EPAS Case study: Update on management and diagnosis of Pregnancy of Unknown Location

RPA/Canterbury ANSC: Educational Case Study Series - June 2022

Hayley Diplock, Clinical Midwifery Consultant (CMC). EPAS, Women and Babies, RPA Hospital

Presentation
Harriet is a 37yo woman who presented to her GP with 2-day history of per vaginal bleeding 1 week after a positive home urine pregnancy test. She is unsure of her last menstrual period. She has no abdominal pain and is otherwise well. This is her first pregnancy, and she has no significant past medical history. She is taking pregnancy multivitamins containing folic acid.

Harriet is advised by her GP to present to RPA EPAS clinic from 0730hrs the next morning unless she experiences abdominal pain prior. She was advised that if she has pain or an increase in PV loss she should present to the nearest emergency department for review.

Harriet remains well overnight but continues to have light spotting, mostly seen on wiping. She presents to the EPAS clinic at RPA hospital the next morning where she is seen by the CMC.

Investigations & Findings:
1. *Pathology:* BhCG 154IU/L, progesterone 15nmol/L and FBC (unremarkable, Hb 98IU/L)
2. *Physical examination:* Normal tone, nil tenderness, rebound or guarding. Nil presyncope or dizziness.
3. *Speculum examination:* Cervix appears closed with nil unusual features, small amount of serous ooze at cervix that stops after wiping with gauze.
4. *Pain assessment:* Nil pain, nil shoulder tip pain.
5. *Ultrasound:* not attended in this case due to the low BhCG and the clinical presentation of stable bleeding with no pain. Had this patient presented with suspicious lower abdominal pain then an ultrasound would be attended at this stage. Ultrasound will be considered if there is a change in clinical condition and/or serial BhCG/Progesterone measurements warrant imaging.

Provisional Dx:
Pregnancy of unknown location and viability

Plan:
Harriet is comfortable, and PV loss is stable, she is sent home to return to EPAS in 48 hours for serial BhCG and reassessment. She is counselled about a provisional diagnosis of pregnancy of unknown location and the risk of ectopic pregnancy and red flags or the same. She is advised to present to ED if she has any concerns about abdominal pain, shoulder-tip pain, or increase in her PV loss.

Follow-up 48 hours later in EPAS:
Harriet represents to EPAS and is feeling well with scant PV loss now and continues to be pain free. BhCG is now 74. Using the M6 risk-prediction model, the ratio between initial progesterone measurement and the two BhCG measurements taken 48 hours apart gives a risk ratio as follows:

Risk of ectopic pregnancy: 4.7%
Risk of failed Pregnancy of unknown location: 94.1%
Chance of intrauterine pregnancy: 1.3%

As Harriet's risk of ectopic pregnancy is low, she is discharged home with a plan to return to EPAS in 1 week for a further BhCG reading to monitor what is likely a failing pregnancy. Harriet is reminded of when to return to ED or EPAS if she has any concerns about her PV loss or pain as red flags for a pregnancy of unknown location vs ectopic pregnancy.

Harriet returns 1 week later, PV bleeding stopped 2 days ago and has nil pain. BhCG is now negative as it has fallen to 4IU/L which is indicative of a complete early miscarriage. Harriet is advised that her next period is expected in 4-6 weeks. The CMC discusses contraception options and optimising health for future pregnancies. Harriet is advised to follow up with her GP. A discharge summary is sent electronically to her GP.

Pregnancy of unknown location and the M6 protocol:
M6 is part of a two-step triage protocol to identify patients at high risk of ectopic pregnancy. The first step triages patients after the first visit using initial progesterone: if the level is ≤2 nmol/L the patient is classified as low risk, failed pregnancy. If the level is >2 nmol/L the patient is scheduled to come back after around 48 hours to have a second hCG measurement (second step). Then M6 is applied, and if the predicted risk of ectopic pregnancy is at least 5% the patient is classified as high risk. If the risk of ectopic pregnancy is <5% then the patient is classified as low risk and likely failed pregnancy or as low risk and likely intrauterine pregnancy, depending on which predicted risk is highest.

The M6 protocol was developed by clinicians and statisticians from Imperial College London and KU Leuven and was based on 2753 PUL from two London-based university teaching hospitals. The model has been externally validated on 2899 PUL recruited between 2015 and 2017 at 8 teaching and district general hospitals in the UK

Protocol and calculator are available at www.earlypregnancycare.co.uk

Did you know?
Human chorionic gonadotrophin (hCG) is a chemical created by the trophoblast tissue that is found in early embryos that will eventually form part of the placenta. The serial measurement of hCG levels is used as a tool to identify a normal pregnancy or pathologic pregnancy (such as ectopic or molar pregnancy) and can be useful following a pregnancy loss or termination to help determine if the process is complete. Molar pregnancies (Partial and Complete), ectopic pregnancies, and miscarriages are all potential risk factors in cases where hCG levels are too high or too low.

In a normal pregnancy the hCG rises rapidly following successful implantation of the fertilised embryo. During the first weeks of pregnancy the hCG will typically double every 48-72 hours. Once the pregnancy reaches week 10 the hCG will usually stabilise and may even decline as the placenta fully takes over production of the hormone.

For clinical advice relating to women who present with pain and/or bleeding in early pregnancy, please call the EPAS CMC on 0429 728 608 (7:30am-3:30pm Monday to Friday)

For general non-urgent clinical enquiries, please call the GP Shared Care CMC Melanie Tulloch on 0425 230 662 (8am-4:30pm Monday to Friday)

References:

1. Bobdiwala, S., Christodoulou, E., Farren, J., Mitchell-Jones, N., Kyriacou, C., Al-Memar, M., Ayim, F., Chohan, B., Kirk, E., Abughazza, O., Guruwadahyarhalli, B., Guha, S., Vathanan, V., Bottomley, C., Gould, D., Stalder, C., Timmerman, D., van Calster, B., & Bourne, T. (2020). Triaging women with pregnancy of unknown location using two-step protocol including M6 model: clinical implementation study. *Ultrasound in Obstetrics and Gynecology*, *55*(1), 105–114
2. Van Calster B, Bobdiwala S, Guha S, Van Hoorde K, Al-Memar M, Harvey R, Farren J, Kirk E, Condous G, Sur S, Stalder C, Timmerman D, Bourne T. (2016). Managing pregnancy of unknown location based on initial serum progesterone and serial serum hCG: development and validation of a two-step triage protocol. *Ultrasound in Obstetrics and Gynecology*, 48, 642-649

Reference ranges for BhCG in normal, non-pathologic pregnancies

Expected value for healthy, non-pregnant female: < 6 IU/L.

Weeks of Gestation	HCG (IU/L, 5th - 95th percentile range)
3	6 - 70
4	10 - 750
5	215 - 7140
6	160 - 32,000
7	3700 - 164,000
8	32,000 - 150,000
9	64,000 - 151,000
10	47,000 - 187,000
12	28,000 - 210,000
14	14,000 - 63,000
15	12,000 - 71,000
16	9000 - 56,000
17	8200 - 56,000
18	8100 - 58,000

Quantitative bHCG performed on Roche Cobas system.

Reference ranges for Progesterone in normal, non-pathologic pregnancies

Female follicular phase: < 4.0 nmol/L
Female mid-cycle: < 5.0 nmol/L
Female luteal phase: 2.0 - 90 nmol/L
Female post menopause: < 2.0 nmol/L
First trimester pregnancy: 36 - 130 nmol/L
Second trimester pregnancy: 120 - 200 nmol/L
Third trimester pregnancy: 330 - 650 nmol/L