was relieved without any medical drugs. She also feels her stomach bloating and full with frequent vomits per day. She could not defecate since three days but the flatus was still present. She has an oral intake difficulty because of the nausea and vomit since three days. No fever reported. Sometimes fresh bloody stool was also complained starting about four months before admission. From the previous examination patient was diagnosed as a new pulmonary tuberculosis case on first week therapy with chief complaint of four weeks productive cough accompanied with night sweat, weight loss, and intermittent fever. Previous bacteriological examination from sputum showed a negative result. It is known that her mother has just finished six month tuberculosis therapy. There were no history of Diabetes mellitus, hypertension, heart disease, lung disease, liver disease, and any drugs consumption. There were no family history of Diabetes mellitus and malignancy. Patient was an administration staff in a private company. She did not consume alcohol and cigarette, no history of intravenous drug use and promiscosity.

Physical examination shows a moderately ill with normal blood pressure, respiratory rate and temperature but tachicardia with heart rate 108 bpm. Body mass index showed normal weight. Examination of head, neck, and thorax was within normal limit. Abdominal examination reveals a bloating abdomen with peristaltic movement that clearly seen, increasing frequency of bowel sound. On percussion tymphanic sound found on all abdominal region, there were no pain and organomegaly. Extremity was warm with good capillary refill time, motoric and sensoric ability was normal in all limb. Digital rectal examination showed a small hemorrhoid mass with normal tonus sphincter, rectum, and no mass was found.

Laboratory examination showed hemoglobin level 11,8 g/dL, leukocyte count 8,360 cell/μL, and thrombocyte 415,000 cell/μL. Renal and liver function test was normal. Electrolyte level and ECG result was normal. Chest X-ray showed an infiltrate process on right lung parenchyme with pleural effusion on the right

lung. Three way abdominal X-ray showed a multiple air fluid level, dilatation and thickening of intestinal wall with bowel air that found in distal part suspicion of partial obstructive ileus. Abdominal ultrasonography showed an ascites in left fossa splenorenal, left praecolic, and perivesical region. Thoracic ultrasound reveal bilateral pleural effusion then continued by diagnostic thoracentesis with result of exudate pleural effusion, with ADA level of 76 U/L suggested tuberculosis infection. At this point, it can be concluded that the patient has a tuberculosis infection of lung and pleural cavity with partial obstructive ileus suspected caused by carcinoma of colon with intestinal tuberculosis was the differential diagnosis.

Colonoscopy examination initially showed an external hemorrhoid, no mucosal abnormality in rectosigmoid, descenden and transversal colon. There was a bloody frail mass occluding the lumen 60 cm from anus and scope cannot move further for evaluation, revealed a possibility of colon carcinoma. A biopsy was done and pathology examination showed a histologically active chronic colitis, mild cript destruction with no sign of malignancy. CT scan with contrast then performed, showed a thickening and contrast enlightenment in caecum intraluminal wall, suggest a malignancy that involved terminal ileum with pericolic and mesentrial lymphadenopathy, plus an obstructive ileus with dilatation of small intestine wall and multiple air fluid level dan form a step ladder. From analysis that pathological result of biopsy was not match to the CT scan result.

As the possibility of intestinal tuberculosis was still present, we decided to undergo second colonoscopy. In second colonoscopy the scope can enter further, then a polypoid granular mass in appendix orifice, ileocaecal valve, distal terminal ileum, and stenosis of ileocaecal lumen was found. An intestinal tuberculosis was suggested and the second biopsy was done. The pathological examination result showed a suggestive tuberculosis infection with granuloma tissue consist of epitheoid cell, datia Langhans cell, and lymphocyte infiltration. A PCR TB was also done, but the result was negative. Patient was finally treated for intestinal tuberculosis with first-line antituberculosis drugs and for the evaluation, patient planned to have colonoscopy evaluation.

