Intravenous tissue plasminogen activator, ischemic stroke, and the risk of Kounis Syndrome

Sir,

We have read with great interest the report by Sweda *et al* that was published in this Journal. It described two patients who developed acute myocardial infarction (MI) following intravenous tissue plasminogen activator (tPA) for acute ischemic stroke.[1] The authors of this report speculated that fragmentation and lysis of any intracardiac thrombus may have resulted in embolization of coronary arteries and development MI after use of tPA. They did not exclude any remote possibility of coincidental occurrence of two atherosclerotic events MI and ischemic stroke. However, both patients died from fatal cardiac arrhythmia. Postmortem examination was not carried out.

The first patient had a history of hypertension and the second patient had a history of hypertension, ischemic heart disease, kidney disease, and diabetes. Both patients developed hypotension, with breathlessness the first, and cardiovascular collapse the second, following the intravenous administration of tPA.

Although the classical symptoms and signs of an allergic, anaphylactic, or anaphylactoid reaction were not described, and therefore such a work up was not performed, these two patients could have suffered type II variant of Kounis syndrome.[2] This syndrome is defined today as the concurrence of acute coronary syndromes with conditions associated with mast cell activation, involving interrelated and interacting inflammatory cells. These inflammatory cells namely mast cells, T-cells, and macrophages activate each other via multidirectional stimuli and behave as a ball of thread. These cells can release inflammatory mediators capable to induce coronary events. Platelets with high and low affinity IgE receptors are involving also in this process.[3] Three variants of this syndrome have been described.[4] Type I variant, which includes patients with normal coronaries in whom the allergic insult can induce either coronary artery spasm or coronary artery spasm progressing to acute myocardial infarction. Type II variant, which includes patients with culprit but quiescent pre-existing coronary disease in whom the allergic insult can induce either coronary artery spasm or plaque erosion or rupture manifesting as acute myocardial infarction. Type III variant, which includes patients with coronary artery stent thrombosis in whom aspirated thrombus specimens demonstrate the presence of eosinophils and mast cells.

Allergic reactions with the use of fibrinolytics have been described in the literature, more often with streptokinase but also with the use of tPA.[5] True and obvious anaphylactic reactions to tPA are rare but anaphylactoid reactions occur in up to 0.002% of patients treated for acute MI and from 1.5% to 1.9% those treated for acute ischemic stroke.[6]

Therefore, Kounis syndrome should be always being considered in such occasions, because this syndrome is not a rare disease but is a rarely diagnosed condition.[4]

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