

Enterobius vermicularis Salpingitis Seen in the Setting of Ectopic Pregnancy in a Malaysian Patient

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We report a rare and unusual case of invasive *Enterobius vermicularis* infection in a fallopian tube. The patient was a 23-year-old Malaysian woman who presented with suprapubic pain and vaginal bleeding. A clinical diagnosis of ruptured right ovarian ectopic pregnancy was made. She underwent a laparotomy with a right salpingo-oophorectomy. Histopathological examination of the right fallopian tube showed eggs and adult remnants of *E. vermicularis*, and the results were confirmed using PCR and DNA sequencing.

CASE REPORT

On 22 January 2014, a 23-year-old woman, who was in her second pregnancy and at 8 weeks of gestation, presented as an outpatient to the Emergency Department (ED) University of Malaya Medical Centre (UMMC), Kuala Lumpur, Malaysia. She was referred by a private general practitioner after complaining of vaginal bleeding for 3 days with small amount of spotting and staining on her undergarment associated with suprapubic pain for a day. The pain was described as sharp pricking, nonradiating, and progressively increasing in severity. She did not have any vaginal discharge or fever. The result of a urine pregnancy test carried out at the private clinic was positive. When she missed her menses in December 2013, no test was done to confirm pregnancy. Bowel and urinary habits were normal. She did not have any medical illnesses or previous surgeries. No known allergies were noted. She had a full-term vaginal delivery in 2009. She attained menarche at the age of 12 years and has a regular menstrual cycle and is free of menorrhagia, dysmenorrhea, dyspareunia, and postcoital bleeding. She is on a natural method of contraception, and a cervical smear test had never been done before.

On physical examination, she appeared pale, with early signs of hypovolemia as evidenced by tachycardia with pulse rate of 110 to 120 beats per min and blood pressure ranging between 90 to 94 and 60 to 70 mm Hg. Fluid resuscitation was immediately started in the emergency department. Her vital signs were monitored continuously. Cardiorespiratory examination revealed no abnormalities. Her abdomen was mildly distended. There was presence of tenderness at the lower abdomen with guarding. Neither an abdominal scar nor organomegaly was noted. Vaginal examination revealed a normal vulvovaginal surface, and her cervix was tubular. The cervical excitation result was positive, with fullness in the Pouch of Douglas. Adnexal tenderness was elicited bilaterally.

Transabdominal pelvic sonography revealed an empty uterus with a right irregular adnexal mass measuring 9 mm and a moderate level of free fluid that was 50 mm deep. Blood investigations revealed anemia, with hemoglobin at 6.7 g/dl and with a normal white blood cell count and platelet level. Preoperative diagnosis of a ruptured right ectopic pregnancy with hypovolemia was made. Informed consent for a laparotomy was provided by both the patient and her husband after they were counseled with respect to the working diagnosis and the intended procedure. She under-

went laparotomy with right salpingo-oophorectomy on the same day. The diagnosis of a ruptured right ovarian ectopic pregnancy was made. She was transfused with 4 U of packed cells. She had an uneventful postoperative recovery and was discharged on the second postoperative day (24 January 2014), with paracetamol prescribed as a pain reliever. She was given a follow-up appointment in the Gynaecology Outpatient Clinic for a date 6 weeks later.

The resected specimens were submitted to the Department of Pathology, Faculty of Medicine, University of Malaya, for histopathological examination. Reports on macroscopic findings described a distended tubular structure measuring 60 mm in length. A ruptured hemorrhagic cystic cavity measuring 40 mm by 25 mm by 20 mm was present. Microscopic findings revealed a fibrotic nodule attached to the wall of the right fallopian tube composed of hyalinized stroma containing rounded structures reminiscent of eggs and adult remnants of pinworms (*Enterobius vermicularis*) (Fig. 1). The nodule was attached to the tubule wall and just impinged on the fallopian tube. There was no obstruction of the tubule lumen noted. Chronic inflammatory infiltrates admixed with histiocytes and a granulomatous reaction showing multinucleated giant cells of a foreign-body type were observed in focal areas within the nodule (Fig. 2). Focal dystrophic calcification was present. Decidual tissue (i.e., suggestive of products of conception) that adhered to the wall of the fallopian tube was observed in focal areas. Fusion of plicae of mucosal folds was seen. The hemorrhagic cystic cavity showed a paratubal cyst.

Paraffin-embedded tissue sections were sent for further species-specific confirmation to the Department of Parasitology, Faculty of Medicine, University of Malaya. The specimens were subjected to a nested PCR targeting the 5-subunit rRNA (5S rRNA) spacer region according to a protocol described previously (1).

