Investigation and Management of Fetal/Neonatal Alloimmune Thrombocytopenia (FNAIT)

New Zealand Maternal Fetal Medicine Network

This guideline was updated in October 2015 by Dr Emma Parry, with input from members of the New Zealand Maternal Fetal Medicine Network, Clinical Directors in Obstetrics and Gynaecology and Neonatology.

Background

FNAIT is a rare condition characterised by thrombocytopenia in the Fetus or Neonate. It occurs in about 1 in 8000 pregnancies. It is secondary to Maternal Platelet specific Alloantibodies which are produced secondary to maternal paternal platelet type incompatibility. It is usually detected as a consequence routine investigations of bruising, purpura or poor condition in a neonate. However it can also be diagnosed at the time of a significant intra cerebral haemorrhage of a fetus in utero or a neonate. These situations are a more rare presentation of FNAIT. Occasionally FNAIT will be diagnosed during the investigations carried out due to a close family member having suffered with FNAIT. The effects of FNAIT can be devastating and for those women management is complex.

Objective

To aid planning and management of a pregnancy where there are Maternal Platelet specific Antibodies.

Differential Diagnosis

Neonatal Thrombocytopenia or IVH secondary to other causes. Maternal thrombocytopenia is secondary to auto immune antibodies and is unrelated to FNAIT.

Important History

Previous pregnancies. Affected fetus and /or neonate. Timing and effect in particular:

- Intracranial Haemorrhage (ICH) and timing
- Cord/ newborn platelet count

- Any maternal Anti-platelet antibody investigation
- Any maternal therapies

Ultrasound

Minimal use except to identify an antenatal ICH

Investigation

- These tests are complex to perform and often difficult to interpret. They should be requested by Doctors with expertise in the area as anxiety can result when the tests are performed when not indicated or results are not correctly interpreted. Members of the NZMFMN are available to advise as to whether testing should be considered
- Maternal Platelet specific Alloantibodies
- Platelet typing and compatibility of both parents (note the lab request blood from BOTH parents)

Note that antibody testing and platelet typing for all NZ patients is performed at the National tissue typing laboratory: (09) 523 5731. If there is a strong clinical suspicion of FNAIT and the antibody screening is negative, discuss the results with the tissue typing laboratory. Antibodies may clear between pregnancies and even be negative in early pregnancy but re-appear later.

Prognosis

This depends on previous Obstetric and Neonatal History. If the couple have had a previously affected child there is an 80% chance of thrombocytopenia in a future pregnancy without treatment. This condition tends to worsen with each pregnancy without treatment.

