



Transient osteoporosis in the third trimester of pregnancy: A case report

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ABSTRACT

A 40-year-old woman presented to the emergency department at 35 weeks of gestation with a six-week history of progressive bilateral hip pain and a severe decline in mobility. Initial investigations were unremarkable and magnetic resonance imaging demonstrated bilateral and extensive femoral bone marrow oedema suggestive of transient osteoporosis (TOP). The patient was managed conservatively and underwent an elective caesarean section at 37 weeks of gestation. There was a gradual postpartum improvement of the patient's symptoms and she attained independent mobility by four weeks postpartum. TOP is a rare presentation and its true prevalence is likely underestimated owing to the diagnostic challenges of the syndrome, which can cause significant delays and often missed diagnoses. It is important for clinicians to be aware of TOP in pregnant women presenting with hip pain and for them to initiate early multidisciplinary involvement to guide diagnosis and management.

1. Introduction

Transient osteoporosis (TOP) is a poorly understood phenomenon with unclear aetiology and an estimated prevalence of 1 in 250,000 amongst pregnant women in the third trimester [1]. Whilst most commonly affecting men, when it occurs in women it almost exclusively affects antenatal women in the third trimester of an otherwise uneventful pregnancy with no specific identifiable risk factors [2]. It can be challenging to differentiate TOP from other causes of hip pain and given that the condition typically affects otherwise healthy young women, it is often overlooked as simple musculoskeletal pain, with no further investigations carried out [3]. However, delays to diagnosis can significantly impact the quality of life as it progressively causes debilitating lack of mobility and can lead to complications such as fractures and avascular necrosis [2]. Once diagnosed, management can also pose a challenge, as traditional treatments for osteoporosis lack robust safety data for pregnant and breastfeeding women [2,4]. The clinical course is typically self-limiting, resolving postpartum with conservative management [4,5].

2. Case Presentation

This case study describes the clinical course of a 40-year-old woman in her first pregnancy who presented to the emergency department at 35 weeks of gestation for worsening bilateral hip pain.

She had had an uncomplicated antenatal course thus far, receiving

routine pregnancy care with the low-risk midwifery clinic. She had no significant medical or surgical history. Her antenatal serology was unremarkable and she was vitamin D replete. Her risk factors included social smoking prior to pregnancy, and a BMI of 28 kg/m [2].

She presented with a six-week history of worsening right hip pain, with involvement of the left hip for the past four weeks. Her emergency department presentation was prompted by a progressive and severe decline in mobility, where she was unable to mobilise to the bathroom using crutches. No history of trauma was identified, and her pain had not improved with paracetamol, heat packs or outpatient physiotherapy. She reported no infective symptoms, and no bowel or bladder deficits. Upon examination in the emergency department she was found to have mild tenderness of her bilateral hips on palpation and a significantly reduced range of motion secondary to pain on bilateral hip flexion, more marked on the right side. No sensory deficits were identified, and there was no involvement of the lower back or sacroiliac joints. Biochemistry was unremarkable, with negative inflammatory markers, and normal vitamin D and serum calcium levels.

There were no obstetric concerns noted by the patient, and cardiotocography upon presentation was reassuring. An obstetric ultrasound scan demonstrated a normally grown foetus of 2704 g at the 45th percentile with a normal biophysical profile.

There was multidisciplinary involvement in the case with the orthopaedic, endocrinology and obstetric teams, given the unusual presentation. Pelvis X-rays were initially suggested by the orthopaedic team to assess for fractures; however, due to foetal radiation concerns, the

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patient underwent magnetic resonance imaging (MRI) of the pelvis and hips. The MRI demonstrated heterogenous bone marrow oedema in the femoral heads bilaterally, more extensive on the right, with extension inferiorly through the femoral neck to the intertrochanteric regions, and no definitive fracture was seen. Her biochemistry including markers of bone metabolism remained unremarkable. This supported a diagnosis of bilateral TOP of the hips.