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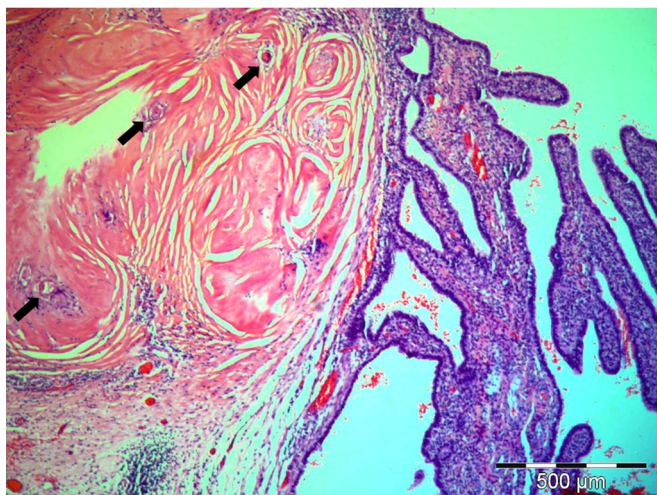


FIG 1 Microscopic findings revealed a fibrotic nodule attached to the wall of the fallopian tube composed of hyalinized stroma containing rounded structures reminiscent of eggs and adult remnants (black arrows) of *Enterobius vermicularis*.

Prior to DNA extraction, the specimen was initially mixed with xylene to remove the embedded paraffin followed by absolute ethanol evaporation. The sample was then digested and incubated at 56°C overnight in an incubator shaker with proteinase K for complete cell lysis followed by genomic DNA extraction following the guidelines of the manufacturer (Macherey-Nagel, Neumann-Nender, Duren, Germany). DNA amplification was performed, and an approximately 200-bp specific amplicon was produced. Additionally, an amplicon representing a positive test result was subjected to DNA sequencing. Homology searching using the National Centre for Biotechnology Information (NCBI) reference sequences with the Basic Local Alignment Search Tool (BLAST) confirmed the species to be *E. vermicularis*. Clinicopathological and molecular findings confirmed the final diagnosis of *E. vermicularis* salpingitis complicated with intra-abdominal bleeding secondary to perforation of vessels of mesosalpinx and complete miscarriage.

On the basis of these findings, the patient was called back to the Gynaecology Outpatient Clinic on 17 February 2014. Upon review, she was pain-free and ambulating well. No pregnancy symptoms were noted. She denied any prior perianal itchiness or abnormal vaginal discharge or itch. Her vaginal bleeding stopped 1 day after discharge and currently at day 2 of menses. Clinically, she was not pale and was hemodynamically stable. Abdominal examination results were normal, with a well-healed scar present. A transabdominal pelvic scan revealed empty uterus without any adnexal mass or free fluid. The result of a urine pregnancy test was negative. The histopathology and molecular results were revealed to her, and she was counseled regarding future fertility implications. She was started on albendazole for a week, and a follow-up examination to review her symptoms was scheduled for a date 2 weeks later.

Enterobius vermicularis, often referred to as pinworm, threadworm, or *Oxyuris*, is an intestinal nematode which commonly infects children throughout the world, particularly in developed temperate

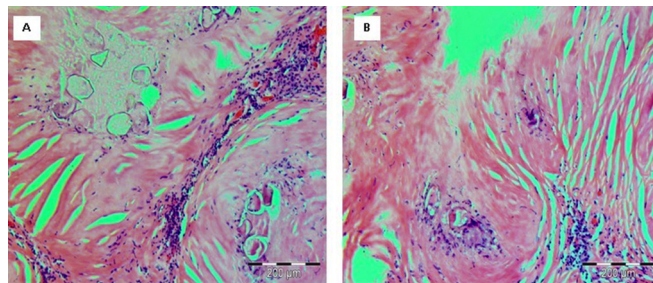


FIG 2 Chronic inflammatory infiltrates admixed with histiocytes (A) and a granulomatous reaction showing multinucleated giant cells of a foreign-body type (B) were observed in focal areas within the nodule.

countries. The worms usually inhabit the cecum of the human gastrointestinal tract. The common route of intestinal infection is via autoinfection (anus to finger to mouth), as the eggs are infective within 4 to 6 h after being laid. Infection through inhalation and swallowing of airborne eggs dislodged from contaminated fomites such as clothing or bed linen may also play a role in transmission. After ingestion, the embryonated eggs hatch and release larvae in the small intestine. Larvae develop into adult worms and reside in the distal ileum, the cecum, the appendix, and the proximal ascending colon, and the majority of infections are asymptomatic (2). After mating, the males die and the gravid female worms migrate nocturnally down to the anus, where the eggs are laid on perianal and perineal surfaces and produce intense irritation and pruritus ani. The life span of the adults is about 2 months. Appendicitis caused by obstruction and inflammation due to the presence of adult worm in the appendix have been reported occasionally. Less commonly, the adult worms can become lodged in the intestinal mucosa and cause intestinal abscess (2).

