Pregnancy and Bone Marrow Failure Diseases

Fertility issues
Precautions to preserve fertility
Risks of pregnancy
Recommended surveillance
Inheritance
Alternative possibilities
Pregnancy and Bone Marrow Failure Diseases

Issues are complex
Little published data or studies available
The law varies for reimbursement for fertility treatment and assisted reproduction
Highly individualized multidisciplinary approach for:
  • Assessment / Counseling
  • Treatment / Surveillance
  • Preservation

Major Factors Influencing Pregnancy in Bone Marrow Failure Diseases

Type of BMF
  • Inherited
    • Acquired
      • PNH
      • MDS

Type of treatment in the past
  • Immune suppression
  • Transfusion history
  • Androgen use
  • Bone marrow transplant

Severity and duration of current disease complications in the past

Fertility Issues in Bone Marrow Failure Diseases

Inherited BMF Acquired BMF PNH MDS

• Reduced fertility is part of the syndrome (primary hypogonadism)
• Anomalies of the reproductive organs
• Fertility may be reduced secondary to chronic illness and previous therapy
• Hormonal anomalies primary or secondary (secondary hypogonadism i.e. iron overload)

• Erectile dysfunction

• Fertility is usually not primarily affected
• Fertility may be reduced secondary to chronic illness and previous therapy
• Hormonal anomalies secondary (i.e. iron overload)
Preserve Fertility in Bone Marrow Failure Diseases

Cryopreservation:
- Sperm
- Egg
- Ovary
- Testes

Erectile dysfunction: Sildenafil, Viagra®
- PNH: Complement inhibitors (Eculizumab, Soliris®)

Assisted Reproduction in Bone Marrow Failure Diseases

Performed in a Fertility Clinic:
- Medication
- Artificial Insemination
- In vitro fertilization (IVF, test tube baby)

In vitro fertilization
Risks of Pregnancy for Mother and Child in Bone Marrow Failure Diseases

(Mothers with BMF or after immune suppressive therapy)

**BMF:**
- **Mother:**
  - Worsening of bone marrow function, relapse of aplastic anemia (30%)
  - Infection
  - Bleeding
  - Anemia
  - Pre/Eclampsia
- **Child:**
  - Early and late fetal loss
  - Low birth weight, prematurity, infection, fetal stress
  - Hemolytic disease of fetus and newborn in multiply transfused mothers
  - Inheritance of genetic disease

**PNH:**
- **Mother:** Blood clots during pregnancy and puerperal period (6-8 wks after birth)

Recommended Surveillance for Pregnant Individuals with BMF

- **Maternal surveillance:**
  - Hematologist familiar with BMF and PNH
  - Obstetrician familiar with high risk pregnancies
  - Neonatologist
  - Frequent monitoring especially third trimester
Recommended Surveillance for Pregnant Individuals with BMF

**Transfusion therapy:**
Red cell transfusion < Hemoglobin 9-10 g/dl
Platelet transfusion <Platelets 20,000

**Prevention of infection:**
Rigorous surveillance for infections (urinary tract infection)
Prophylactic antibiotic if low white blood cell counts (ANCs)
Prophylactic antifungal therapy if low white blood cell counts (ANCs)

**Delivery:**
Spontaneous vaginal delivery if possible
Epidural/spinal anesthesia depending on platelet counts, and experience (ultrasound guided)

**Medication:**
United States FDA Pharmaceutical Pregnancy Category
Cyclosporine Pregnancy Category C
ATG or ALG Pregnancy Category C

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United States FDA Pharmaceutical Pregnancy Category

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
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<tbody>
<tr>
<td>Pregnancy Category A</td>
<td>Adequate and well-controlled human studies showed no risk to fetus in first trimester of pregnancy (and there is no evidence of risk in later trimesters).</td>
</tr>
<tr>
<td>Pregnancy Category B</td>
<td>No risk to fetus in animal studies but there are no adequate studies in pregnant women. Off animal studies have shown an adverse effect, but adequate studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester.</td>
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<tr>
<td>Pregnancy Category C</td>
<td>Animal studies have shown an adverse effect on the fetus and there are no adequate studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.</td>
</tr>
<tr>
<td>Pregnancy Category D</td>
<td>Positive evidence of human fetal risk from human studies, but potential benefits may warrant use of the drug in pregnant women despite potential risks.</td>
</tr>
<tr>
<td>Pregnancy Category X</td>
<td>Positive evidence of human fetal risk in animal or human studies, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.</td>
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http://en.wikipedia.org/wiki/Pregnancy_category&oldid=367143184
**Recommended Surveillance for Pregnant Individuals with BMF**

*First/Second trimester screening:*
Red cell antibodies: D and Kell
Viral screening
Ultrasound

**Genetic surveillance:**
Prenatal genetic counseling
Genetic testing by amniocentesis or chorionic villus sampling
Preimplantation genetic diagnosis (PGD)

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**Recommended Surveillance for Pregnant Individuals with PNH**

*PNH specific:*
- PNH clone size by flow cytometric analysis
- Full therapeutic anticoagulation with low molecular weight heparin (LMWH) if PNH clone ≥50% and platelet count ≥80,000/µl during pregnancy and full anticoagulation 6-12 wks after delivery, monitor anti-Xa activity
- Discuss whether to initiate or continue complement inhibitors (Eculizumab, Soliris®). Successful pregnancies have been reported - long term effects are yet unknown
- Adjust dosing of complement inhibitors (Eculizumab, Soliris®)
- Rigorous surveillance for infections (urinary tract infection)
- Epidural/spinal anesthesia depending on platelet counts, anticoagulation, and experience (ultrasound guided)
- Folic acid substitution

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**Inheritance of BMF Diseases**

Our genes are unique

Half of your genes are from your mother, the other half are from your father

Adapted from Human Genome Project
Can you pass bone marrow failure disease on to your child?

Bone marrow failure or the predisposition to develop bone marrow failure may be inherited. An inherited bone marrow failure disease always has to be excluded especially in children and the young adult who presents with BMF. If an inherited BMFS is suspected or diagnosed, genetic counseling is advised. The inheritance varies for different bone marrow failure diseases.

PNH is NOT passed on to our child, however the predisposition to develop bone marrow failure may be inherited.

MDS or the predisposition to develop MDS may be inherited or develop out of an inherited form of BMF. An inherited form of MDS or BMF has always to be excluded especially in children and young adults who present with MDS. If an inherited form of MDS or BMF is suspected or diagnosed, genetic counseling is advised. The inheritance varies for different bone marrow failure diseases.

Alternative Possibilities for Becoming a Parent

- Adoption
- Surrogate Pregnancy = substitute mother in the place of the natural mother. Legal contract, laws differ between countries and states.
  - Traditional surrogacy (straight method) the surrogate is pregnant with own biological child, but child was conceived with the intention of its being raised by others.
  - Gestational surrogacy = gestational carrier = the surrogate becomes pregnant via embryo transfer with a child of which she is not the biological mother.
  - Altruistic surrogacy is a situation where the surrogate receives no financial reward for her pregnancy.
  - Commercial surrogacy is a form of surrogacy in which a gestational carrier is paid to carry a child to maturity.

Pregnancy in Bone Marrow Failure Diseases

Pregnancy in BMF diseases is often complex and requires a highly individualized, multidisciplinary approach.

"Planning is bringing the future into the present so that you can do something about it now!" 
(Latin proverb)