DISCUSSION

Gastrointestinal tuberculosis was the most commonly forms of abdominal tuberculosis with incidence rate of 70-78%, with ileocaecal, colon,

and jejunum as the most location found. Abdominal tuberculosis diagnosis was hard because of its unspecific clinical presentation, lack of positive finding for acid fast staining, and mycobacterial culture.^{4,6}

Intestinal tuberculosis was found mostly in young women, two third among them was 21-40 years old. The possible risk factor was malnutrition, healthcare accessibility, and spread of salphingitis tuberculosis into abdominal organs. Its has a wide clinical spectrum from asymptomatic to acute, chronic, and even acute exacerbated manifestation.^{4,7}

A study by Khan et al, showed that among abdominal tuberculosis, intestinal tuberculosis was the highest frequency (49%), followed by peritonitis tuberculosis (42%), intraabdominal visceral tuberculosis (5%), and lymphadenitis tuberculosis (4%). Bhansali et al, Prakash et al, and Horvath et al reported that the predilection of intestinal tuberculosis was in ileum and caecum.^{4,7,9} Ileocaecal was the preferred location of tuberculosis mycobacterium infection because of it was a physiologic stasis area where fluid and electrolyte absorption was high, minimal digestion activity, and lot of lymphoid tissue that can be found there. M cell in Peyer's plaque will fagositized M. Tuberculosis bacteria and would be the entry point for M. Tuberculosis to spread to the adjacent organs.^{7,9} Our patient has several risk factors for intestinal TB infection that is women in young age (23 years old) with abnormalities on ileum and ileocaecal region was the part of intestine that having similar to intestinal tuberculosis in general.

In histopathologic examination, granulomatous tubercle with confluent shape in various size was the main characteristic of intestinal tuberculosis, although sometimes it was also found in submucosal layer below the ulcer. Tuberculous ulcer was superficial and rarely infiltrate muscularis layer. This is a transversal ulcer that if affect all intestinal mucosa will result in stricture formation. A deeper lesion would show a different stages of fibrosis. Most of it showing a nonspecific chronic inflamation without any granuloma. Mesenteric lymph nodes could also infected so that it enlarged followed by caseous formation. Granuloma was only found in patients consuming tuberculosis drugs.⁷ In this patient, a hypertrophic lesion of polypoid mass was found in ileocaecal region. This was match for colon carcinoma, but its pathological examination showed an tuberculosis infection with dathia langhans cell found on the tissue.

Symptoms of intestinal tuberculosis have two main course, constitutional such as fever, lethargy, anemia, night sweat, and weight loss and local such as in Table below.⁷

Table 1. Type of TB lesion and clinical manifestation

Type of Lesion	Clinical manifestation
Ulcerative	Chronic diarrhea, malabsorption, bowel perforation, rectal bleeding (Colonic TB)
Hypertrophic Stricture/constriction	Bowel obstruction or ileocecal lump Subacute bowel obstruction (vomiting, constipation, colic and abdominal distention). Bowel dilatation and movement on inspection to acute intestinal obstruction.
Anorectal	Stricture or fistula ani
Gastroduodenal	Ulcer peptikum with or without <i>gastric outlet</i> obstruction or perforation
Hepatosplenic	Hepatosplenomegaly and granuomaotus hepatitis on microscopic examination (part of disseminated TB)
Peritoneum	Abdominal distention and ascites
Lymph nodes	Lump or mass on central abdomen may be felt as dull pain on abdomen.

A specific symptoms of ileocaecal tuberculosis is bomborygmi bowel sound and frequent vomiting. Several findings on physical examination was intraabdominal mass with clear border, mobile in right lower quadrant. Ascites and bowel dilatation with peristaltic movement seen could be the physical finding on intestinal tuberculosis, although in some cases there were nospecific findings. Several disease with similar sign is lymphoma or carcinoma, inflammatory bowel disease, liver cirrhosis with ascites, ileocaecal mass, or chronic appendicitis.^{4,7,9} The main symptoms reported in this patient was abdominal pain with some constitutional tuberculosis symptoms and bowel obstruction symptoms such as nausea, vomiting, with problems in defecation on physical examination a distended and dilated abdomen with more frequent bowel sound. For younger patient with symptoms mention above should be suspected for intestinal tuberculosis with suggestive a stricture or constriction lesion.