On-going Management

See chart below

Prenatal Testing

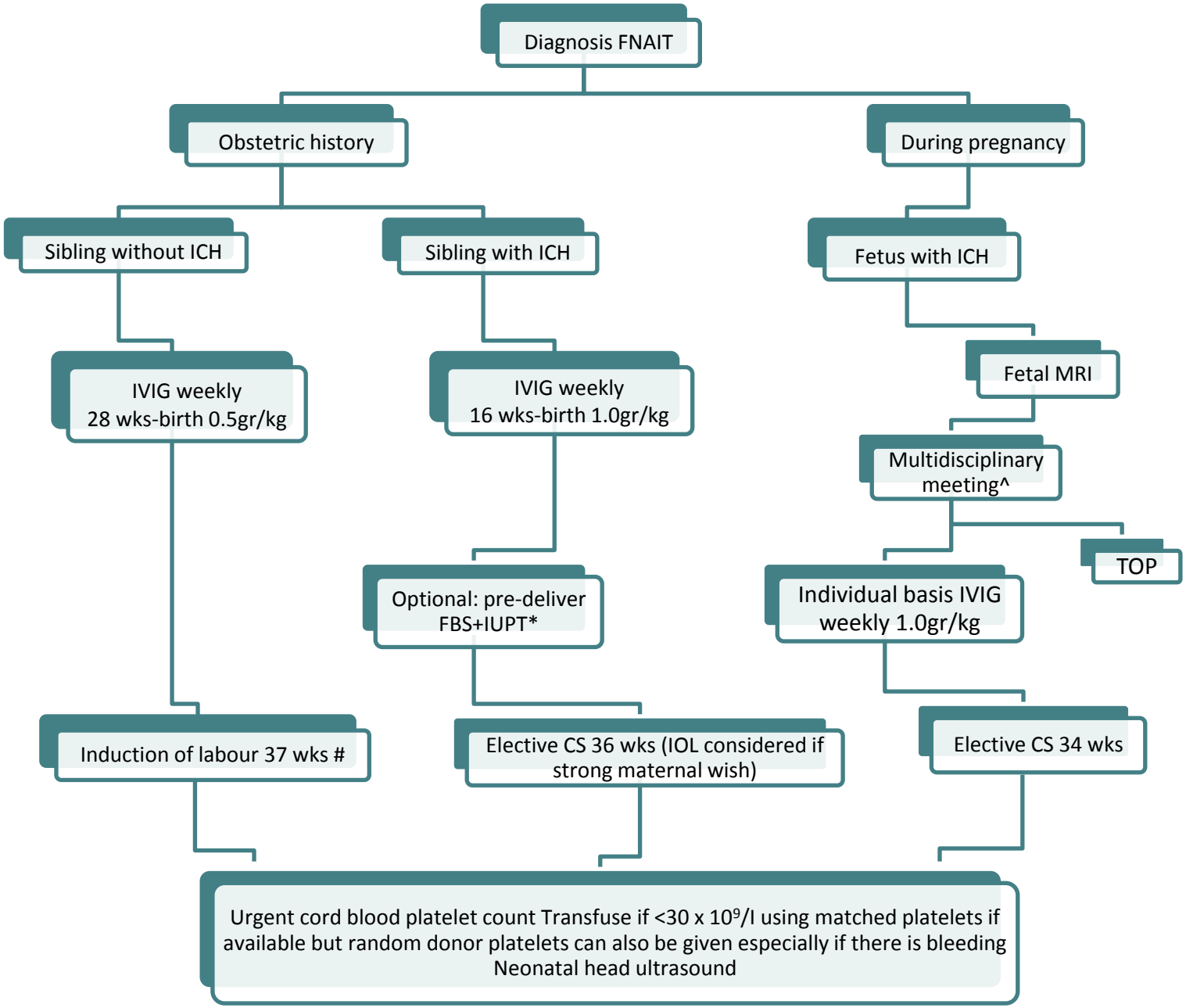
If the father has heterozygosity for the particular antibody producing antigen, invasive testing of the pregnancy can be offered to tissue type the fetus. Tissue typing laboratory should be consulted prior to procedure (09) 523 5731. If the fetus is compatible to the mother on-going treatment and surveillance is not required. At the time of writing there may be some availability to perform non-invasive testing for platelet type overseas and if a father is heterozygous it is recommended to contact the tissue typing laboratory to get the most up to date information.

IVIG and Steroids

IVIG has been shown to improve platelet count in fetuses at risk of FNAIT. The dose used has varied between studies with a higher dose being used for more serious previous events. The addition of steroids has not been well shown to improve platelet counts but could be considered at a dose of 0.5mg/kg/day for women at high risk of poor outcomes if the benefits outweigh the risks.

Platelet sampling and transfusions

FBS carries a higher risk in a pregnancy at risk of FNAIT due to the risk of bleeding from the puncture site. In addition transfused platelets have a short half-life of 2-5 days unlike transfused red blood cells. Recent approaches have reserved Platelet sampling and transfusion for the time of delivery planning. If a procedure is planned it will generally be performed in a setting where a move straight to caesarean section delivery is possible.


Diagnosis FNAIT
Obstetric history
During pregnancy
Sibling without ICH
Sibling with ICH
Fetus with ICH
IVIG weekly
28 wks-birth 0.5gr/kg
IVIG weekly
16 wks-birth 1.0gr/kg
Fetal MRI
Multidisciplinary meeting^
TOP
Optional: pre-deliver FBS+IUPT*
Individual basis IVIG weekly 1.0gr/kg
Induction of labour 37 wks #
Elective CS 36 wks (IOL considered if strong maternal wish)
Elective CS 34 wks
Urgent cord blood platelet count Transfuse if <30 x 10⁹/l using matched platelets if available but random donor platelets can also be given especially if there is bleeding
Neonatal head ultrasound

