Emerging Applications of Argatroban in the Management of Systemic Malignancies
Potential Benefits Besides Its Primary Role as an Antithrombin Agent

The recent article by Coppens et al1 provided for highly stimulating reading. Argatroban may exert several antineoplastic effects besides its antithrombin effects.

Argatroban exerts significant antineoplastic effects in gliomas.2 Thrombin, in general, augments the growth and progression of gliomas.3 Thrombin mediates its neoplastic role by increasing DNA synthesis within the cancer cells. It also accentuates intratumoral production of vascular endothelial growth factor. Thrombin-induced vascular endothelial growth factor production by the neurons is markedly mitigated by argatroban.4 Administration of argatroban blocks and reverses these neoplastic effects of thrombin. Neurological deficits secondary to gliomas are decreased,5 and concurrent brain edema is also decreased. Simultaneously, the survival time is increased markedly.

Argatroban also attenuates bone metastasis from breast carcinomas. It mediates its antineoplastic role by inhibiting thrombin-induced secretion of vascular endothelial growth factor.6 These effects have been seen both in vivo and in vitro. Argatroban also inhibits osteopontin-dependent cancer cell migration in breast cancers.7 Adhesion is also markedly altered. As a result, lymphatic metastases in mammary malignancies are markedly decreased. Similarly, argatroban attenuates metastasis in melanomas.8 These effects are dose-dependent. Interestingly, argatroban also attenuates ischemia/reperfusion-induced liver metastasis from colon carcinomas. It mediates this effect by accentuating prostaglandin 12 production. As a result TNF-α-induced expression of E-selectin is markedly decreased.9

The above examples clearly illustrate that argatroban has a significant role to play in the management of various systemic tumors and that further research is needed in this regard.

Disclosures

None.

References

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