Orthopaedic advice was to remain non-weight-bearing and commence venous thromboembolism prophylaxis with enoxaparin and calf compressors, given no definitive fractures on imaging. A joint decision was made with the patient for a caesarean section, given the patient's significantly reduced mobility and range of motion, and the postulated additional risk of fracture associated with trial of vaginal delivery. The patient was steroid covered and had an uncomplicated elective caesarean section at 37 weeks of gestation.

Post-operatively, the patient was advised to weight-bear as tolerated and she received inpatient physiotherapy and occupational therapy to assist the transition from hospital to home. A DEXA scan postpartum demonstrated osteoporosis of the right femoral neck ($T - 2.5$) and osteopenia of the right proximal femur ($T - 1.6$) with a normal lumbar spine ($T - 0.8$). Following this, the endocrinology team advised the patient to avoid breastfeeding, given the risk of further decrease in bone density, fragility fractures and delay in recovery of her transient osteoporosis. Given limited evidence for anti-resorptive therapy in the postpartum period, she was not commenced on any medical therapy.

The patient was discharged home 13 days after her caesarean section, once she was able to safely mobilise with crutches. She was reviewed by the orthopaedic surgeon two weeks after discharge, by when she had experienced a significant improvement in pain and mobility and was able to independently care for herself and her newborn.

3. Discussion

Transient osteoporosis (TOP) is a rare entity characterised by progressive pain and a decline in mobility, most commonly of the hip joint. It is less common in females, and when it does manifest in females the predominant group affected is women in their third trimester of pregnancy. It is a benign condition with no clear aetiology and appears to gradually resolve postpartum.

The pathophysiology of TOP in pregnancy and lactation is unclear. Antenatally it is hypothesised to be secondary to increased calcium needs of the foetus for skeletal mineralisation and growth, particularly in the third trimester [6,7]. Up to 80% of foetal calcium is obtained in the third trimester of pregnancy, which is aided by a doubling of maternal intestinal calcium absorption [6]. This is hypothesised to be secondary to the increasing concentration of calcitriol detected in each subsequent trimester of pregnancy, however this has not been definitively demonstrated in animal or human studies. Additionally, vitamin D deficiency is not a consistent finding in women affected by osteoporosis in pregnancy [6]. The placental calcium gradient maintains the relative hypercalcaemic state of the foetus and is supported by the activity of foetal parathyroid hormone (PTH) and parathyroid hormone-related protein (PTHrP) [6]. Breastfeeding is associated with increased PTHrP and decreased oestrogen levels, which are believed to contribute to osteoporosis however, the clinical data on this is conflicting [6,8]. The pathophysiology of osteoporosis in pregnancy and breastfeeding is still unclear, as is the reason for it existing only as a transient entity, with spontaneous resolution observed postpartum.

Given the conflicting observations and unclear pathophysiology, a recommendation cannot be made for calcium and vitamin D supplementation specifically for the prevention of TOP in pregnancy. However, optimal maternal calcium and vitamin D levels are crucial for foetal skeletal development and should be emphasised in routine obstetric care.

TOP is likely under-diagnosed as it is not a widely recognised

medical condition. This is an issue particularly in the antenatal population, as pelvic pain is often simply thought to be musculoskeletal and there is a reluctance to perform imaging on pregnant women secondary to the risk of foetal radiation exposure. Missed diagnosis can affect the quality of life of women and result in a debilitating loss of mobility, as seen in the present case, where the patient was unable to ambulate to the bathroom. Additionally, if unrecognised and not appropriately managed it could lead to complications such as fractures and avascular necrosis.

Whilst often retrospectively realised, the clinical course of TOP usually presents in three stages. The first stage is characterised by increasing pain affecting the woman's ability to walk and eventually even to transfer from a supine to standing position [2,4]. In the next stage these symptoms are reflected on imaging studies as bone marrow oedema [2,4]. The third stage describes the gradual recovery, usually postpartum, aided by gradual return to controlled weight-bearing and simple analgesia [2,4].