Laboratory examination was an important tool in intestinal tuberculosis diagnosis. In general, anemia, leukopenia, and increase erythrocyte sedimentation rate could be found. In 55-70% patients, Mantoux test was positive. Radiologic examination, even its less specificity, was still needed for intestinal tuberculosis diagnosis.^{7,9,10}

Radiologic examination has an important role in intestinal tuberculosis diagnosis. Among several modalities, plain x-ray of thorax and abdominal region, ultrasonography, CT scan, and barium meal was the most commonly used. Khan et al reported 53% of intestinal tuberculosis suggestion using combination of USG, CT scan and barium study, while barium study alone showed a 60% positive result. Abdominal CT Scan was one of the best modalities to examine abdominal organs. From radiologic examination, pulmonary tuberculosis coincidence was found in 64% patients, while 4,7% among them have an

active disease. Abdominal X-ray may showed an enterolith, bowel obstruction (dilatation with multiple air fluid level ascites, perforation, or intusussepsion), lymph node calcification, granuloma, and sometimes hepatosplenomegaly. This was patient's abdominal x-ray during hospital admission. This patient also having an active pulmonary tuberculosis with intestinal tuberculosis.^{4,7-9}

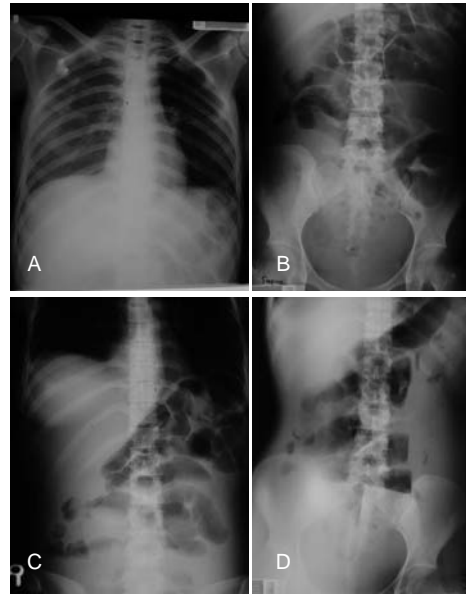


Figure 1. Thorax and abdominal x-ray result A. right lung infiltrate with pleural effusion in thorax x-ray, B, C, and D, Three position abdominal x-ray showed a distal bowel air, bowel dilatation with wall thickening, multiple air-fluid level, and no extraluminal free air, suggestive for partial bowel obstruction.

Barium meal study showed a hypersegmentation in small bowel with multiple stricture, segmental dilatation, and intestinal wall thickening. Barium enema would show spasm and edema in ileocaecal region. Double contrast examination may showed irregularity of distal ileum wall.^{7,9} Ultrasonography could show an ascites, lymphadenopathy with caseous zone or calcification, and ileocaecal wall thickening.^{7,8} In CT scan, ileocaecal tuberculosis was seen as hyperplastic lesion with symmetrical circumferential thickening in caecum and terminal ileum. A further disease would cause an adherent loop, local and mesentrial lymph node enlargement seen as central mass in ileocaecal junction, and also intraluminal node in ileum terminal. Sometimes, narrowing of intestinal lumen, ulceration, and lesion in hepatic flexure was present.^{7,11} This radiologic examination was relatively fast and cost effective, but cannot exclude Chron's disease and abdominal malignancy as differential diagnosis.⁴

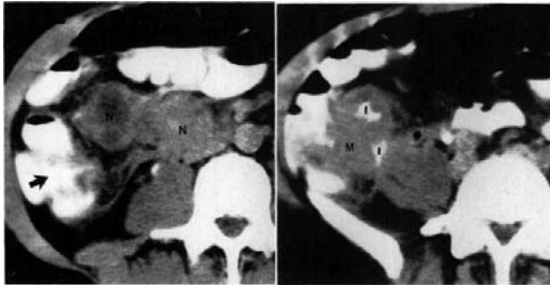


Figure 2. CT scan result of ileocaecal tuberculosis: (A) Thickening of ileocaecal valve (arrow) and extensive lymph node enlargement, seen as mesentria mass (N), low density area showed an caseous necrosis; (B) Soft tissue mass (M) in ileum terminal and ileocaecal valve.

