cox-2 protein expression and treatment failure in early-stage laryngeal cancer treated with radiotherapy. They found that overexpression was significantly associated with radio-resistant tumors \( (P=0.004) \) and suggested that cox-2 inhibitors might have a role in enhancing the effects of radiotherapy. Two important and recently published randomized trials clearly showed that in patients with operable high-risk head and neck cancer, concurrent use of radiotherapy and chemotherapy is superior to radiotherapy alone with regard to disease-free survival and/or overall survival \([2, 3]\). In these trials, in the concurrent arm, radiotherapy was combined with cisplatin, which is the most common and effective radiosensitizer of all chemotherapeutic agents. A recent study reported that the cox-2 inhibitor JTE-522–cisplatin combination elicited a synergistic and additive antitumor effect in different gastric cancer lines \([4]\). A study by Peng et al. \([5]\) also demonstrated that the cox-2 inhibitor NS398 potently augmented chemotherapeutic drug-induced apoptosis in hypopharyngeal cancer. NS398 also radiosensitizes head and neck squamous cell carcinoma cell lines, possibly by inhibiting radiation-induced expression of cox-2 \([6]\). These preclinical and clinical data suggest that the cox-2 inhibitor–cisplatin combination may be more useful than cisplatin alone as a radiosensitizer in the treatment of head and neck cancer that overexpresses cox-2 protein.

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Complete disappearance of multiple periorbital xanthelasmata after chemotherapy for primary extragonadal germ-cell mediastinal tumor

Xanthelasmata is a benign localized collection of lipid-laden histiocytes, which is usually idiopathic, while it commonly occurs with primary or secondary plasma lipid abnormalities \([1, 2]\). Moreover, xanthelasmatas have been rarely reported in association with various hematological malignancies \([3–6]\). We report on a 30-year-old male with primary mediastinal germ-cell tumor and simultaneous occurrence of multiple bilateral periorbital xanthelasmata. He was successfully treated by surgical resection of the mediastinal tumor, followed by cisplatin-based adjuvant chemotherapy, without complications. He achieved complete remission of the germ-cell tumor, while the periorbital xanthelasmata had completely disappeared immediately after chemotherapy. The tumor markers simultaneously returned to normal. During the 5-year follow-up post-operatively, neither the tumor nor the xanthelasmata recurred. We consider the periorbital xanthelasmata of our patient as a possible paraneoplastic manifestation of the primary mediastinal germ-cell tumor, which successfully responded to the chemotherapy given for the primary tumor. According to literature available to us, multiple periorbital xanthelasmata in relation to extragonadal primary mediastinal germ-cell tumor has not been reported previously, while little is known about the possible pathogenic mechanism in these cases. Moreover, complete regression of the xanthelasmata after effective chemotherapy has been only rarely described in isolated case reports \([6, 7]\).

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Acute neurotoxicity as a serious adverse event related to rasburicase in a non-Hodgkin’s lymphoma patient

Hyperuricemia and tumour lysis syndrome are well known complications during induction treatment for aggressive non-Hodgkin’s lymphomas (NHLs) [1]. Recently, rasburicase, which converts uric acid into the soluble compound allantoin, has been shown to control hyperuricemia faster and more reliably than allopurinol in adults and paediatric patients with acute leukaemia and lymphoma [2].

Here we report an unusual case of rasburicase neurotoxicity in an NHL patient after rasburicase infusion. The patient, a 35-year-old female, was referred to our unit for consideration for repeated high-dose therapy followed by autologous stem cell transplantation as primary treatment for high risk, aggressive NHL. Pertinent pre-treatment laboratory evaluations included the following: white blood cells, 10.1 x 10⁹/l; platelet count, 186 x 10⁹/l; haemoglobin, 10.2 g/dl; blood urea nitrogen, 23 mg/dl (8.2 mmol/l); creatinine 1.1 mg/dl (100 mmol/l); lactate dehydrogenase, 640 IU/l; alkaline phosphatase, 80 U/l; sodium, 140 mmol/l; calcium, 8.5 mg/dl (2.12 mmol/l); potassium, 4.7 mmol/l; and uric acid, 9.1 mg/dl.

As planned, administration of rasburicase was started the day before initiation of chemotherapy at a dose of 0.20 mg/kg. Within the first 2h after administration, the patient became confused and agitated, she had generalised myoclonus and muscular spasticity characterised by extension of her neck to the left, and protracted deviation of the mouth to the left followed by decorticate positioning of the arms and legs. She became mute. At the time when these symptoms occurred, there were no significant abnormalities in the patient’s serum electrolyte, renal function, calcium level, arterial blood gases or hepatic function to suggest other metabolic causes of the observed symptoms, but uric acid levels decreased to 0.2 mg/dl after rasburicase administration. Results of a brain computed tomography scan with contrast were normal.

Twenty-five milligrams of intravenous diphenhydramine were given, which produced an immediate relaxation of all myoclonus and muscular spasticity, but did not change the mutism. Over the next 24h the patient had several episodes of myoclonus and muscular spasticity, which were resolved by intravenous diphenhydramine. After 36h, the confusional state and myospasticity disappeared and she was able to speak. The uric acid level was 0.4 mg/dl at this point. Abnormalities not were found on the electroencephalogram. Electrophysiological studies, including nerve conduction, were normal.

The exact mechanism of this unusual toxicity, not commonly seen during treatment with rasburicase, is beyond our understanding. In current oncological practice, most of the characteristic acute pharmacological neurotoxicities reported to date can been referred to acute channelopathy [3, 4]. Na⁺, K⁺-ATPase is an enzyme embedded in the cell membrane that is necessary to maintain neuronal excitability. This enzyme activity is highly susceptible to free radicals, and in this context it has been shown that uric acid has a significant anti-oxidant activity and a neuroprotective role in both in vitro and in vivo models of cerebral ischaemia [5]. Curiously, in our patient, symptoms of acute neurotoxicity coincided with the drop in uric acid level. Whether uric acid acts on the sodium channels, modifying the action potential, remains to be explored. With increasing clinical use of rasburicase in adult and paediatric patients, a clearer understanding of the real incidence of this toxicity should become apparent.

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