Eur J Cancer, Vol. 28, No. 1, pp. 243, 1992.
Printed in Great Britain
0964–1947/92 $5.00 + 0.00

Meningeal Fluid Granulocytosis After Cytarabine

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WE REPORT recurrent meningeal fluid granulocytosis after intermediate-dose intravenous cytarabine. The indication for therapy was first relapse of acute lymphoblastic leukaemia (ALL) in a 33-year old man.

14 years ago the patient had undergone subtotal nodal irradiation and splenectomy for Hodgkin's disease. After 12 years without disease he developed ALL and was treated with combination chemotherapy and prophylactic central nervous system (CNS) irradiation with 24 Gy [1], with some modifications including cytarabine and mitoxantrone as consolidation therapy and prophylactic treatment for CNS relapse with intrathecal application of cytarabine, methotrexate and dexamethasone (AMD). He achieved complete remission and stayed on maintenance therapy with mercaptopurine, methotrexate and bimonthly intrathecal AMD for 8 months before he was admitted with clinical signs of acute meningitis. Microbiological examination of the cerebrospinal fluid (CSF) revealed pneumococcal bacteria and the patient recovered after antibiotics.

2 months later bone-marrow biopsy showed relapse of ALL and the patient was put on a 3 h intravenous infusion of cytarabine 1 g/m^2 every 12 h for 8 doses with aclacinomycin 20 mg/m^2 on days 2–6. Prophylactic oral ofloxacin was started on the first day. After 5 doses of cytarabine, chemotherapy was halted because the patient developed a sterile meningitis. CSF analysis revealed a pleocytosis of 6600/3 granulocytic cells, increased protein levels in the absence of lymphoblasts or viral, bacterial or fungal microorganisms. Nevertheless, broad specific antibiotics were administered. Nuclear magnetic resonance scans of the brain did not show any abnormalities. The symptoms and the pleocytosis disappeared within 4 days.

Because of persisting blasts in the bone marrow a second course of chemotherapy was started 4 weeks later. Again, on the second day of the treatment, the patient showed the clinical signs of a meningitis with a granulocytic pleocytosis (1200/3 cells) without evidence of any microbiological agents in the CSF. This time chemotherapy was continued with concomitant antibiotics. Symptoms improved within a few days. Because of a residual blastic infiltration of the bone marrow, a third chemotherapy course was administered 4 weeks later. After 3 doses, meningeal symptoms occurred and the patient again soon recovered despite continuing chemotherapy.

The neurotoxicity of high-dose cytarabine regimens has been frequently reported. It appears to be age-related [2] and to occur in a dose-dependent manner, increasing rapidly beyond a total dose of 48 g/m^2 per course [3]. The major sign is the cerebellar syndrome with some other features such as seizures, leukoencephalopathy and peripheral neuropathy occurring significantly less often [4]. Pre-existing CNS disorders as well as the cumulative amount of cytarabine received may play a role in the development of neurological symptoms [4, 5].

Our patient developed a sterile meningitis with classical clinical symptoms and granulocytic pleocytosis shortly after the onset of three courses of cytarabine. Several CSF analyses were performed without detection of any microorganisms. Each time the patient recovered quickly, as opposed to the prolonged recovery time observed for bacterial meningitis. No other neurological toxicity was observed. To our knowledge, meningitis or meningitis-like syndromes have not been previously described after cytarabine. The fact that severe and reproducible neurotoxicity occurred in our case with only intermediate-dose cytarabine may be explained by the pre-existing CNS disorder (pneumococcal meningitis 2 months ago) and the previously received cytarabine as part of induction and consolidation.

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Received 15 Aug. 1991; accepted 19 Sep. 1991.

Eur J Cancer, Vol. 28, No. 1, pp. 243–244, 1992.
Printed in Great Britain
0964–1947/92 $5.00 + 0.00

Mitozantrone-induced Onycholysis

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MITOZANTRONE IS an anthracene derivative with substantial cytotoxic activity in breast cancer, lymphoma and some leukaemias. Only 2 cases of onycholysis have been described with mitozantrone as a single agent [1] and a further 4 cases in

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Received 18 Sep. 1991; accepted 10 Oct. 1991.