^Consulting paediatric neurologist, neonatologist regarding outcome

*with platelet transfusion if platelet count <50x10^9/l

#avoid any potential traumatic events, like scalp electrode, scalp blood sampling or assisted vaginal delivery

ICH=intracranial haemorrhage, IVIG=intravenous immunoglobulins, TOP=termination of pregnancy

CS=caesarean section, FBS=fetal blood sampling, IUPT=intrauterine platelet transfusion

Figure 1 - Flowchart for perinatal management of fetal and neonatal alloimmune thrombocytopenia

References

- M.M.Kaphuis and D.Oepkes, Prenat Diagn 2011; 31: 712-719. DOI: 10.1002/pd

Additional Information

Adobe Acrobat Document

Additional Information

NZBLOOD
Te Ratonga Toto O Aotearoa

REQUEST FOR TISSUE TYPING DIAGNOSTIC TESTING

- Disease Association
- Platelet Tests, Transfusion Reaction Investigation
- Hypersensitive Drug Reactions

National Tissue Typing Laboratory

NZ Blood Service
Private Bag 92071
Victoria Street West
Auckland 1142
NEW ZEALAND

Telephone: (09) 523 5731
Fax: (09) 523 5761

Tissue Typing use only:

Received by _____ Registered by _____

Event No.

FULL AND ACCURATE COMPLETION OF THIS FORM IS ESSENTIAL

Step 1. PATIENT/DONOR DETAILS - sections marked * are mandatory

*(Tick box indicating if detail relate to a patient or donor. Attach identification label or complete **all** written details).*

❑ **Patient** ❑ **Donor implicated in TRALI/Transfusion Reaction**

*NHI No. _____ *DOB _____ *Gender ____

*Family Name _____

*Given Names _____

Ethnicity _____

*DHB of Patient _____

*Progesa ID of Donor _____
(TRALI/Transfusion Reaction investigation only)

FOR URGENT TEST REQUESTS PLEASE PHONE TISSUE TYPING – (09) 523 5731

Step 2. TESTING REQUIREMENTS – see reverse for sample requirements

Disease Association
- ❑ B27 (ankylosing spondylitis)
- ❑ Coeliac Disease (HLA-DQ)
- ❑ Narcolepsy (HLA-DR,-DQ)
- ❑ Other – please specify _____

Hypersensitive Drug Reaction
- ❑ HLA-B*57:01 (Abacavir)
- ❑ HLA-B*15:02 (Carbamezapine/Tegritol)
- ❑ Other – please specify _____

Platelet Immunology & TRALI/Transfusion Reaction
- ❑ Platelet (HPA) antibody screen
- ❑ NAIT Investigation (includes HPA genotyping and maternal/paternal crossmatch)
- ❑ Investigation of Platelet Refractoriness (includes HPA/HLA antibody screen and HLA/HPA typing if required)
- ❑ TRALI/Transfusion Reaction
- ❑ Other – please specify _____

Step 3. CLINICAL INFORMATION INCLUDING FACTORS WHICH MAY INTERFERE WITH TESTS

Step 4. NAME OF REQUESTING PRACTITIONER / CO-ORDINATOR

Practitioner / Co-ordinator / Nurse: _____ Signature: _____

Contact ph: _____ Date: _____ DHB: _____

Full Address: _____

Copy report to and Address _____

Step 5. SPECIMEN COLLECTOR DECLARATION

* I certify that the blood specimen(s) accompanying this request form was drawn from the patient named above.
* I established the identity of this patient by direct enquiry and/or inspection of their wristband.
* Immediately upon the blood being drawn I labelled and signed the specimen(s) in the presence of the patient.

Date/Time of collection _____ Contact No/Pager _____

SIGNATURE OF COLLECTOR _____ Print Name _____
Doctor/Co-ordinator/Nurse (please circle)

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Abbreviation(s)

BMT = Bone Marrow Transplant	MUD = Matched Unrelated Donor	SOT = Solid Organ Transplant
CDC = Complement-Dependent Cytotoxicity	PAA = Platelet Associated Antibody	SPA = Serum Platelet Antibody
HPA = Human Platelet Antigen	PRA = Panel Reactive Antibody	SSP = Sequence Specific Primers
HLA = Human Leucocyte Antigen	SBT = Sequencing Based Typing	

