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Letter to the editors

Potentiation of anticoagulant effect of coumadin by 5-bromo-2′-deoxyuridine (BUDR)

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Sirs,

The investigational agent 5-bromo-2′-deoxyuridine (BUDR) is widely used in cancer clinical trials as a radiation sensitizer for a variety of tumors [1]. We wish to report evidence for a possible adverse interaction between BUDR and coumadin in a patient receiving BUDR for a primary brain tumor.

The patient was a 65-year-old white man with a diagnosis of grade III anaplastic astrocytoma of the left temporal lobe, who was registered on a Northern California Oncology Group clinical trial of combined radiation therapy and BUDR 1400 mg daily by iv. infusion on 4 days each week. The patient had a prior history of a deep venous thrombosis of the right calf and developed a recurrent thrombosis of the same calf after his brain biopsy. He was treated with a short course of intravenous heparin and was then given oral coumadin (5 mg alternating with 2.5 mg per day) before initiation of radiation therapy. As Fig. 1 demonstrates, the patient's prothrombin time remained stable through his first course of BUDR, but with successive courses of the drug the prothrombin time became progressively prolonged. A prothrombin time in excess of 40 s necessitated the administration of intravenous vitamin K. The figure also demonstrates an increase in the prothrombin time following a single oral 490 mg dose of the drug given as part of a pharmacokinetic study. However, this rise occurred shortly after the patient had been receiving loading dose of coumadin, thus clouding the interpretation of that increase. Following a fifth cycle of intravenous BUDR at 990 mg/day, there was another significant increase in his prothrombin time, which necessitated discontinuation of his anticoagulation.

These observations demonstrate that repeated exposures to intravenous BUDR resulted in significant prolongation of the prothrombin time in a patient receiving stable doses of coumadin. It should also be noted that the patient had no changes in his other medications. We did not obtain serum coumadin levels, so we cannot comment on the mechanism of this interaction. Clinical investigators using BUDR should be aware of this potential adverse interaction in patients receiving oral anticoagulants.

Reference

1. Phupanich S, Levin EM, Levin VA (1984) Phase I study of intravenous bromodeoxyuridine used concomitantly with radiation therapy in patients with primary malignant brain tumors. Int J Radiat Oncol Biol Phys 10:1769-1772 1984.

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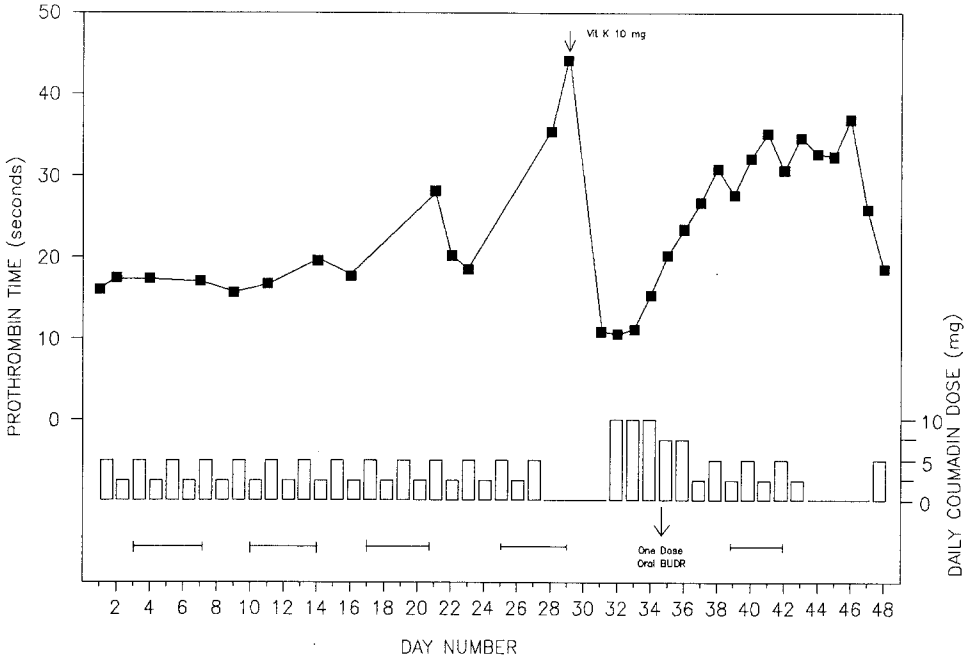

Fig. 1. Time course of administration of coumadin (vertical bars) and BUDR (⊢⊣) with serial prothrombin times (–■–■–)