given six cycles of carboplatin (300 mg/m²) that resulted in a partial remission of her lung metastases. She became asymptomatic soon after the second cycle.

Five months later, lung lesions again began increasing in size. Since she was asymptomatic and elderly she was challenged with oral megestrol acetate, 160 mg daily. Six months later, chest radiography showed partial remission of her lung metastases. Today, after 20 months on megestrol the patient is in good health. Two of the lung metastatic deposits have disappeared but a third has begun increasing in size.

Hormonotherapy in granulosa cell tumours of the ovary has attracted little attention to date. One published study on leuprolide acetate, a gonadotrophin-releasing hormone analogue shows moderate activity in patients treated for refractory or persistent ovarian granulosa cell tumour [2] and there is a recently reported anecdotal case of a response that occurred on dexamethasone [3].

This is the first published report on megestrol acetate activity in a granulosa cell tumour of the ovary. Megestrol is a well-known hormonal agent which is active in metastatic breast and endometrial cancers. It also has a role in the management of prostatic carcinoma. Megestrol acetate is a synthetic progesterational agent that produces serum steroid hormone changes through feedback effects on the pituitary and hypothalamus. It has been shown to suppress gonadotrophins [4] and the pituitary-adrenal axis [5]. Although the mechanism of the anti-tumour effect of megestrol acetate is unclear in other tumours, we postulate that gonadotrophin suppression can be considered a common mechanism of anti-proliferative activity in granulosa cell tumour of the ovary for both megestrol and leuprolide acetate. The possibility that gonadotrophin hyperstimulation has a role in the pathogenesis of this cancer [6] supports such a consideration.

We conclude that the observed activity of megestrol in this case of granulosa cell tumour of the ovary calls for greater attention to be paid to hormonotherapy in these tumours. Megestrol acetate warrants further investigation as a potential non-toxic alternative to platin-based treatment. We propose that this tumour should perhaps be considered as another hormone-responsive cancer.

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References


Ataxia following docetaxel infusion

In June 1995, a 51-year-old woman was diagnosed with breast cancer. She was initially treated with adjuvant cyclophosphamide, methotrexate and 5-fluorouracil (5-FU) chemotherapy (CMF) following surgery in her local hospital. During this period she had a localized Borrelia Burgdorferi infection (IgEIA 31, normal range <1 U/ml), IgM 16, normal range <1) which was adequately treated with oral doxycycline. After four CMF courses she developed cerebellar ataxia, which was attributed to 5-FU as it subsided completely after withdrawal of 5-FU. In February 1996, she experienced erythema around the left knee and was again successfully treated with oral doxycycline for recurrence of Lyme disease (IgG 0.6, IgM 1.2).

In June 1996, she was admitted to our hospital with a supraclavicular lymph node as the only manifestation of advanced breast cancer and started with docetaxel (100 mg/m²) every three weeks. Co-medication included ondansetron, ranitidine and dexamethasone. Two weeks after the third course, she complained of unsteadiness, especially of the legs and trunk. In retrospect, she had experienced the same symptoms, although less severe after the first and second course, but these symptoms had disappeared completely before each next docetaxel cycle. The neurologist diagnosed cerebellar truncal and gait ataxia.

Laboratory testing revealed no abnormalities. Borrelia Burgdorferi IgG- and IgM-titres were negative. A brain CT-scan was normal. Cerebrospinal fluid (CSF) showed a slight increase in total protein (0.67 g/l, range 0.20-0.55), but a normal IgA, IgG and IgM index. CSF glucose was low (1.2 mmol/l, range 2.2-4.4), and CSF/serum glucose was decreased (0.29, range 0.50-0.75). T. pallidum hemagglutination test (TPHA) in serum and CSF was negative. No evidence of neuroborreliosis (negative IgG and IgM titres) or metastatic disease was found in the CSF. Antineural antibodies in serum were negative. Six weeks later CSF glucose (3.0) and CSF/serum glucose ratio (1.00) had both normalized. Again, no evidence of metastatic disease in the CSF was found. Therefore, we concluded that the previous docetaxel infusion was the most probable cause. Docetaxel infusions were withdrawn. Within eight weeks she recovered completely.

Possible causes for ataxia in patients with cancer receiving chemotherapy are metastatic disease, paraneoplastic cerebellar degeneration (PCD) or chemotherapy toxicity and in this case we had to exclude the possibility of recurrent Lyme disease in the CNS. Until now, ataxia as the only neurological symptom following infusion with taxoids has not been reported. Sensory polyneuropathy is the most frequent neurological side effect of docetaxel [1]. CNS toxicity of paclitaxel has been described in a few reports [2-5]. One report described a patient with advanced ovarian carcinoma experiencing multi-embolic cerebral infarction three days after infusion with paclitaxel [2]. Brown et al. observed seizures in two patients following paclitaxel treatment [3]. However, one patient had brain metastases. In a recent report by Perry et al. [4], a transient encephalopathy in two patients was observed following paclitaxel. In this report one patient with advanced breast cancer (bone and liver metastases) also experienced short episodes (4-6 hours) of ataxia following paclitaxel infusion after the second and third cycle. She received a total of six cycles without further neurological symptoms.

The mechanism involved in our patient with ataxia following docetaxel infusion is not clear, but this patient illustrates
that docetaxel should be considered a candidate for transient ataxia in patients receiving this chemotherapeutic drug.

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