TEST REQUESTS	SAMPLE REQUIREMENTS
Bone Marrow Transplant - patient/donor Initial and confirmatory HLA typing	2 x 10ml CPDA (If cell count low - 4 x 10ml CPDA) 1 x 10ml clotted 1 x 6ml EDTA (with initial typing only)
Solid Organ Transplant - patient/donor Initial and confirmatory HLA typing Lymphocyte crossmatch (Flowcytometry and CDC) Monthly transplant tray sample	 4 x 10ml CPDA; 1 x 10ml clotted and 1 x 6ml EDTA 4 x 10ml CPDA; 1 x 10ml clotted and 1 x 6ml EDTA 1 x 10ml Clotted or, 3 x 5ml or 2 x 7ml Clotted
Disease Association (e.g. B27, Coeliac, Narcolepsy)	1 x 10ml CPDA
Platelet Immunology & TRALI/Transfusion Reactions TRALI/Transfusion Reactions Refractory patients (includes HLA/HPA typing if required) NAIT (includes HPA genotyping and maternal/paternal XM) Platelet Antibody screen (PAA and SPA)	 Donor: 2 x 10ml clotted; Patient: 2 x 10ml CPDA 4 x 10ml CPDA and 2 x 10ml clotted Mother: 4 x 10ml CPDA and 2 x 10ml clotted Father: 4 x 10ml CPDA 4 x 10ml CPDA and 1 x 10ml clotted
Hypersensitive drug reaction (HLA-B*57:01, HLA-B*15:02)	1 x 10ml CPDA

NOTE: FOR YOUNG PATIENT/DONOR WHERE SAMPLE VOLUMES MIGHT BE PROBLEMATIC CONTACT THE TISSUE TYPING LABORATORY AT (09) 523 5731.

SAMPLE LABELLING & ACCEPTANCE CRITERIA

1. Both tube and request form **MUST** contain the following information:
   - Family name and given name(s)
   - NHI No or DOB
   - Date and time of sample collection
2. Request form and sample(s) **MUST** be signed by physician/transplant co-ordinator/nurse who collected the samples.
3. Details on tubes **MUST** match those on the accompanying form.

DELIVERY INSTRUCTIONS FOR TISSUE TYPING TEST REQUESTS

Monday to Friday	After Hours – Weekends and Public Holidays
Tissue Typing Laboratory New Zealand Blood Service 71 Great South Road Epsom AUCKLAND	Blood Bank Auckland City Hospital Park Road AUCKLAND

TURNAROUND TIMES

Bone Marrow Family Study	1 month	Renal Transplant List (HLA and ABO)	2 weeks
MUD Confirmatory HLA typing	2 weeks	Live Donor Renal workup	4 weeks
HLA Type	2 weeks	Other Solid Organ workup	2 weeks
B27 / Disease Association	2 weeks	CDC PRA/Antibody Screen (SOT)	6 weeks
Platelet Refractoriness	*1 day – 1 week	Cadaver Report	4 weeks
NAIT	*1 day – 1 week	Post Transplant Monitoring	2 days
Platelet Crossmatch	*1 day – 1 week		
HPA Genotype	1 week	*Verbal report given within 24 hours	

TESTS PERFORMED	TECHNIQUE
HLA typing uses DNA techniques and is at intermediate resolution except where stated.	
BMT	
Initial HLA Typing: patient HLA-A,-B,-DR or potential related donor HLA-A,-B, and if a HLA-A,-B match HLA-DR	Luminex DNA typing
Confirmatory HLA Typing - HLA-A,-B,-DR	CDC/Luminex/SSP
Patient High Resolution HLA-DR Typing for Unrelated Donor Search	SSP/SBT
High Resolution HLA-A,-B,-C,-DR,-DQ typing for patient and unrelated donor	SSP/SBT
SOT	
Initial HLA Typing patient and donor - HLA-A,-B,-DR	Luminex DNA typing
TRALI/Transfusion Reactions	Luminex
Confirmatory HLA Typing - HLA-A,-B,-DR	Luminex DNA typing
Crossmatch (patient serum v donor cells)	Flow cytometry/CDC
HLA antibody screening	Luminex/CDC
Disease Association	SSP/Luminex DNA typing