## Maternal Medicine – Miscellaneous

<table>
<thead>
<tr>
<th>M2-01</th>
<th>Risk factors and outcome of pregnancy with cardiac disease.</th>
</tr>
</thead>
<tbody>
<tr>
<td>M2-02</td>
<td>Maternal and neonatal outcomes in pregnancy complicated with pulmonary hypertension: a case series from west China.</td>
</tr>
<tr>
<td>M2-03</td>
<td>Pelvic Tuberculosis complicated by meningitis with radiological changes appears within 24 hs.</td>
</tr>
<tr>
<td>M2-05</td>
<td>A case of an unexpected pregnancy in a woman undergoing treatment for metastatic melanoma.</td>
</tr>
</tbody>
</table>
Risk Factors and Outcome of Pregnancy with Cardiac Disease

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Objective:
To assess risk factors and outcomes of pregnancy with cardiac disease

Place:
dr. Wahidin Sudirohusodo hospital, Makassar

Design:
Cross-Sectional Retrospective Study

Methods:
Samples are pregnant women with congenital or acquired cardiac disease and treated at Dr.Wahidin Sudirohusodo Hospital during January 2016 - December 2017. During the study period we found 29 pregnant women with cardiac disease. Data were analyzed using chi square test using SPSS software. P value <0.005 considered as significant.

Results:
Most of our study samples were multiparous (65.5%), and not obese. Gestational age at admission mostly was ≥34 weeks (69%). Majority of our samples had no history of hypertension (51.7%) but had a history of cardiac disease (58.6%). Based on maternal and neonatal outcomes, most of infants who were born had mild-to-moderate asphyxia (65.5%), and born with birth weight <2500 gram (55.2%). Most woman were hospitalized ≤4 days. We did not find significant association between parity, body mass index, gestational age, history of hypertension, extent of aortic valve, mitral valve area and left ventricular fraction ejection with incidence of cardiac failure (p < 0.05). There was a significant association between history of cardiac disease and risk of heart failure (p = 0.03).

Conclusion:
Previous history of heart disease affects maternal outcomes of pregnant women with heart disease.

Keywords: cardiac disease, risk factors, maternal outcome, perinatal outcome

REFERENCES
OBJECTIVE

To determine maternal and fetal outcomes in patients with pulmonary hypertension (PH).

METHOD

A retrospective analysis was carried out of 71 pregnancies in women with PH who delivered at a tertiary care center in west China between January 2009 and May 2015.

RESULTS

One pregnancy resulted in spontaneous abortion and six were electively terminated. The cardiac complications were encountered in 26.8% including 3 maternal mortalities. At least one adverse obstetric event and neonatal complication occurred respectively in 28.2% and 56.3% of the 64 ongoing pregnancies. Diagnosis after the third trimester, severe PH and/or right ventricular systolic dysfunction were predictive of adverse fetal/neonatal events.

CONCLUSION

A pre-pregnancy baseline assessment can identify women at the highest risk. Pregnancy is strongly discouraged especially in those patients with baseline NYHA functional class III or IV or severe PH and/or right ventricular systolic dysfunction.
Pregnancy in a woman on treatment for metastatic melanoma

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Introduction

Women of childbearing age make up approximately 1/3 of women diagnosed with melanoma, making it one of the most common malignancies diagnosed in pregnancy (Todd, 2017). Management during pregnancy however remains unclear (Todd, 2017), and depends on when it is diagnosed and the extent of disease. There appears to be no significant impact on maternal prognosis when primary disease is diagnosed prior to pregnancy, based on retrospective cohort data (Lens, 2004).

The primary concerns with management surround progression of disease in the mother, embryofetal toxicity during treatment, and metastasis to the placenta and fetus. Progression of disease is thought to be either due to the cessation of treatment, or the relative immunosuppression and hormonal changes during pregnancy that may increase the growth rate of existing localised melanomas or increase metastasis.

Melanoma is the most common tumour to metastasize to the fetus and can occur in widespread metastatic disease of the mother. It is reported that the fetus will be affected in 25% of cases when placental involvement is identified (Alexander, 2003).

This case describes the management and outcome of a pregnancy diagnosed when undergoing treatment with Nivolumab for stage 4 melanoma BRAF mutation (not previously reported).

Nivolumab is a human IgG4 monoclonal antibody that acts as a checkpoint inhibitor immunotherapy agent which targets programmed cell death protein 1 (PD-1) and decreases tumour growth. It is approved for the treatment of advanced melanoma. Human IgG4 is known to cross the placenta. There is no available human data recording drug associated risk and hence women are counselled on potential harm to a fetus in the case of a pregnancy.

Case

A 32-year-old nulliparous female who had experienced 10 years of primary infertility was undergoing treatment for stage IV melanoma (BRAF mutation) diagnosed 1 year prior. Melanoma was first diagnosed in 2011 with a lesion on her forehead which was excised. She was on a clinical trial of Nivolumab with treatment under a specialist oncologist for her recurrence. She smoked 2 cigarettes and 7 cones of marijuana per day whilst undergoing treatment and had been using condoms and a combined OCP as per the conditions of the trial, when she unexpectedly fell pregnant. She had received her last dose of Nivolumab at approximately 8 weeks when she was referred to Maternal and Fetal Medicine (MFM) specialist at RBWH.

Through the MFM department, she received close specialist monitoring and regular ultrasounds every 3 weeks, including a low risk combined first trimester screen and normal morphology. All other antenatal investigations were unremarkable.

Progression of melanoma was also monitored antenatally with regular chest X-RAYS and liver USS.

Small for gestational age baby was diagnosed on a 31-week growth scan. A subsequent ultrasound at 32+5 showed decreasing growth velocity. Delivery via caesarean section was performed at 33+1 weeks following pre-term labour. A healthy infant was delivered and admitted to the nursery. The placenta was sent for detailed histology that showed no evidence of metastatic melanoma. The patient’s post-partum CT showed stable disease with no new metastasis.

Discussion

Antenatal counselling focused on potential fetal risks from Nivolumab, and potential maternal risks in progression of disease. One key function of the pathway blocked by Nivolumab, is preserving pregnancy by maintaining maternal immune tolerance to the fetus. By disrupting this pathway in mouse models there was increased spontaneous abortion.

Animal studies also reported increased premature infant death, though no apparent malformations or effects on neurobehavioral, immunological or clinical pathology parameters throughout the 6-month postnatal period.

It was uncertain whether Nivolumab would cause embryo-fetal toxicity. The drug is also thought to potentially cross the placenta as it is an IgG4, with effects thought to be greatest in 2nd and 3rd trimester.

The chance of transplacental melanoma spread was also discussed antenatally and raised concerns for potential transmission to the baby.

Conclusion

It is difficult to comment on the safety profile of Nivolumab during pregnancy after 1 case report, however there did not appear to be any adverse effect to the fetus during organogenesis when the drug was still being taken.

In those with advanced disease, it is recommended to wait 2-3 years before becoming pregnant due to the risk of recurrence. Birth control is recommended, and there does not appear to be an increased risk of melanoma in those using the OCP.

References:
1/ Todd, S. Driscoll, M. (2017); Int J Womens Dermatol. “Prognosis for women diagnosed with melanoma during, before, or after pregnancy: Weighing the evidence