Letters to the Editor

The emerging antineoplastic effects of nitidine chloride

Dear Editor,

We read with great interest the recent article by Kang et al. [1] published in JBUON identifying that nitidine chloride can inhibit proliferation and induce apoptosis of nasopharyngeal carcinoma cells with upregulation of p53 gene in a time- and dose-dependent manner. Interestingly, recent data suggests that nitidine chloride may exert antineoplastic effects in a number of other systemic malignancies.

For instance, nitidine chloride shows an inhibitory effect on tumor growth in renal carcinomas. It mediates these effects via suppressing the ERK signaling pathway [2]. Subsequently, nitidine chloride decreases the phosphorylation of ERK and Akt. Increased levels of Bax are observed within the tumor cells. Simultaneously, the level of Bcl-2 is downregulated, thus inducing apoptosis of cancer cells. Interestingly, the pro-apoptotic effects of PD98059, a specific inhibitor, is markedly accentuated secondary to the administration of nitidine chloride. Besides, nitidine chloride can also show anti-metastatic activity in renal cell carcinomas by mediating the AKT signaling pathway [3]. The phosphorylation of AKT is seen within the tumor cells, and the downregulation of MMP-2 and MMP-9 accompanies the above changes. When treating cancer cells by nitidine chloride combined with AKT inhibitors such as LY294002, a synergistic anti-metastatic effect is observed.

A similar impact has also been seen in hepatocellular carcinomas [4]. Nitidine chloride acts by blocking the activation of JAK1 and STAT3 signaling pathway. As a result, it decreases the tumor volume and weight. The expression of cyclin D1, CDK4 and Bcl-2 is downregulated while the levels of p21 and Bax are upregulated within the tumor cells. Similarly, nitidine chloride has a negative impact on mammary carcinomas [5]. It mediates the tumor cells migration and invasion by attenuating the c-Src/FAK signaling pathway. It decreases PDGF-induced phosphorylation of c-Src, FAK and MAPKs. And activation of RhoA, Rac1 and AP-1 transcriptional activity is also seen following the above changes.

The above examples clearly illustrate the significant antineoplastic effects of nitidine chloride and the need for further studies.

References

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Recurrent parathyroid carcinoma with spinal metastases unresponsive to cinacalcet therapy

Dear Editor,

Parathyroid carcinoma is a rare cause of primary hyperparathyroidism, and its incidence is no more than 0.5 - 3% of parathyroid neoplasms. It is slow-growing, and distant metastases occur late in the course of the disease. Death is commonly attributed to the metabolic complications of recurrent or persistent primary hyperparathyroidism rather than to tumor growth. Because external beam radiation and chemotherapy are general-
Calcium levels [2]. Calcium were observed in patients with particularly high parathyroid carcinoma and greatest reductions in serum percalcemia in two-thirds of patients with inoperable concentrations for as long as 3 years [4,5]. Silverberg et al. acalcet therapy has resulted in decreased serum calcium.

The initial surgery for neck disease [3]. Occasionally, detection of these metastatic foci might not be possible. In patients with primary hyperparathyroidism, cinacalcet therapy has resulted in decreased serum calcium concentrations for as long as 3 years [4,5]. Silverberg et al. demonstrated that cinacalcet effectively reduces hypercalcemia in two-thirds of patients with inoperable parathyroid carcinoma and greatest reductions in serum calcium were observed in patients with particularly high calcium levels [2].

Although not curative, resection of distant metastases palliates and prolongs life for a number of years by relieving the symptoms and improving the metabolic disturbances. Patients who achieved a favorable response from metastectomy are more likely to have a peripherally situated single lesion. Patients with multiple lesions are more likely to undergo major surgery, but complications secondary to hyperparathyroidism develop like in our patient.

**References**


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**Figure 1.** MRI scan of lumbar spine demonstrates a metastatic lesion (arrows) in the right lateral region of L3 vertebral corpus (A: axial and B: sagittal sections).
Dear Editor,

Some types of solid tumors overexpress epithelial growth factor receptor (EGFR), which activates cellular signalling, migration and proliferation. Cetuximab is a human/mouse monoclonal antibody that inhibits EGFR [1]. It has been approved for the treatment of metastatic k-ras wild type colorectal cancers and head neck cancers [1,2]. Rash and diarrhea are the more frequent side effects of this agent [1]. Herein we report a case of bowel perforation which might be associated with the cetuximab-containing chemotherapy for the treatment of metastatic adenocarcinoma of sigmoid colon.

A 65-year-old male patient with metastatic sigmoid adenocarcinoma was admitted to the emergency service with the major complaint of abdominal pain and constipation. The patient had received one cycle of irinotecan and cetuximab combination regimen (one cycle consists of 4 weekly doses of irinotecan and cetuximab) 4 weeks ago and the second cycle was delayed due to significant weight loss. The patient’s vital signs and physical examination were normal except abdominal tenderness on deep palpation. The patient was hospitalized with suspected ileus. Oral intake was stopped. The general status of the patient improved after 2 days of supportive treatment and the second cycle of irinotecan and cetuximab started. Abdominal pain reappeared and hypotension was noticed after the completion of cetuximab infusion. An allergic reaction due to cetuximab was suspected and 1 mg/kg methylprednisolone and 10 mg chlorphenoxamine hydrochloride were administered parenterally, while a consultation with the Department of General Surgery led to urgent laparotomy for acute abdomen, during which small bowel perforation was observed. Partial small bowel resection and drainage were carried out. The patient deceased 12 days after the operation due to sepsis.

Cetuximab is a monoclonal antibody that inhibits EGFR competitively and therefore blocks cancer cell growth, induces apoptosis and decreases the production of vascular endothelial growth factor (VEGF) [3]. Cetuximab may cause perforation via antitumor activity, reduction of VEGF levels or by causing mucositis. EGFR inhibitors may also prolong wound healing time [4] and this may cause perforation due to a pre-existing ulcer. As of 2014, to our knowledge, there is only one case of bowel perforation after cetuximab administration in the English literature [5]. We claim that bowel perforation should be considered in the differential diagnosis of patients with abdominal pain receiving cetuximab.

References

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