

## Preface

## Cancer and Thrombosis—An Update

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In his lecture to his colleagues at Hotel Dieu in 1856, Trousseau described the clinical presentation of migrating phlebitis in two of his patients preceding the discovery of gastric carcinoma and speculated that “in cancer, the blood is modified....”<sup>1</sup> This led to our recognition of the “Trousseau syndrome” that venous thrombosis in cancer is associated with hypercoagulability. Tragically, Trousseau predicted his own fate of cancer when he, too, developed phlebitis. Although it is debatable to which of the multiple thrombotic complications this term is applied today,<sup>2</sup> there is little question of the association between cancer and thrombosis. Indeed, new findings on the changes in the hemostatic function in cancer are continually on the rise. In 1999, an issue on this topic appeared in *Seminars in Thrombosis & Hemostasis*.<sup>3</sup> In the past decade, more exciting findings were discovered. The present issue is therefore devoted to an update of these developments in both the pathogenesis of thrombosis in different types of cancer and the improved clinical management.

To begin with, some of the recent progress in our understanding of the scientific basis of the relationship between cancer and thrombosis are presented in several articles. Among the latest findings on the pathogenesis of cancer is a potentially new role of neutrophils within the tumor micro-environment. Under certain stimulation, these cells produce DNA-containing neutrophil extracellular traps (NETs), which can induce the activation of platelets and of coagulation. As part of the first article, Demers and Wagner described their work demonstrating that these neutrophils, through the action of NETs, can promote tumor growth in animals.<sup>4</sup> As the NETs can be removed readily with DNases, this discovery may open up a new approach to cancer treatment. Next, D’Asti and colleagues describe the complex relations between several genetic mutations that increase the thrombogenic potential of cancer, while also pointing out the adverse effects of tumor-associated coagulopathies.<sup>5</sup> In addition to changes in coagulation, platelets also play an important part in tumor growth and metastasis. This is summarized by Goubran et al.<sup>6</sup> A therapeutic agent, erythropoietin, which was extensively used in the past to treat the anemia of cancer, is now believed to play a

contributory role to thrombosis, and possibly may enhance tumor growths since the erythropoietin receptors have now been identified in some tumor cells. Thus, erythropoietin use in cancer patients has been curtailed by regulatory agencies. On the contrary, there is also new evidence that erythropoietin increases the well-being of many cancer patients. This controversial subject is dissected thoroughly by Glaspy.<sup>7</sup> The reciprocal relationship between thrombosis and cancer is complex as each can inflict further harmful effects on the other. This topic is analyzed by Arora and Wun.<sup>8</sup>

As there is a greater recognition of the adverse effects of thrombosis on the cancer patient, clinicians are looking for ways to assess the risk of thrombosis in each individual patient. Several scoring approaches, including the widely used Khorana scores, are available. Their respective merits are discussed by Gomez and Khorana.<sup>9</sup>

The incidence of thrombosis varies widely from one form of cancer to the other. Although all cancers share a common predisposition to thrombosis, each form of cancer has its own contributing factors that determine their degree of thrombogenicity. A notable example is seen in glioblastoma, being the solid tumor with highest risk of thrombosis. The pathogenic factors are thoroughly discussed by Jo et al.<sup>10</sup> Similarly, acute promyelocytic leukemia has unique characteristic changes in coagulation and fibrinolysis that lead to a very high risk of both bleeding and thrombosis, as pointed out by Kwaan.<sup>11</sup> In some cases, the choice of therapeutic drug regimens is a major thrombogenic risk factor, such as in multiple myeloma. This is reviewed by De Stefano et al.<sup>12</sup> In another neoplastic disorder, namely, myeloproliferative neoplasms, thrombogenic factors in which thrombosis is the major cause of morbidity and mortality is reviewed by Falanga and Marchetti.<sup>13</sup> In lymphoproliferative disorders, bleeding and thrombotic complications can be caused by perturbation of the immune system. This is discussed by Lechner et al.<sup>14</sup>

The remaining articles are devoted to the management of thrombosis in the cancer patient. van Ommen and Chan review measures in supportive care in pediatric cancer patients.<sup>15</sup> As the use of central venous catheters remains a major cause of

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thrombosis in the cancer patient, especially in children, new recommendations in the management of these catheters are presented by Linnemann.<sup>16</sup> Thromboprophylaxis is now an essential part in treating a cancer patient. Evidence-based findings of use of anticoagulants are presented by Carrier and Lee.<sup>17</sup> As anticoagulant therapy in a cancer patient may not be possible due to impaired platelet or coagulation functions, the use of inferior vena cava filters has gained in popularity. Ryu and Lewandowski provide an update on the indications as well as the merits of various newer devices.<sup>18</sup>

It is hoped that with this assembly of these articles written by experts in their respective fields, the readers of this issue of this journal can get an in-depth and updated view on the subject of cancer and thrombosis.

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