Watchful waiting for pediatric ITP: what does that actually mean?

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The incidence of pediatric ITP is between 1.4 and 6 per 100,000 children per year, which is very similar to that of acute leukemia. Many parents when they first see the bruising and characteristic small red spots in the skin (petechiae) go to the internet and are already worried about the diagnosis of leukemia before they meet the hematologist. The first visit is often spent discussing the diagnosis of ITP and the typical course in childhood: most cases are self-limited and resolve within 3-6 months and are rarely associated with more serious bleeding. The job of the hematologist is to establish the diagnosis and provide guidance to the family. But in this disease where there is no diagnostic test to definitely ***prove*** a patient has ITP, a dialogue between the family and physician practice is critical to promote effective communication about important changes in the status of the patient.

Most pediatric patients with ITP have resolution of their ITP eventually. Even during the course of their disease, the platelet count generally improves from the very low platelet count (often less than 10) at the time of diagnosis and increases to a level that is much more "comfortable" to parents and treating physicians. More importantly, the bleeding symptoms that initially prompted evaluation often improve, and the majority of children with ITP have symptoms limited to only bruising and petechiae. The majority of children even have limited degrees of skin findings. In these children, the guiding principle, as a physician, is to "do no harm." We expect that most of these children will get better and that their overall risk of bleeding is very small. Clinical studies in the US and in other countries have demonstrated the safety of cautious treatment with observation without drug therapy in this population. Clinical practice guidelines support the safety of observation in most children with ITP based on the fact that there have not been significant differences in rates of major bleeding or mortality between countries with vastly different rates of observation.[1-4] As long as there are no changes in bleeding symptoms, observation with good communication between family and provider for changes in symptoms is preferred, to avoid the toxicities and side effects associated with many ITP therapies. The recent randomized trial of IVIG in newly diagnosed patients with ITP (called the TIKI trial), again showed that observation was safe as long as children with changes in symptoms had evaluation and intervention at that point if needed.[5] The therapies most often employed for children with ITP: IVIG, corticosteroids, anti-D Ig are all associated with significant side effects. Since most children will get better, and treating early doesn't change the ultimate outcome with regard to whether ITP becomes chronic, early on it is usually safe to observe most children.

But there are a small number of patients, perhaps 1 in 2,500,000 children per year, with difficult to treat, profoundly low platelet counts associated with significant bleeding symptoms (frequent or severe nosebleeds, spontaneous bleeding in the mouth, blood in the urine or stool).[6] These children have a much more serious and different disease from other children with ITP and require a different approach. Identification of these children in the initial presentation can be challenging, but certain characteristics are more common among these patients. First, these patients generally have more bleeding symptoms, which ***by itself*** are a reason to

intervene and treat regardless of platelet count. Second, these patients tend to have persistently low platelet counts beyond the first few weeks after diagnosis without the characteristic early rise from <10 to ~30 platelet count.

Pediatric hematologists wouldn't be concerned about observation in children with ITP if not for the fear of death or significant injury due to intracranial hemorrhage (bleeding in the brain). This complication is quite rare, with a quoted of incidence of ~1% of pediatric ITP patients. However, this number is highly dependent on the denominator (total number of patients at risk). If we examine the cases of ICH in the literature, most of these do NOT occur at the time of presentation with ITP with over half of the cases occurring more than a month from diagnosis (at a time when most children no longer have a platelet count <20) and over 25% occurring >6 months from diagnosis. ICH is unlikely to occur when platelet counts are >20.[7,8] Therefore, risk probably increases with prolonged duration of very low platelet counts.[6] Data also suggests that in many patients with ICH, children presented with a "herald" bleed prior to the ICH: another bleeding event that required medical attention, either severe nosebleed, bleeding in the gastrointestinal tract or blood in the urine. Therefore, the combination of very low counts for a long time and bleeding symptoms defines a population at risk for ICH and these patients probably deserve more therapy directed at increasing platelet counts. However, early on with diagnosis, the risk of ICH is quite low, 0.1-0.2%.[9]

Two other important points to note about ICH in ITP: first, in many cases (as many as 50% of reported cases), ICH is not spontaneous and occurs in the setting of serious head trauma (25%)[10], arteriovenous malformation, or features of associated disease that suggest possible other diagnoses (beyond ITP).[9] Second: bleeding in ITP is slow (oozing), allowing time for intervention when it occurs as long as the symptoms of hemorrhage are recognized and communicated with the medical team. With modern ITP treatment and aggressive management, most children with ICH will do well with no sequelae of their event, and mortality (while still unacceptably high) is 10-21%.[11,12] Important factors are early recognition and intervention, and aggressive management at the time of detection.[13,14]

So, while bleeding can happen in ITP, most children have symptoms limited to skin bleeding and will do well with observation. Observation is an active form of treatment requiring communication between the family and physician practice and if symptoms change, changes in the therapy plan may be needed. This means that even if your child isn't getting frequent labs (which may not be needed if they aren't bleeding), any changes do need some sort of evaluation. If your child has new bleeding symptoms, a CBC may be needed. If the count is very low and symptoms continue, a conversation with your provider about best next steps is important. If your child has persistent or worsening headache, particularly with vomiting or nausea, even if fever is present, evaluation by a medical professional is important. Early intervention and discussion about escalation of treatment if needed are key in the setting of new symptoms, but most children with ITP eventually resolve without the need for mediations that have serious side effects.

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