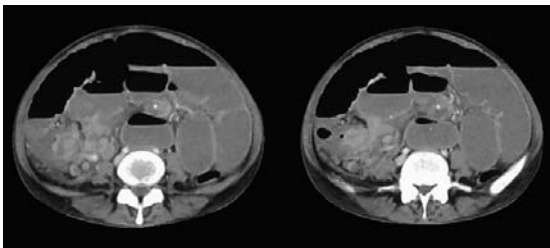


Figure 3. CT Scan patient thickening and enhancement of caecum wall, suspected malignancy intralumen of caecum, extent to terminal ileum. Limphadenopathy parakolika and menesterium. Obstructive ileus with thickening and dilatation of small intestinal lumen.

From colonoscopy examination, intestinal TB can be manifest as nodule in intestinal mucosa, vary from 2 to 6 mm and also discrete ulcer sized 4 to 8 cm. Mostly it was found as pink nodule in caecum with ulcer between nodules vary from small (3-5 mm) to large (10-20 mm). A stricture could also be found. Other possible findings was edematous pseudopolypoid ileocaecal folds and deformity in ileocaecal valve. Differential diagnosis of this findings was colon carcinoma.^{7,12}

During colonoscopy examination, biopsy was also can be done for pathologic and microbiologic examination. Actually, pathologic examination was nor reliable because of its lesion that found in submucosal layer while colonoscopy procedure can only take mucosal layer. In a case report, granuloma with caseation was found in 8-48% of one third positive result. Acid fast staining result was varous. Positive culture did not always correlate to the presence of granuloma. Combination of both histopathology and culture from biopsy was expected to increase diagnostic ability in more than 60% of cases.^{7,8,10,12}

This patient has been undergo two colonoscopy procedure. First colonoscopy found mass of ascenden colon with fragile and bloody characteristic that occlude lumen about 60 cm from anus. Pathologic examination of biopsy sample from first colonoscopy

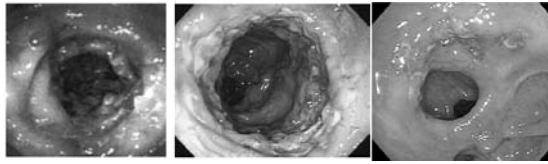


Figure 4. Colon tuberculosis with multiple ulcer and nodule during colonoscopy examination

showed an infiltrate within lamina propria with chronic inflammatory cell and also eosinophil with mild cript distortion suggestive for active chronic colitis without any sign of malignancy. Because of there is contradiction among colonoscopy and pathology result, the secondary colonoscopy was proposed.

Second colonoscopy showed a granular polypoid mass in appendix, ileocaecal valve, and distal terminal ileum with ileocaecal stenosis then biopsy

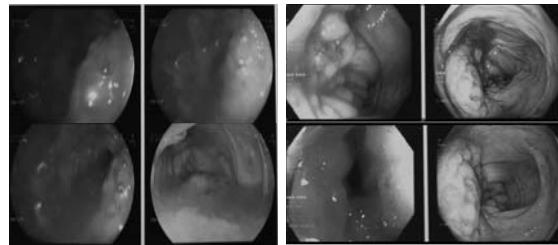


Figure 5. (A) First colonoscopy procedure showed a colon mass that is fragile and bloody, suspected for colon carcinoma, the scope cannot go further above the mass; (B) Second colonoscopy found granular polypoid mass on appendiceal region, ileocecal valve and terminal ileum with stenosis ileocecal lumen.

was done for PCR TB and pathologic examination. Secondary pathologic examination showed an infiltrated lamina propria from chronic inflammatory cell, PMN cell, and eosinophil with fibrotic tissue and wider cript distances. There were also found a granuloma composed of epitheloid cell, dathia langhans cell, and lymphocyte infiltration. Villious shortening, concluded as granulomatous ileitis caused by *Mycobacterium tuberculosis* infection. PCR TB esamination showed a negative result, but clinical examination, epidemiological data, colonoscopy, and pathology examination result as mention above made intestinal tuberculosis as the final diagnosis of this case.

