

## EDUCATION SESSION 13: PLATELET DISORDERS



### Diagnosis and Management of Immune Thrombocytopenia

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Idiopathic thrombocytopenic purpura (ITP) may be of the acute, self-limited variety, or may be chronic. While it may be difficult to distinguish between these two forms at onset, they are distinct entities.

The *acute, self-limited form of ITP* most commonly occurs in children, often becoming apparent 2 to 3 weeks following a viral infection (varicella, rubella, mumps, upper respiratory tract infection, gastroenteritis, flu-like illnesses, etc.). The peak age is 2-7 years, and the disorder is characterized by the sudden appearance of petechiae, ecchymoses, and mucous membrane bleeding (epistaxis, gum bleeding, and less commonly, gross hematuria or gastrointestinal bleeding). Intracranial hemorrhage rarely occurs. There may be shotty lymphadenopathy and a palpable spleen tip, reflecting the recent viral infection. Males and females are equally affected.

Laboratory tests characteristically show severe to moderately severe thrombocytopenia (the platelet count is often  $< 10,000/\text{mm}^3$ ), with the few platelets seen on peripheral blood film being larger than normal. There may also be anemia (secondary to blood loss) and a relative increase in lymphocytes and monocytes (reflecting the recent viral infection). In most instances, it is not necessary to perform a diagnostic bone marrow aspirate.

In this acute, post-viral form of ITP, management should be individualized. The child should be protected from head injury during the phase of severe thrombocytopenia. Depending on the age, degree of activity, and parental understanding of the need for close observation of the child, some (very young, hyperactive children) may benefit from a brief period of hospitalization in a padded bed or crib. Older children often can be followed on an out-patient basis from the start, with "common sense" precautions (no bicycle riding or skate-boarding, avoidance of situations where accidental head injury may occur).

Anemia due to acute blood loss (if any) can be managed with a packed red blood cell transfusion. (Platelets are rarely of benefit, as the transfused platelets will be rapidly destroyed in the patient's circulation.) Most children (85-90%) will have a spontaneous remission within a few days to a few months (average time: 3 weeks). If there is a perceived need to increase the patient's platelet count quickly (for instance, in a child with extensive mucocuta-

neous purpura, or hyperkinetic behavior and worry about head injury), one can give one or two daily doses of high-dose intravenous immunoglobulin (IVIG) (dosage 0.5 to 1.0 gm/Kg body weight), given I.V. over a period of 6-8 hours). In the majority of children this will result in an increase in circulating platelet count to a safe range within one or two days. By the time the effects of IVIG have worn off, many children will have had a spontaneous remission of ITP. (Disadvantages of high-dose IVIG include its cost, and side effects which can include severe headache, nausea and vomiting, and aseptic meningitis.)

In a few children, the course of ITP ultimately proves to be "chronic" (see below). In an occasional child, there is a spontaneous remission but one or more subsequent episodes of acute ITP (usually in association with another viral infection), with normal platelet counts in-between.

The "*chronic, autoimmune form of ITP (AITP)*" is the form usually seen in adolescents and adults. While AITP occurs in both males and females, there is a higher incidence in females. The onset of bleeding may be acute or insidious, with excessive bruising and mucous membrane bleeding (epistaxis, gum bleeding, menorrhagia, gross hematuria). Intracranial hemorrhage, although not common, may occur in the autoimmune form of ITP. (It is more likely to occur in AITP than in the acute post-viral form of ITP described above.) One can often (but not always) elicit a family history of systemic lupus erythematosus (SLE), Hashimoto's thyroiditis, rheumatoid arthritis, or other autoimmune disorder. In addition to thrombocytopenia (with or without anemia secondary to blood loss), IgG and IgA levels may be below normal. One should also obtain the following laboratory tests: direct antiglobulin test (Coomb's test), antinuclear antibody test (ANA), and (if clinically indicated) tests of thyroid function and rheumatoid factor. If the ANA is positive, one should obtain an anti-DNA test. (If this is positive, the patient has SLE, a more generalized autoimmune disorder, and should be more thoroughly evaluated.) If the direct Coomb's tests is positive, but ANA is negative, the patient would fall into the category of Evans' syndrome (autoimmune hemolytic anemia as well as AITP).

Spontaneous remission rarely occurs in AITP; thus, some form of intervention is warranted in most cases. However, again, management should be individualized, depend-

ing on the patient's platelet count and type and degree of bleeding manifestations. Those with platelet counts of 50,000/mm<sup>3</sup> or more can be merely followed with periodic blood counts unless bleeding manifestations develop. Those with < 30,000/mm<sup>3</sup> and bleeding can be treated with high-dose IVIG (one or two doses of 0.5-1.0 gm/Kg body weight); when the platelet count falls again, IVIG can be tried again. Ultimately, most individuals will become refractory to IVIG.

Another good therapeutic option is methylprednisolone, and many physicians would use this before using IVIG. However, as with IVIG, patients usually become refractory to methylprednisolone over time. In addition, methylprednisolone may cause glycosuria and behavioral changes, and is expensive.

If the patient is Rh (D) positive (and not splenectomized), one can next try I.V. anti-D (Rho) (WinRho SD). (By hemolyzing some of the patient's [Rh positive] red cells, an Fc receptor blockade occurs, and the patient's autoantibody coated platelets are not phagocytosed by the reticuloendothelial system to the same extent. Thus the circulating platelet count rises.) The recommended dose is 75 mg/Kg body weight. The response is generally transient (median of 5 weeks).

In many instances all of these approaches ultimately fail. If the patient with AITP remains severely thrombocytopenic with bleeding manifestations, splenectomy should be considered. Approximately 80% of patients will have an excellent response to splenectomy (the spleen in the primary site of production of the patient's autoantibody directed against his or her platelets *and* is the primary site of platelet destruction). Often the patient's platelet count will rise dramatically as soon as the splenic pedicle is clamped in the operating room.

The main complication of splenectomy is that of overwhelming post-splenectomy infection (so-called "OPSI Syndrome"). This risk is considerably less if one gives the patient polyvalent pneumococcal vaccine and H. influenza vaccine a few weeks prior to splenectomy, and then prescribes daily oral penicillin for at least several years post-splenectomy. (It is also recommended that a "booster" dose

of pneumococcal vaccine be given 5 years later.)

In young women who have a history of AITP, their offspring may have neonatal thrombocytopenia. Even if the mother's platelet count has normalized post-splenectomy, she may still have circulating anti-platelet antibodies that can cross the placenta and destroy the baby's platelets. Here, the baby's platelets are merely the substrate on which the maternal antibody acts. The neonate may be born with severe thrombocytopenia, petechiae and bruising. However, as soon as the maternal antibody dissipates from the infant's circulating (in approximately 6 weeks), the infant's platelet count will normalize.

## References

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