Immune thrombocytopenic purpura: Major progress in knowledge of the pathophysiology and the therapeutic strategy, but still a lot of issues

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In 1996, the American Society of Hematology (ASH) published guidelines focused on the diagnosis and treatment of immune thrombocytopenic purpura (ITP): corticosteroids were considered the best first-line treatment and splenectomy was proposed early for patients who did not respond to corticosteroids [1]. However, authors have highlighted that most of the recommendations were based on expert opinion rather than the results of randomized studies. Almost 20 years later, major progress has been made in knowledge of the pathophysiology of ITP and the development of new therapeutic strategies mainly based on the results of prospective studies. Despite these advances, steroids and splenectomy remain useful treatments and the therapeutic strategy for ITP appears paradoxically more complex.

For a long time, ITP has been considered a disorder characterized by antibody-mediated platelet destruction, mainly by splenic macrophages. We know now that for most patients with ITP, thrombocytopenia results from both increased platelet destruction and decreased platelet production. However, the pathogenesis of ITP has been proven complex, and the potential relations among ITP, infection, genetic predisposition and/or the underlying autoimmune repertoire remain elusive [2]. The roles of B- and T-cells in the initiation and/or perpetuation of ITP are better understood, but whether the immune abnormalities associated with ITP play a causative role in the disease or are secondary phenomena remains unclear [3]. Better knowledge of the ITP pathogenesis continues to be a major objective for the near future. It should help reveal new therapeutic strategies, as shown by the review by the group of Dave Arnold in this issue of Quarterly Medical Review, and perhaps, help in understanding the resistance to some treatments.

The management of ITP has changed dramatically in the past 10 years. Rituximab is increasingly used, and we now have a clear view of its short-term efficacy, which is attractive, with an overall response rate of about 60% [4]. Recent data confirm that tolerance is acceptable. However, relapses are frequent, and the long-term response is modest. The challenge for the future should be to potentiate the long-term efficacy. Several options that may be tested include giving rituximab early after the diagnosis or combining it with other treatments able to modulate the...
T-cell compartment. Thrombopoietin mimetics (TPO-mimetics) have been found effective in well-conducted and robust randomized studies, which explain why eltrombopag and romiplostim have been licensed in most countries. In theory, the strong efficacy and the good short-term tolerance would argue for expanded use of these drugs. However, the long-term tolerance of these treatments is a concern and as shown by the review of Jim Bussel in this issue, important questions remain about the use of these still-novel agents.

To date, the respective places of splenectomy, rituximab and TPO-mimetics and the optimal time to administer or perform treatment are debated [5]. We lack randomized trials to help guide the decisions, but controlled face-to-face studies comparing these options are not likely to be conducted. The ASH [6] and an international panel of experts [7] produced the recent recommendations, with great variability in opinion and interpretation of current data for treatment of adults with ITP, as is shown by Francesco Rodeghiero in this issue. The important message is that unlike the great improvement in the management of ITP for the last 10 years, the indications for treatments should be personalized and should be adapted to the patient’s condition and opinion.

I sadly close this editorial by paying tribute to Dr Roberto Stasi, who recently died. Roberto was an exceptional researcher who conducted many major scientific studies that greatly contributed to better knowledge of the pathogenesis and treatment of ITP. His death is a tragedy and a great loss for the scientific community and all colleagues, and I, who participated in this issue of the Quarterly Medical Review, lost a close friend. I would like to dedicate this editorial to his memory.

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References


