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Mutagenicity of topoisomerase targeting anticancer agents

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Among the anticancer drugs currently used in the treatment of human malignancies, as well as several new series of drugs under development, are targeted at topoisomerase enzymes. Besides of inducing cell death due to both 'mitotic catastrophe' and the induction of apoptosis, topoisomerase-targeted drugs can increase the frequency of cells bearing mutations. These cells can develop resistance to the therapeutic agents or may lead to the development of secondary tumours and abnormal reproductive outcomes. This talk focuses on the mutagenic properties of the topoisomerase inhibitors, which are front-line therapies for a variety of malignancies. In addition, the topoisomerase catalytic inhibitors that are in clinical trials as anticancer agents will be discussed. An understanding of the mechanisms of mutagenicity is important not only in advancing our understanding of the action of mutagens but also in terms of improving cancer chemotherapy. This will, in turn, help us to design and bring safer drugs to the market. The demonstrated mutagenicity profile of topoisomerase inhibitors may support further development of effective topoisomerase inhibitors with less mutagenicity because such genomic alterations might result in an increased risk of birth defects, genetic disease or cancer in the children of cancer survivors.

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Upper tract urothelial tumor: Usefulness of urine cytology in the initial diagnosis

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Objective: To analyze 101 radical nephroureterectomies that were performed between 1992 and 2011

Methods: A retrospective, descriptive, and analytical study was carried out with a total of 101 radical nephroureterectomies that were performed for upper tract urothelial tumors between 1992 and 2011.

Results: All patients underwent a radical nephroureterectomy and we grouped our results in descriptive results and oncological results, with a survival estimate was performed using the Kaplan Meier method, with a survival rate of 86% (95% CI; 78-95) and a mean follow-up of 41 months (1-108).

Conclusions: Upper tract urothelial tumors currently represent a diagnostic and therapeutic challenge, and radical nephroureterectomy is fully applicable in their management. Urine cytology is a clearly efficient diagnostic tool and yields a higher benefit in high-grade tumors.

Behavior of advanced gastrointestinal stromal tumor in a patient with Von-Recklinghausen disease: Case report

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Gastrointestinal stromal tumors (GISTs) represent a malignant gastrointestinal tumor of type-1 neurofibromatosis (NF1) Von Recklinghausen disease. In the current case, we report a 27-year old woman with NF1, who presented with a lower abdominal mass, symptomatic anaemia, and significant weight loss. We employed multiple approaches to assess the tumor behavior, including computed tomography (CT) scan, surgical tumor resection, histological and immunohistochemical analysis and gene sequencing. Additionally, the patient was given imatinib mesylate (Gleevec) as adjuvant therapy. CT scan delineated a large thick wall cavity lesion connecting to the small bowel segment. Resection of the tumor yielded a mass of 17cmx13cm with achievement of safety margins. The diagnosis was GIST, confirmed by immunohistochemical expression of CD117, CD34, and Bcl-2. Sequencing revealed no mutations in either KIT or platelet-derived growth factor receptor-alpha (*PDGFR-α*), genes which are mutated in over 85% of sporadic GIST cases. Further, there was no evidence of recurrence, metastasis or metachronous GIST for over three years in our patient. From our analyses, we believe selective genotyping is advisable for high risk patients to predict potential tumor behavior.