Hematologic Malignancies Therapy and Cardiotoxicity: New Biomarkers

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During the last two decades, relevant improvements in the treatment of different hematologic malignancies have occurred, with a significant increase in the overall survival of patients. Increasingly aggressive chemotherapy (CT), however, has caused a comparable rise in serious adverse effects. Cardiotoxicity is a well-known and potentially serious complication of hematologic malignancies therapy that can significantly impair the patient's quality of life and substantially increase health care costs. A wide range of chemotherapeutic agents (CA) are associated with cardiotoxicity including Anthracyclines, Alkylating Agents, Monoclonal Antibodies. Cardiac toxicities associated with chemotherapy include left ventricular systolic dysfunction (LVSD), heart failure, conduction abnormalities, QT prolongation, acute coronary syndrome, and hypertension. Early identification of patients who are at risk for cardiotoxicity should be a primary goal for hematologists in the development of personalised antineoplastic therapeutic strategies or interventions [1].

Recently, biochemical markers of cardiac injury, especially cardiac troponins and natriuretic peptides, have been investigated in the assessment of cancer therapy-induced cardiotoxicity [2,3]. The role of cardiac troponin determination to stratify the risk of cardiotoxicity is currently based on strong evidence clearly suggesting the routine use of this biomarker [4]. Thus, Cardiac troponin troponins have been included into National Cancer Institute (NCI) classification of cardiotoxicity of anticancer therapy.

Moreover, natriuretic peptides have been investigated in detection of chemotherapy-induced cardiotoxicity. However, definitive evidence of their diagnostic and prognostic role in this context is still lacking and natriuretic peptides have not been routinely used for monitoring of cardiotoxicity in clinical practice [5-7].

More recently, new markers of myocardial ischaemia and necrosis such as heart-type fatty acid-binding protein (H-FABP) and glycogen phosphorylase BB (GPBB) have been reported to also increase in severe adverse effects. Cardiotoxicity is a well-known and potentially serious complication of hematologic malignancies therapy that can significantly impair the patient's quality of life and substantially increase health care costs. A wide range of chemotherapeutic agents (CA) are associated with cardiotoxicity including Anthracyclines, Alkylating Agents, Monoclonal Antibodies. Cardiac toxicities associated with chemotherapy include left ventricular systolic dysfunction (LVSD), heart failure, conduction abnormalities, QT prolongation, acute coronary syndrome, and hypertension. Early identification of patients who are at risk for cardiotoxicity should be a primary goal for hematologists in the development of personalised antineoplastic therapeutic strategies or interventions [1].

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More recently, new markers of myocardial ischaemia and necrosis such as heart-type fatty acid-binding protein (H-FABP) and glycogen phosphorylase BB (GPBB) have been reported to also increase after chemotherapy [8,9]. However, although these markers are highly sensitive, they have relatively low cardiac specificity and available data are insufficient to propose their use in the follow-up of oncology patients.

The increase of markers of inflammation, such as cytokines, has also been described after CT. Mercuro et al. [10] reported a correlation between interleukin-6 (IL-6) increase and early changes in systolic function when analysed by tissue Doppler imaging in a small population of patients treated with CT containing epirubicin. More recently, the same group showed that the angiotensin II receptor blocker telmisartan can reduce CA-induced radical species, antagonise the inflammation, and reverse the early myocardial impairment [11].

These preliminary results warrant confirmation by further, larger prospective investigations.

In January 2011, a position statement from the Heart Failure Association of the European Society of Cardiology on "Cardiovascular side effects of cancer therapies" was published [12]. The main recommendations among others include that identification and validation of reliable biomarkers for the prediction and detection of cardiotoxicity of chemotherapeutic agents is urgently required. The use of simple biomarkers such as troponins and natriuretic peptides should be strongly considered but is not a substitute for objective evaluation by echocardiography or similar modalities.

The Expert Working Group on Biomarkers of Drug-Induced Cardiac Toxicity developed the following list of characteristics of "ideal biomarkers", which includes specificity, sensitivity, kinetics of appearance in accessible media, robust assay, and ability to bridge between preclinical and clinical applications [13].

Strategies to minimize cardiotoxicity during treatment are crucial to prevent severe lasting effects on health and quality of life. An interdisciplinary approach is needed to foster communication between healthcare providers, and ensure optimal patient outcomes.

References


