P434

P434 -Severe systemic toxicity following intra-sac methotrexate treatment of an ectopic caesarean scar pregnancy

Dr Sarah Gleeson[1], Dr David Semple[1], Dr Audrey Long[1], Dr Ian Kando[1]
[1]*Auckland City Hospital, Auckland, New Zealand*

A 30-year-old G3P2 Tokeluan woman with haemodialysis-dependent end stage renal failure, secondary to diabetic nephropathy, presented with an unplanned pregnancy. One of her previous children had been delivered by caesarean section. Fetal ultrasound scan at 8 weeks showed an ectopic caesarean scar pregnancy. This ectopic pregnancy was treated with an intra-sac injection of 50mg methotrexate and fetal intracardiac injection of 2mls 20mmol/ml potassium chloride. The procedure was uneventful.
On day 1 post procedure she became unwell with Escherichia. coli bacteraemia. Despite appropriate antibiotic treatment she deteriorated, with persistent pyrexia, worsening mucositis, rash and pancytopenia. On day 5, methotrexate toxicity was suspected; serum methotrexate level was 0.30umol/L (normal< 0.02). Despite folinic acid and granulocyte colony stimulating factor administration, she developed severe neutropenia, complicated by both Candida albicans and dubliniensis fungaemia, requiring intensive care unit admission and prolonged inpatient treatment. Bone marrow synthetic function recovered at 14 days and she self-discharged on day 55.

Discussion
Caesarean scar pregnancy (implantation of the embryo into a uterine scar, usually following previous caesarean section), carries a significant risk of uterine rupture, severe haemorrhage and death if pregnancy is continued. Prompt treatment is advised. Treatment options include systemic or local methotrexate, uterine artery embolization and surgery.
Methotrexate preferentially affects rapidly dividing cells, e.g. bone marrow, blastocysts and mucous membranes. In patients with normal renal function, high-dose administration can lead to toxicity. Folinic acid is often co-administered with methotrexate to limit or prevent toxicity, and methotrexate concentration is carefully monitored. In patients with impaired renal function, in whom methotrexate clearance is reduced, the risk of toxicity is heightened. There have been 2 previously reported cases of methotrexate toxicity in dialysis patients after systemic methotrexate administration for ectopic pregnancy, 1 fatal.

In patients with renal dysfunction, locally administered therapies are often considered safe and devoid of systemic toxicity. The systemic clearance of locally administered treatment is rarely considered. As exemplified by this case, this approach can have devastating consequences.

This is the first reported case of methotrexate toxicity following intra-sac methotrexate administration. In this case local methotrexate administration into the gestational sac was erroneously considered safe due to a misperception of it having only local effects, with little systemic absorption. However, a study in tubal ectopic pregnancies showed that mean peak serum methotrexate levels after local injection to the ectopic amniotic sac were comparable to those obtained with systemic dosing.

In the face of a rising incidence of both caesarean scar ectopic pregnancies (growing trend of operative deliveries) and renal disease, cases such as this serve as a timely reminder to renal physicians of the potential for methotrexate toxicity in patients with renal disease, even with local administration. A high clinical index of suspicion, methotrexate blood level monitoring, folinic acid administration and high flux dialysis are integral to the diagnosis and management of such situations. This almost- fatal case also

highlights the need for proactive management of contraception and pregnancy planning in dialysis patients of child-bearing age.