Platelets: Pathophysiological Relevance and Therapeutic Potential

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Platelets play key roles in physiological and pathological haemostasis, inflammation, wound healing and immune responses. This issue of the IJHBT contains several articles on the relevance of these tiny, enucleate, discoid cellular fragments across different clinical settings.

Among the quantitative platelet disorders, immune thrombocytopenia (ITP) of childhood is the most prevalent. Most children with acute ITP undergo rapid resolution. However, chronic ITP, i.e. platelet counts less than $100 \times 10^9/L$ persisting for over 12 months, persists in nearly 10–20% patients. Clinical risk factors for chronicity, elegantly delineated in a recent meta-analysis [1], include older age, female gender, a lack of preceding infection or vaccination, gradual onset of symptoms and the use of a therapeutic regimen combining intravenous immunoglobulin (IVIg) with standard-dose methyl prednisolone. The last is especially interesting since IVIg alone was found to confer a protective effect, possibly due to its ability to restore regulatory T-cell numbers in responsive patients [1].

Chronic ITP possibly develops more commonly in children with less profound thrombocytopenia at diagnosis, higher mean platelet volumes and lower total leukocyte and lymphocyte counts. Serological studies show that the presence of anti-nuclear antibodies increases risk while the presence of platelet-associated IgM and anti-glycoprotein antibodies lowers it [1]. Genetic factors have been analysed by several studies, with almost uniformly disappointing results. Only *TGFβ1* cd 25 allele A and *IL4* intron 3 allele RP1 were shown to correlate consistently with the risk of

development of chronic ITP [2, 3]. The need for new and accurate biomarkers of prognosis is therefore real and urgent.

In this context, the study by Saeidi et al. in this issue [4] represents yet another attempt to utilize a genetic marker to predict treatment response. They quantitated *CXCR4* gene mRNA in 35 acute ITP patients using real-time PCR, and found that while levels differed between patients-versus-controls as well as among patients, they did not correlate with the 1-week responses to first-line ITP therapies. However, what is noteworthy that they found *CXCR4* levels to uniformly *decline* after treatment in *acute* ITP, whereas two prior papers had found *CXCR4* levels to *increase* in *chronic* ITP [5, 6]. This hints that the marker may have potential value in predicting chronicity. A follow-up of their cohort would be clearly very interesting. Another intriguing aspect of their paper is that 18 out of 35 of their patients were born of consanguineous marriages and two had a family history of ITP. The cDNA of this Iranian pediatric patient group could therefore be invaluable in future high-throughput studies to identify genetic lesions that might modulate risk of developing acute ITP.

In the other papers on platelets, two studies deal with the influence of platelet mass components (typically defined as platelet count multiplied by the mean platelet volume, MPV) on a neoplastic and an infectious disorder. In the first of these, Ayer et al. [7] from Turkey studied the roles of MPV and JAK2 mutational status on thromboembolic events in essential thrombocythemia (ET) and polycythemia vera (PV) patients. While MPV was marginally lower in ET than in PV and in controls, it had no significant influence on thromboembolic events. This result is in line with recent opinion that advises caution in extrapolating physical parameters like MPV, plateletcrit and platelet distribution width as surrogates for activation and functional status of platelets [8].

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The other paper by Sridhar et al. [9] looks at contributions of various parameters including clinical findings, degree of thrombocytopenia and D-dimer levels in predicting the risk of early disseminated intravascular coagulation (DIC) and thus bleeding in 60 children with dengue fever. Their conclusion, that clinical features of shock need to be factored in over and above the platelet count and D-dimer level, underscores the lesson that DIC is a clinic-pathological diagnosis and the choice and intensity of component therapy needs to be guided by several indicators rather than just one or two lab parameters.

And finally, Arora et al. [10] have reviewed platelet-derived biomaterials in this issue. Biomaterials are substances used in medical therapeutic or diagnostic procedures that have been processed or engineered to interact *in vivo* or *in vitro* with components of living systems. Examples of their use include fibrin glue or sealants to attain surgical hemostasis, platelet gels to promote wound healing and bone regeneration and platelet lysates with applications in *ex vivo* stem cell expansion. The production and marketing of biomaterials on an industrial scale entails stringent good laboratory practices as well as regulatory and quality control issues in addition to the robust evaluation of their clinical efficiency. The review touches upon all of these aspects.

In summary, the intrigues and the controversies around platelets as well as the diagnostic and therapeutic opportunities they promise truly cement their status as small cells with large impacts.

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