Enterobius vermicularis salpingitis seen in the setting of ectopic pregnancy in a Malaysian patient: A case report

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We report a rare and unusual case of invasive Enterobius vermicularis infection in a fallopian tube. The patient is a 23-year-old woman from Malaysia 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 was confirmed using PCR and DNA sequencing.

CASE REPORT
On January 22, 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, non-radiating and progressively increasing in severity. She did not have any vaginal discharge or fever. 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 twelve, has regular menstrual cycle, free from menorrhagia, dysmenorrhea, dyspareunia and postcoital bleeding. She is on natural method of contraception and cervical smear test has never been done before.

On physical examination, she appeared pale with early signs of hypovolemia as evidenced by tachycardia with pulse rate of 110-120 beats per minute and blood pressure ranging between 90-94/60-70 mmHg. Fluid resuscitation was immediately started in the ED. 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 abdominal scar nor organomegaly were noted. Vaginal examination revealed normal vulvovaginal surface and cervix was tubular. Cervical excitation was positive with fullness in the Pouch of Douglas. Adnexal tenderness was elicited bilaterally.

Transabdominal pelvic sonography revealed empty uterus with right irregular adnexal mass, measuring 9 mm and moderate free fluid of 50 mm deep. Blood investigations revealed anemia with hemoglobin of 6.7 g/dl with normal white count and platelet level. Pre-operative
diagnosis of ruptured right ectopic pregnancy with hypovolemia was made. Informed consent was taken from both patient and her husband, for a laparotomy, after being counseled of the working diagnosis and the intended procedure. She underwent laparotomy with right salpingo-oophorectomy on the same day. The diagnosis of ruptured right ovarian ectopic pregnancy was made. She was transfused with 4 units of packed cells. She had an uneventful postoperative recovery and was discharged on second postoperative day (January 24, 2014) with paracetamol as pain relief. She was given a follow up appointment in the Gynaecology Outpatient Clinic 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 were of a distended tubular structure measuring 60 mm in length. A ruptured hemorrhagic cystic cavity measuring 40 mm x 25 mm x 20 mm was present. Microscopic findings revealed a fibrotic nodule attached to the wall of the right fallopian tube composed of hyalinised stroma containing rounded structures reminiscent of eggs and adult remnants of pinworms (*E. vermicularis*) (Figure 1). The nodule was attached to the tubule wall and just impinged on to the fallopian tube. There was no obstruction of the tubule lumen noted. Chronic inflammatory infiltrates admixed with histiocytes and granulomatous reaction containing foreign body types of multinucleated giant cells were observed in focal areas within the nodule (Figures 2 and 3). Focal dystrophic calcification was present. Decidual tissue (i.e., suggestive of products of conception), 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.

The paraffin-embedded tissue sectioned was sent for further specific-species confirmation to the Department of Parasitology, Faculty of Medicine, University of Malaya. The specimens were subjected to a nested polymerase chain reaction (PCR) targeting the 5
Subunit ribosomal RNA (5S rRNA) spacer region according to the protocol described previously (1). 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 incubator shaker with proteinase K for complete cell lysis followed by genomic DNA extraction following the manufacturer’s guideline (Macherey-Nagel, Neumann-Neander, Duren, Germany). DNA amplification was performed and approximately 200 bp specific amplicon was produced. Additionally, positive amplicon was subjected to DNA sequencing. Homology search using the National Centre for Biotechnology Information (NCBI) reference sequences with Basic Local Alignment Search Tool (BLAST) confirmed the species as *E. vermicularis*. Clinicopathological and molecular finding confirms the final diagnosis of *E. vermicularis* salpingitis complicated with intraabdominal bleeding secondary to perforation of vessels of mesosalpinx and complete miscarriage.

Based on these findings, the patient was called back to the Gynaecology Outpatient Clinic on February 17, 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 one day after discharge and currently at day 2 of menses. Clinically, she was not pale and hemodynamically stable. Abdominal examination was normal with a well-healed scar. Transabdominal pelvic scan revealed empty uterus without any adnexal mass or free fluid. 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 with a follow up in 2 weeks time to review her symptoms.
*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 countries. The worms usually inhabit the caecum 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 – 6 hours 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 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 which 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 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 young girls have also been indentified (16,17). We describe a case of *E. vermicularis* salpingitis seen in the setting of ectopic pregnancy in a patient from Malaysia. In this case, salpingitis due to ectopic infection by *E. vermicularis* might have contributed to the ectopic pregnancy. Nevertheless, the 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 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 female genital tract and the first case was reported in 1950 (12). Infection involving the female genital tract occurs due to the migration of gravid female worm from perianal and perineal areas up to the vagina and may ascend to the peritoneum through the fallopian tubes. This hypothesis is supported by several reports which documented presence of only female adult worm and ova on cervical smears and in peritoneal granuloma (3,6,8). Another possible mechanism is by the passage of 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, the clinical manifestations due to 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 have been reported including salpingitis, fallopian tube infiltration, urinary tract infection, pelvic mass, tubo-ovarian abscess, generalized peritonitis, granulomata of the vulva, uterus and ovaries (3-8,10-13). In addition, several cases of invasion of the human embryo by *E. vermicularis* have also been reported (14-15). These patients all underwent hysterectomy and/or oophorectomy and the diagnosis of enterobiasis was made postoperatively after 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 specimen might suggest *E. vermicularis* infection which prompts appropriate treatment.

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

Experience with treatment of extraintestinal enterobiasis is not standardized and is 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 malformation of fetal compared with control group (20). Although no significant teratogenic effects were seen, nevertheless it should be used with caution in pregnancy especially in the first trimester. Treatment should also be given to family members due to the high incidence of infection in the same household especially family members who are in close contact with the patient.

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Figure 1: Microscopic findings revealed a fibrotic nodule attached to the wall of the fallopian tube composed of hyalinised stroma containing rounded structures reminiscent of eggs and adult remnants (black arrows) of Enterobius vermicularis.
Figure 2 (A) and (B): Chronic inflammatory infiltrates admixed with histiocytes and granulomatous reaction containing foreign body type of multinucleated giant cells was observed in focal areas within the nodule.