The difficulty of the diagnosis of TOP is compounded by the fact that there are no specific risk factors linked with its development and it is a diagnosis of exclusion. Traditional risk factors for osteoporosis such as age, smoking, alcohol consumption and low vitamin D levels are not always reflected in this group of antenatal women in third trimester affected by TOP [2]. Differential diagnoses include fractures, avascular necrosis, primary or secondary malignancies and complex regional pain syndrome [4]. Multidisciplinary teamwork is crucial in the diagnosis and management of TOP.

Investigating hip pain in the pregnant woman is challenging, as discussed above. Biochemistry is typically unremarkable in TOP, but can be useful in distinguishing TOP from other causes of hip pain, including malignancy and infective aetiologies. The choice of imaging can be difficult, particularly in a public hospital setting. In a presentation of debilitating hip pain and significantly reduced range of motion, a fracture is one of the top differential diagnoses. Ideally, plain radiographs should be avoided in pregnancy; however, it may be most easily accessible option in a public hospital setting and should be considered in the case of significant delays to MRI. If other diagnoses are excluded, MRI is the most sensitive method of detecting changes typical of TOP and is effective at distinguishing it from avascular necrosis [2,5]. MRI findings suggestive of TOP include diffuse bone marrow oedema without focal changes [2,5].

Once diagnosed, there are several management factors to be considered. There is no consensus on the appropriate mode of delivery for a woman with TOP, given the limited data available [2,4]. Often TOP results in a severe functional limitation of the range of motion of the hip, which becomes a strong indication for an elective caesarean section. It is also hypothesised that a caesarean section may be protective for birth-related trauma and complications of TOP, including fractures, and the limited observational data indicates a 74% rate of caesarean section in women with TOP [9].

The mainstay of treatment of TOP in the absence of complications is conservative management centred around non-weight-bearing strategies and simple analgesia [4,5]. Bisphosphonates are the most common treatment for osteoporosis; however, data regarding their use in antenatal and breastfeeding women is scant. There is evidence that bisphosphonates cross the placenta; however, their effects on foetal development are unknown. Animal studies demonstrate growth restriction and reduced bone density of the foetus whilst the few documented human case studies indicate no significant impact on the foetus, with normal birth weights and no adverse impacts observed [10]. The case studies in pregnant women largely comprise those with malignancies and bone metastases necessitating urgent treatment with bisphosphonate therapy [10]. Given this, there is an understandable reluctance to use it in otherwise healthy pregnant women with TOP, especially as there is a lack of robust data, and as conservative management and delivery most often lead to recovery. Similarly, calcitonin was demonstrated to decrease time to recovery in two case studies [11] but it requires more extensive research before it can be routinely

recommended for use in TOP for pregnant women.

The data on bisphosphonates in breastfeeding is also scarce. Pamidronate has been found to be undetectable in breast milk 48 h following a 30 mg infusion and was used in a case study where the woman experienced severe postpartum hip pain not amenable to opioid analgesia [12]. She received two infusions on day 3 and day 8 postpartum, expressing and discarding her breastmilk for 24 h after infusion. The child was observed to have no adverse effects at one-year follow-up [12]. Whilst this is encouraging, this should be reserved for cases where other management options for pain have been exhausted, as there is no extensive safety data available. Breastfeeding in itself may also a risk for further decreased bone density secondary to an increased expression of bone-resorbing markers [13], which is why the patient was recommended to cease breastfeeding.

Observational data suggests that recovery is spontaneous postpartum, usually occurring within six weeks [4,5]. Whilst data is limited by the rarity of the disease, TOP does not seem to recur in subsequent pregnancies or have any familial links [4]. Long-term follow-up should be aimed at ensuring that the woman is pain free, regains full mobility and is able to independently care for herself. Traditional risk factors for osteoporosis, such as smoking, should be controlled and a DEXA scan should be repeated in 18–24 months to assess for improvement in bone density.

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Patient consent

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The author declares no conflict of interest regarding the publication of this case report.

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