Case Study: Ectopic Pregnancy

Introduction

Ectopic pregnancy (EP) is defined as the implantation of a conceptus outside of the uterine endometrium (1). Major risk factors include history of pelvic inflammatory disease, tubal ligation and smoking as well as other factors age and intrauterine device usage (2). In New South Wales (NSW) the incidence of EP was found to be relatively common, at 16.2 per 1000 live births in a 1998 analysis of the NSW Department Inpatient Statistics Collection (3). Consequences of delayed diagnosis and rupture of EP includes haemorrhage, shock and death. Hence, timely diagnosis and management of EP is necessary for good outcomes. Although maternal mortality is uncommon as a consequence of EPs in high-income countries, there remains significant morbidity relating to pain, transfusion and operative complications (1). The following case discusses a 24-year-old's presentation, diagnosis and progression of treatment of EP in comparison to clinical practice guidelines and literature.

Case

Mrs. VL, a pregnant 24-year-old at 3 weeks and 6 days gestation presented to Blacktown Hospital Emergency Department (ED) with per vaginal (PV) bleeding and lower abdominal pain. Earlier that day, she had been discharged from Mount Druitt Hospital (MDH) ED with a diagnosis of miscarriage. She received an outpatient transvaginal ultrasound scan (TVUS) prior to coming to Blacktown Hospital ED. Her imaging results showed a right adnexal solid mass.

The patient complained of a 2-week history of scant PV spotting and a 3-day history of a constant and crampy right iliac fossa (RIF) pain which had worsened that day. The pain radiated down the anterior aspect of her legs. She denied having abdominal symptoms of nausea, vomiting, diarrhoea as well as urinary symptoms of frequency, urgency and dysuria. She was otherwise well with no recent fevers.

This was her first pregnancy (gravida 1 parity 0) and has had outpatient serum -hCG blood tests (1+6 weeks: 205IU/L, 2 weeks: 305IU/L, 3 weeks: 985IU/L). Mrs. VL menstrual history revealed a last menstrual period starting 3 weeks 6 days ago which lasted 7 days. Prior to this, she had regular 28 days menstrual cycles with regular flow (4-5 pads per day) and menses lasting 5 days. She denied intermenstrual bleeding or heavy menstrual bleeding. The patient had no previous sexual activity before marriage with her partner 2 months ago. No forms of contraception had been used and there was no history of sexually transmitted infections. She denied PV discharge or post-coital bleeding. She has not had previous cervical screening tests and her human papillomavirus immunisation status was unknown.

Mrs. VL had no relevant past medical or surgical history and does not take any regular medication. She has a known drug allergy to amoxicillin which results in urticaria. Her family history was unremarkable. She denied smoking and illicit substance use however there was occasional consumption of alcohol.

On general inspection, Mrs. VL appeared alert and comfortable. Her vitals were in the normal

ranges and remained stable throughout her admission. On examination, her abdomen was soft with tenderness and guarding in the right lower quadrant. However, there was no rebound tenderness or rigidity. A complete pelvic examination was performed. Speculum examination showed scant dried blood on the pad, a long, closed cervix and scant dark blood in the posterior fornix. No cervical excitation, adnexal tenderness, masses or enlargements were found on bimanual examination.

Mrs. VL was investigated with a urinalysis, full blood count (FBC), group and hold (G+H), C reactive protein, electrolytes, blood sugar level and serum -hCG. Her investigations were unremarkable apart from slight elevations of leukocytes, neutrophils and monocytes. Her blood group was A positive. Her -hCG level was 816IU/L at 3+6weeks, a decrease from 6 days prior. Her outpatient TVUS revealed endometrial thickening at 15mm, intrauterine fluid, right adnexal solid mass separate from the ovary (measuring at 2.7x2.4x3.6cm) and a normal left ovary.

