FETAL AND NEONATAL ALLOIMMUNE THROMBOCYTOPENIA (FNAIT): ALGORYTHM OF LABORATORY INVESTIGATION AND TREATMENT MODALITIES IN CROATIAN INSTITUTE OF TRANSFUSION MEDICINE (CITM)

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Background

Fetal and neonatal alloimmune thrombocytopenia (FNAIT) is the result of maternal alloimmunization against paternally inherited specific platelet antigens (HPA) of the fetus, during pregnancy. FNAIT is a rare but potentially life-threatening disorder. The incidence is estimated to 1:1000 to 1:2000 births in white populations. Clinical course varies from asymptomatic to severe cases with intracerebral hemorrhage (ICH) resulting in death or long-term disability. In most cases ICH develops due to HPA-1a alloantibodies. Serologic testing for FNAIT in case of isolated thrombocytopenia in the newborn contributed considerably to timely detection of this disease. Platelet transfusions are needed in severe cases to prevent ICH. Current guidelines recommend transfusion of HPA compatible apheresis platelets or mother's washed and irradiated platelets (threshold above 30x10^9/L). According to the ISBT Working party on platelet serology and genotyping (expert group consensus recommendations) IVIG (corticoids) treatment is over the FBPS and platelet intrauterine transfusions. Usage of IVIG during pregnancy in case of confirmed anti-HPA-1a ab contributes significantly to the prevention of FNAIT.

Aim

The aim of this study was to analyse laboratory and clinical data of 90 new-borns undergoing serologic testing for isolated neonatal thrombocytopenia during the 2004 to 2020 period in Croatian Institute of Transfusion Medicine.

ALGORYTHM /METHODS OF SEROLOGICAL INVESTIGATION

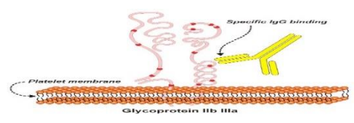
Screening for HPA alloantibodies in maternal/neonatal sera (MAIPA method)
⇩ POSITIVE
Specificity of HPA antibodies (EIA-MAIPA and luminex-bead method)
⇩
HPA genotyping (PCR-SSP method)
⇩
CONFIRMATION OF FNAIT DIAGNOSIS

Results

RESULTS OF LABORATORY INVESTIGATION OF FNAIT IN CITM

In the period from 2004 to February 2017, in the Croatian Institute of Transfusion Medicine, Department of platelet and leukocyte diagnostics and hemostasis 90 FNAIT suspected cases were analyzed. Serologycal screening was positive in 40 of 90 cases.

- Anti-HPA antibodies were detected in 20 (48,8 %) of 41 cases of serologically positive FNAIT :
  * 12 (60%) of 20 anti-HPA-1a
  * 5 (25%) of 20 anti-HPA-5b
  * 2 (10%) of 20 anti-HPA-1b
  * 1 (5%) of 20 HPA-5a

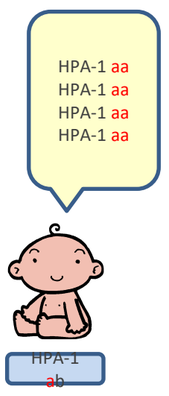


  - In 5 (12,2%) of 41 pan-reactive (anti GP IIb-IIIa, Ia-IIa, Ib-IX) maternal autoantibodies
  - 9 (21,9%) of 41 cases only anti-HLA class I antibodies were detected
  - Serological results were confirmed by antibody identification and HPA genotyping
- In 9 neonates only anti-HLA I were detected, laboratory investigation revelved no anti-HPA alloantibodies of IgG class , cross match of neoanates /fathers platelets and mothers sera done by MAIPA method (by using beta microglobulin) was positive
  - HPA extended genotyping done by IDHPA XT (Luminex, multiplex) showed no presence of low incidence HPA's.
  - In another 7 (17,7%) of 41 confirmation test was negative.

RESULTS OF LABORATORY AND CLINICAL DATA OF EIGHT NEWBORNS WITH FNAIT *DUE* TO ANTI-HPA-1A WHO RECEIVED 9 ANTIGEN POSITIVE PLATELETS FROM RANDOM DONORS

- Five of 8 newborns were male and three female.
- Six of 8 were born to prim parous women.
- All neonates had skin hemorrhage (localized or generalized petechia) and two had intracerebral hemorrhage.
- Serologycal and molecular confirmation of FNATP due to anti-HPA alloantibodies of IgG class in all eight neoanates
- Maternal antibody status was known in one of 8 newborns at the time of transfusion.
- Average platelet count before transfusion was 28x10^9/L (range 7x10^9/L to 34x10^9/L).
- Seven neonates received apheresis platelets in dose of 10 mL per kg BW and two received one single unit of platelet reach plasma (PRP) platelets.
- Five of 8 newborns showed an increase of platelets above 40 x10^9/L (range 47 x10^9/L to 87 x10^9/L) after random donor platelet transfusions.
- Two newborns needed more than one transfusion.
- In addition to platelet transfusion, two newborns received immunoglobulins (IVIG), one received IVIG and corticosteroids and one corticosteroids only

All neonates reached full recovery !



In the period from 2016 to 2020 four mothers were successfuly treated with IVIG (0.8 g/kg BW) from 28 weeks of gestation, along with monitoring of anti-HPA-1a alloantibody titers.

Conclusion

* Serologic testing for FNATP in case of isolated severe thrombocytopenia in the newborn contributed considerably to timely detection and favorable outcome.
* Random donor platelet transfusion is an acceptable approach in urgent situations, when antigen negative platelets are not readily available.
* In addition, intravenous immunoglobulins (IVIG) and corticosteroids can be given to prolong the survival of the incompatible platelets and prevent FNAIT.

Poster presentation
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