Complications Of Secondary Immunodeficiency, Diagnosis and Treatment of Leukopenia in Patients with Acute Leukemia

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ABSTRACT

The characteristic manifestations of NL are intracranial hypertension, meningeal syndrome, and cytosis in the cerebrospinal fluid. However, on the one hand, there has not yet been an idea of the course of NL with modern tactics for the treatment of acute hemoblastoses, on the other hand, the appearance of even reduced neurological symptoms significantly worsens the clinical course of the disease, aggravates the prognosis and requires an immediate change in the tactics of therapy.

Keywords: intracranial hypertension, meningeal syndrome, cytosis

Introduction. Neuroleukemia (NL), or neuroleukemia, is one of the severe complications of acute leukemia (AL), which previously occurred in 30-50% of adult patients with AL and in 70% of children. With the beginning of the introduction of NL prevention (1970s) in the form of early intrathecal administration of cytostatic agents, this complication is observed in 5–10% of patients with AL. The clinical picture of this complication has also changed. All this is considered as the most important success of modern hematology [2,5].

The occurrence of NL is due to metastasis of leukemic blasts into the arachnoid and pia mater of the brain and spinal cord. Leukemic infiltration of the cranial and peripheral nerves can be observed with a variety of sensory and motor disorders [1]. The characteristic manifestations of NL are intracranial hypertension, meningeal syndrome, and cytosis in the cerebrospinal fluid [3]. However, on the one hand, there has not yet been an idea of the course of NL with modern tactics for the treatment of acute hemoblastoses, on the other hand, the appearance of even reduced neurological symptoms significantly worsens the clinical course of the disease, aggravates the prognosis and requires an immediate change in the tactics of the therapy [1,4].

Purpose of the study. The aim of the study is to improve methods for diagnosing and treating complications of secondary immunodeficiency, leukopenia in patients with acute leukemia.

Materials and research methods. For 5 years, 18 patients with OL (11 men and 7 women; mean age 37 years) were observed in the hematology department of the clinic of the ASMI in Gandijan, in which the disease was complicated by HL. The diagnosis of NL in 15 patients was established during the first 1-3 days of stay in the clinic based on the study of cerebrospinal fluid (CSF), in 3 - during the period of relapse of the disease. The basis for the diagnosis of NL was the detection of cytosis

in the CSF above 10 in 1 μl and blast cells, regardless of the presence of neurological symptoms. 14 patients were treated for lymphoblastic AL (ALL), 3 for acute myeloid leukemia, 1 for promyelocytic AL. The difference in the number of observed patients was due to the fact that NL in ALL develops much more often than in other clinical and hematological variants of AL. The diagnosis in all cases was confirmed by the results of bone marrow puncture.

All patients were prescribed treatment with cytostatic agents, prophylaxis and treatment of NL was carried out, which covered all three periods of AL therapy (remission induction, consolidation and maintenance therapy) and corresponded to modern recommendations. Repeated intrathecal injections of methotrexate, cytrabin, and dexamethasone were performed. At the same time, the dose of intravenously administered cytostatics (vincristine, cyclophosphamide, doxorubicin, etc.) was increased in order to have a more intense systemic effect on the underlying pathological process. If necessary, radiation therapy was prescribed with irradiation mainly of the head.

Research results. All 18 patients with NL were treated for this complication of AL in the form of intrathecal administration of cytostatics according to the available schemes. At the same time, 14 (77.8%) patients developed clinical signs of damage to the nervous system. In other words, these patients manifested a complete clinical and laboratory syndrome of NL in the form of both typical changes in the CSF and a variety of symptoms characteristic of damage to the nervous system. Neurological symptoms of NL in 11 patients occurred in the acute period of the disease, which was manifested by fever, anemia, thrombocytopenia, ossalgia, general intoxication, bleeding, enlarged lymph nodes, spleen, hyperleukocytosis. It should be especially noted that 2 patients initially consulted a neurologist due to severe headache, and only after a blood test was performed, AL was suspected. In 3 patients, the complete clinical and laboratory syndrome of NL manifested itself only during the period of ALL recurrence after remission was achieved, in 2 of them, damage to the nervous system was its first sign.