Mrs. VL was admitted with a suspected right-sided EP which was clinically subacute and had not ruptured. This impression was formed based on history, clinical features and investigation results. She was kept nil by mouth (NBM) and intravenous (IV) fluids were administered. Her pain was well controlled by analgesia (regular paracetamol and oxycodone as needed). Conservative, medical and surgical management options were discussed with the patient and family. Prior to discharge, serum -hCG levels were repeated and follow-up in the outpatient Early Pregnancy Assessment Clinic (EPAC) was organised. She was to return for repeat bloods (FBC and -hCG) and further discussion of treatment. The patient was advised to return to ED immediately if there was further PV bleeding or the severity of her pain increased. Upon presenting for EPAC follow-up, the patient chose conservative expectant management and continued to return to EPAC for serial -hCG levels. These levels were found to be decreasing (3 days after discharge: 629IU/L, 6 days after discharge: 287IU/L). This was consistent with a resolving EP.

One and a half weeks after her discharge from Blacktown Hospital, Mrs. VL represented to ED with an acute worsening of the RIF pain. This pain had a pain score of 7/10, radiated to the back and down her legs, and was associated nausea. She had noticed fresh PV bleeding and blood clots of 5cm in diameter on her pad. The patient denied chest pain, dyspnoea, palpitation, pre-syncopal symptoms, visual changes or vomiting. Examination findings were consistent with the previous admission. On a TVUS, no intrauterine gestational sac was visible, and a complex mass was found in the right adnexa. Mrs. VL was consented for diagnostic laparoscopy with or without salpingectomy or dilatation and curettage. Before the operation, blood tests were repeated (-hCG: 174IU/L, G+H, FBC), she was kept NBM, given IV fluids, prophylactic antibiotics and TED stockings. Laparoscopically, an unruptured right tubal EP was visualised and a right salpingectomy was performed. A specimen of the right tube was analysed, and the diagnosis was later confirmed histologically. Post-operatively, the patient recovered well and was discharged 2 days after surgery. Follow-up at the gynaecology clinic 4 weeks later was arranged. During her follow-up consultation, Mrs. VL was advised of the risk of recurrence of EP. Early dating scans as well as preconceptual folic acid were recommended for future pregnancies.

Discussion

The management of Mrs. VL can be evaluated with a focus on her initial presentation,

diagnostic work-up and treatment options. EP commonly presents with abdominal pain and vaginal bleeding between 6 to 10 weeks' gestation. However, abdominal pain and vaginal bleeding are common symptoms in early pregnancy and atypical presentations are also relatively common (4, 5). Other signs and symptoms include shoulder tip pain, syncope and shock which occur in up to 20% of women and are usually indicative of rupture of EP (4). Delayed or incorrect diagnosis and treatment may result in rupture and ultimately haemorrhage and early pregnancy maternal death (6). Hence clinicians should be suspicious of EP in women of reproductive age who present with abdominal or pelvic symptoms. In the context of a positive -hCG, it is recommended to refer to an early pregnancy assessment service (EPAS), as per National Institute for Health and Clinical Excellence guidelines (7). Due to incomplete documentation prior to discharge from MDH ED, it was unclear how a miscarriage was diagnosed, whether EP was considered and if a referral to an EPAS was made.

The recommended initial investigation on suspicion of miscarriage or EP is TVUS (8). The use of TVUS has been supported by previous studies reporting up to a 73.9% rate of visualising EPs in a single scan. However, this is complicated by EPs which may be too small to visualise if scanned early during pregnancy (9, 10). If imaging results are found to be indeterminant, serial quantitative serum -hCG is advised (8). The combined use of TVUS and serial quantitative serum -hCG for the diagnosis of EP have been found to be approximately 96 percent sensitive and 97 percent specific (11). A TVUS referral was appropriately arranged to be performed at an outpatient imaging clinic to identify location of implantation, products of conception and pelvic organ structure. However, serum -hCG levels were below the discriminatory zone of 1000-1500IU/L and hence the diagnosis of pregnancy of unknown location was made (1). Upon presentation to Blacktown Hospital ED, Mrs. VL was appropriately worked up with a suspicion of right tubal EP based on her symptoms and ultrasonographic findings.