Extraintestinal enterobiasis is rare and mostly involves the female genital and reproductive tract, which includes the vagina, uterus, ovaries, fallopian tubes, and pelvic peritoneum or even the human embryo (3–15). In addition, recurrent urinary tract infections (UTIs) as a complication of aberrant migration in women, particularly in young girls, have also been identified (16, 17). We describe a case of *E. vermicularis* salpingitis seen in the setting of ectopic pregnancy in a Malaysian patient. In this case, salpingitis due to ectopic infection by *E. vermicularis* might have contributed to the ectopic pregnancy. Nevertheless, risk of infertility from chronic low-grade asymptomatic salpingitis due to enterobiasis has been reported in the literature (13, 18).

Extraintestinal *E. vermicularis* infections involving the female genital and reproductive tract are unusual. Although vaginal enterobiasis is rare, a review of the English-language literature revealed several reports on *E. vermicularis* infection in the female genital tract and the first case was reported in 1950 (12). Infection involving the female genital tract occurs due to the migration of the gravid female worm from perianal and perineal areas up to the vagina, and the worm may ascend to the peritoneum through the fallopian tubes. This hypothesis is supported by several reports which documented the presence of only female adult worms and ova on cervical smears and in peritoneal granuloma (3, 6, 8). Another possible mechanism is the passage of the adult worm through the intestinal wall to produce pelvic peritoneal granulomas; however, this hypothesis is difficult to prove, as the infection is rarely found in the bowel wall (19).

In most cases, clinical manifestations due to the presence of adult worms or eggs outside the gastrointestinal tract are minor, with many lesions reported as incidental findings upon surgery or autopsy (10). However, several cases of invasive female genital tract enterobiasis with overt clinical symptoms, including salpingitis, fallopian tube infiltration, urinary tract infection, pelvic mass, tubo-ovarian abscess, generalized peritonitis, and granulomata of the vulva, uterus, and ovaries, have been reported (3–8, 10–13). In addition, several cases of invasion of the human embryo by *E. vermicularis* have been reported (14, 15). The patients all underwent hysterectomy and/or oophorectomy, and the diagnosis of enterobiasis was made postoperatively after a histopathological examination. Preoperative diagnosis is difficult, as only past or concomitant gastrointestinal enterobiasis or the finding of parasites in cervical smears, vaginal wet mounts, and vaginal pooled specimens might suggest *E. vermicularis* infection and prompt appropriate treatment.

Moreover, the preoperative symptoms and complaints, including lower abdominal pain, fever, dyspareunia, nausea, and vomiting, are usually nonspecific, while results of biochemical examination such as blood test also lack specificity (3, 6–11). Histological examination is also difficult, as the egg of this parasite might be easily confused with *Schistosoma* eggs, particularly in the epidemiological setting, in which infections by both species are endemic. Nevertheless, since *Schistosoma* infection is not endemic in Malaysia and the patient lacked a travel history, combined with the PCR and DNA sequencing results, this case excluded the possibility of schistosomiasis.

Experience with treatment of extraintestinal enterobiasis is not standardized, and the available treatment choices are limited. According to The Centers for Disease Control and Prevention (CDC) guidelines, the recommended treatment for enterobiasis is oral pyrantel pamoate. Alternatively, a single dose of mebendazole may also be given to the patient followed by a second dose in cases where the infection persists, typically as a result of autoinfection. In most reported cases, patients were treated with mebendazole after surgery (3–11). However, the use of mebendazole in pregnancy remains controversial with regard to fetus safety (9). A study conducted to examine the pregnancy outcome after gestational exposure to mebendazole reported no significant increase in fetal malformation compared with control group results (20). Although no significant teratogenic effects were seen, nevertheless, mebendazole should be used with caution in pregnancy, especially in the first trimester. Treatment should also be given to family members, especially to family members who are in close contact with the patient, due to the high incidence of infection in the same household.

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