In 4 patients during the follow-up (in 1 patient for 7 years), AL recurrences repeatedly occurred, cytosis and blasts in the CSF were recorded, however, with intensive treatment and prophylaxis, there were no clinical manifestations of NL. In these cases, one could speak of an incomplete NL syndrome. Apparently, with this variant of NL, we can talk about the persistence of blast cells in the brain tissue and the fact that these leukemia cells periodically break through the blood-brain barrier, leading to the development of AL recurrence.

Judging by the literature data [1, 2], another variant of the incomplete NL syndrome can occasionally be observed — neurological signs of damage to the nervous system are present in the absence of pronounced cytosis and blast cells in the CSF.

It is necessary to note several common features of the course of AL in patients with NL. They concern both patients with complete and incomplete NL syndrome. First of all, it should be emphasized that patients

NL were younger than 60 patients with AL without this complication (24.6 ± 2.65 and 44.3 ± 4.27 years, respectively; $p < 0.01$) with no differences in gender. Further, it should be noted a more severe course of AL in patients with NL. Thus, leukocytosis more than 20 x 109/l, blastosis more than 50 x 109/l, anemia less than 90 g/l, which is considered poor prognostic signs of OL, was observed in 12 (66.6%) patients with CL out of 18, while in the group compared, in 15 (25%; $p < 0.001$) out of 60. It is believed that this pronounced peripheral blood blastosis is directly related to damage to the nervous system, since it causes leukostasis in small vessels and the penetration of leukemic cells into surrounding tissues.

A variety of neurological symptoms, which were identified in 14 patients with clinically developed NL, can be combined into several syndromes.

The syndrome of leukemic meningoencephalitis was observed most often - in 7 (50%) of 14 patients who had a complete

clinical picture of NL. Usually it developed sharply. The occurrence of meningoencephalitis in 6 patients was associated with severe clinical signs of AL, and in 1 it preceded the appearance of classical manifestations of AL, which is consistent with the observations of other authors [9]. Patients developed a severe headache, nausea, vomiting, photophobia along with drowsiness, lethargy and increasing apathy. Already within the next day, signs of damage to the meninges (rigidity of the neck muscles, Kernig's symptom, etc.), congestive optic discs, bouts of blurred vision, and damage to the oculomotor nerves were usually detected. All this testified to intracranial hypertension, which was confirmed by lumbar puncture and computed tomography (n = 3), namely, narrowing of the brain ventricles.

In 3 patients with clinical manifestations of leukemic meningoencephalitis, along with signs of intracranial hypertension, signs of focal brain damage were observed: nystagmus, diplopia, deviation of the tongue, etc. Within 1–2 days, these symptoms became more pronounced, but were inferior to increasing clinical manifestations increased intracranial pressure and lesions of the meninges. CSF revealed hypercytosis and a large number of blast cells (85–95%). 6 patients with OL with leukemic meningo-encephalitis syndrome died in the acute period of the disease, 1 was able to achieve remission.

The second most common was the syndrome of predominant damage to the cranial nerves. It was noted in 4 (28.6%) patients with NL. The most common was dysfunction of the oculomotor (III), trigeminal (V) and facial (VII) nerves. In 1 patient, NL manifested itself as a bilateral lesion of the facial nerve. In 1 patient with ALL, the first attack of the disease began with a unilateral multiple lesion of the cranial nerves (trigeminal, facial, auditory-vestibular, vagus, sublingual), which caused him to initially turn to a neurologist.

In 2 (14.3%) patients, the manifestations of NL were in the form of damage to the peripheral nerves. The pathogenesis of this syndrome is based on leukemic infiltration of the nerves, which was clinically expressed by the appearance of signs of polyneuropathy (paresthesia, decreased sensitivity, movement disorders, pain, areflexia) in one patient and peroneal nerve neuropathy in another.

Conclusion. Thus, NL is a very dangerous complication of AL, which can manifest itself both as a complete (clinical and laboratory) and incomplete (only changes in the CSF or only damage to the nervous system) syndrome. Neurological manifestations of NL in AL can be recorded in the form of leukemic meningoencephalitis, syndrome of predominant cranial nerve damage, in the form of peripheral nerve damage and local leukemia of the brain. The development of NL in patients with AL indicates an unfavorable prognosis and requires intensification of treatment in the form of both intrathecal administration and systemic use of cytostatic agents.

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