Serial quantitative serum -hCG is frequently used to monitor the progression of foetal development and viability. An increase of 66% over 48 hours is commonly used as a threshold for normal development (12). In EP, -hCG may demonstrate atypical trends of falling, rising or plateauing. Due to this variability, -hCG is useful for confirming foetal viability but does not rule out EP (13, 14). Hence it should be interpreted in the context of clinical and sonographic findings (13). Mrs. VL's decreasing -hCG and haemodynamic stability is commonly associated with a resolving EP (15). Other investigations including serum progesterone levels and diagnostic laparoscopy may be performed. Previous reports have suggested that serum progesterone value may be a useful predictive biomarker in ectopic pregnancies however this is not concordant with the NICE 2012 guidelines and was hence appropriately not performed (1, 12, 16). Diagnostic laparoscopy is 'gold standard' and may be indicated when ultrasound is inconclusive (12). Additionally, diagnostic laparoscopy is frequently done in conjunction with laparoscopic surgical management. However, Mrs. VL's clinical impression of ectopic pregnancy was quite definitive and did not require further invasive diagnostic investigation or management.

EP has 3 main forms of treatment – expectant, medical and surgical. Expectant management involves the spontaneous resolution of EP through regression or tubal abortion. It is offered only when TVUS fails to show the location of the gestational sac and serum levels of -hCG are low and declining (12). Expectant management is an option for clinically stable asymptomatic women with an ultrasound diagnosis of EP and a decreasing serum hCG initially less than 1000IU/L (7). Fertility outcomes following expectant management are comparable to those following surgical intervention (17). Medical therapy involves systemic methotrexate offered to

patients with no significant pain, hemodynamically stable, adnexal mass of less than 35mm, no intrauterine pregnancy or serum -hCG less than 5000IU/L (8, 12). When administered to appropriate patients, there is a success rate of 94% (18). Surgical management in the form of salpingectomy or salpingotomy is also offered to these patients who are suitable for medical management if serum -hCG is greater than 1500IU/L. Surgical management can be offered as first-line treatment when there is significant pain, haemodynamically unstable, adnexal mass greater than 35mm, fetal heartbeat visible on ultrasound scan or -hCG greater than 5000IU/L (NICE guidelines). On initial presentation to Blacktown Hospital ED, Mrs. VL was mildly symptomatic. However, she was clinically stable, and the pain was well controlled. Additionally, her serum -hCG was less than 1000IU/L and decreasing. Hence it was appropriate for both expectant and medical management to be offered. Falling -hCG levels is usually an indication for less invasive therapy but rupture of EP may still occur (19, 20). Therefore, as the patient had requested for expectant management, regular outpatient follow-up with continued serial -hCG every 2 days was appropriate to monitor her progress.

Upon representing to Blacktown Hospital ED with significant pain, Mrs. VL was consented and prepared for surgery. This was concordant with the NICE guidelines' indications for surgical intervention (7). A laparoscopy salpingectomy, which involves the removal of the ipsilateral fallopian tube, was performed. This procedure is often compared to the more conservative procedure, salpingostomy, which allows for the preservation of the fallopian tube. Despite Mrs. VL's loss of a fallopian tube, compared to a salpingostomy, there is no significant difference in impact on future fertility as she has a healthy unaffected contralateral tube (21, 22). Additionally, salpingostomies are associated with a small increase in risk of persistent trophoblasts and reoccurrence of EP (23). Hence, Mrs. VL's salpingectomy is appropriate given she has a healthy contralateral fallopian tube with no known risk factors of EP. The laparoscopic approach that was performed was appropriate given the shorter operation times, improved haemorrhage control and increased safety compared to a laparotomy (24, 25). There is also no associated difference in reproductive outcome after treatment of EP by laparoscopy or laparotomy (18).

Conclusion

Ectopic pregnancy is a common cause of early pregnancy bleeding. It has good outcomes when managed appropriately however late diagnosis or inadequate treatment can result in a rupture of ectopic pregnancy. This is a medical emergency which can result in maternal morbidity and mortality. Hence, immediate investigation with transvaginal ultrasound and serial quantitative -hCG as well as appropriate selection of management options, including expectant, medical or surgical, is recommended.

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