Based on WHO guidelines for extrapulmonary TB infection, patient received standard first-line drugs for TB. Short-course chemotherapy was proven to be effective as standard therapy in pulmonary tuberculosis case, and also for extrapulmonary tuberculosis because of paucibasilar condition that commonly found. Tuberculosis standard therapy was divided into two main phase, initial phase or bactericidal phase and continuation phase or sterilization phase.

During initiation phase, majority of bacil in tubercle was eliminated and clinical condition was improved. Continuation phase was aimed to kill the remaining mycobacterium and to prevent relapse.^{1,6,13,14}

Extrapulmonary TB there were not determined yet in drug duration, therapy may vary between 6 to 24 months, depends on evaluation and clinical manifestation. Several RCT reported the effectivity of 6-months therapy but clinical judgement could make the therapy longer.^{14,15} Intestinal tuberculosis therapy was similar to other extrapulmonary tuberculosis with drug regime given for at least 6 month. The first two months was an intensive phase, consist of rifampycin, isoniazide, ethambutol, and pyrazinamide. Balasubramaniam et al compared 6 and 12 months therapy (with streptomycin in the first two weeks) in 193 patients in India showed a successful rate of 99% and 94%, respectively. Conventional and short course therapy was slightly better, but in daily clinical practice, a longer therapy for 12-18 months could be decided based on clinical findings.^{6,8,14} Corticosteroid effectivity in tuberculosis infection in animal study caused an increase in virulence of *Mycobacterium tuberculosis*, but if administered with antituberculosis drugs, the effect was not seen.^{5,16} Corticosteroid could be used in life-threatening tuberculosis. Steroid use in first 2-3 month will reduce complication such as adhesion in intestinal tuberculosis. Usual dosage used is 40-60 mg/day prednisone or equivalent and titrated for 4-8 weeks.^{17,18} In diagnostic-problems case, several expert recommended antituberculosis drug as a trial, but should not delay the diagnostic procedure for other possible disease such as malignancy, lymphoma, and Chron's disease.^{7,9,12}

Surgical management for intestinal TB was used to treat any complication such as bowel obstruction, perforation, or massive bleeding that unresponsive to conservative therapy. Perforation was treated by resection and anastomosis, while stricture with stricturoplasty. Bypass surgery such as enteroenterostomy and ileotransverse colostomy was not yet recommended because of malabsorption and fistulation risk. Nowadays, antituberculosis treatment for bowel obstruction should be succesfull and not followed by surgical management.⁸

In this patient, antituberculosis drug was previously prescribed for active pulmonary tuberculosis is continued, so that there were no additional drugs used for intestinal tuberculosis. Patients has been receiving 450 mg rifampycin, 300 mg isoniazid, 750 mg pyrazinamide, and 750 mg ethambutol. This

regime was planned initially for 6 month therapy with colonoscopy evaluation at the end of therapy.

Intestinal tuberculosis complication was bowel obstruction caused by lumen narrowing from caecum hyperplasia, stricture, and adhesion. Lymph node involvement could lead to bowel loop disorder by altering traction, narrowing, and fixation. Malabsorption was also commonly found in intestinal tuberculosis, the possible mechanism is bacterial overgrowth in stasis bowel, bile acid deconjugation, and reduced intestinal surface area for nutrition absorption as the present of ulcer and infection in lymphatic system.⁷

Basically, extrapulmonary tuberculosis therapy was showing a good result, except for meningitis and spondilitis tuberculosis where only few cases that fully healed. Khan et al reported that antituberculosis drug treatment for abdominal tuberculosis was responsive in 76% with 17% among them undergo further surgical management because of complication. Other literature reported a surgical approach in 20-40% cases. High mortality among surgical management was predicted due to previous complication such as perforation, malnutrition, and sepsis. Abdominal tuberculosis mortality was about 8-50%, with worsen risk factor is older age, delayed therapy initiation, and liver cirrhosis as comorbid.^{4,7,9}

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