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RECURRENT PURULENT MENINGITIS IN A PATIENT WITH BRUTON'S DISEASE*

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Pyogenic meningitis in children is a serious infection with significant morbidity and mortality despite the availability of potent antimicrobial drugs. The most common etiologic agents are Hemophilus influenza, Streptococcus pneumonia and Neisseria meningitidis. In the majority of cases, the pathogenesis of this disease is not well understood. Predisposing factors such as anatomical defects of the central nervous system or parameningeal foci of infection, such as chronic sinusitis or chronic otitis media can be found in the small number of children having recurrent meningitis[1].

Pyogenic meningitis has been reported to be one of the most common infections seen in immunodeficiency diseases. Primary complement deficiencies, particularly late component deficiencies are associated with recurrent meningitis and it may be seen in children with untreated hypogammaglobulinemia. These patients respond properly to antibiotic therapy which may delay the diagnosis of immunodeficiency[2-4]. The presented case with Bruton's disease and recurrent meningitis is typical of the late diagnosed disease. The main aim of this report is to emphasize the importance of evaluating patients with recurrent infections and meningitis for immunodeficiency diseases.

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Case Report

A five-year-old boy was admitted to the hospital with fever and vomiting. It was learned that he had been hospitalized for meningitis in 1985, pneumonia in February 1986, and sepsis with meningitis in May 1986, and had bilateral otitis media for the last three years.

On physical examination, the patient was unconscious with a temperature of 39.3 °C. His tympanic membranes were dull with central pseudomembranes, and this finding was not interpreted as an active infection. He did not have nuchal rigidity, but the Kernig and Brudzinski signs were slightly positive. Left central facial paresis, spasticity of the left arm and leg, and the bilateral Babinsky sign were other neurological findings. Diffuse rhonchal rales were detected by auscultation of the lungs. There were no palpable lymph nodes and tonsillar tissue was not visible.

Initial laboratory findings showed the hemoglobin valve to be 12.20 g/dl, and white blood cell count 17,400 per mm^3 with polymorphonuclear leukocytes predominating in the peripheral blood smear. The cerebrospinal fluid (CSF) was turbid with a protein content of 84 mg/dl, glucose 132 mg/dl and simultaneous blood glucose 132 mg/dl. On microscopic examination there were 7,040 erythrocytes, 80% of which were old, 99 polymorphonuclear leukocytes and 55 mononuclear leukocytes per mm^3. The old erythrocytes could have been the result of a subarachnoid hemorrhage caused by a clotting defect. But the prothrombin and partial prothrombin times were within normal limits. Thus, the hemorrhage was explained by meningitis itself. The normal glucose level of the CSF was attributed to the previous antibiotic treatment administered in a state hospital from where the patient was referred. There was no gram-stained bacteria on the CSF smears and the infectious agent could not be cultured in blood, urine or CSF. Computerized brain tomography revealed the presence of diffuse cerebral edema.

After admission to the hospital, penicillin G (500,000 units/kg/day) plus chloramphenicol (100 mg/kg/day) were started intravenously.

The patient's general condition improved in two days and oral feeding was started. On the fifth day of treatment, the second LP was performed which revealed a clear CSF which contained 11 lymphocytes and 10 old erythrocytes per mm^3 with normal protein and glucose levels. Then procaine penicillin i.m. and chloramphenicol per os replaced the i.v. therapy.

The child's recurrent meningitis might be explained by chronic otitis media, but immunodeficiency should not be ruled out. The determination of serum immunoglobulin levels revealed that the IgG was 23 mg/dl, IgM was below 20 mg/dl and the IgA was undetectable. The delayed hypersensitivity skin tests were negative against streptokinase-streptodornase, candida and PPD, but positive

(12 x 11 mm) for phytohemagglutinin (PHA). The CH50 value and lymphoblastic transformation with PHA were normal. E rosette-forming cells were 76 percent. Surface Ig bearing B cell percentages were 2% with polyvalent antiserum, 0.5% for IgA and 0% for IgG and IgM (normal values were 22 ± 5, 9.1 ± 3.6, 8.2 ± 4.2 and 4.5 ± 3.1 percent respectively). Neutrophil chemotaxis against ZAS (zymosan-activated serum) was within normal limits. HLA antigens were A_2A_{10} (A_{26}) $B_5B_{35}CW_4$.

The family history of the patient, whose parents were unrelated, did not reveal any other case of this disease. The patient's only sister, who was eleven years-old, was healthy. In spite of the absence of known cases of hypogammaglobulinemia in the family, the fact that the serum Ig levels were below 100 mg/dl, the presence of a very low number of circulating B cells and the absence of palpable lymph nodes and invisible tonsils suggested that our patient had X-linked hypogammaglobulinemia.

After evaluation of the results of the serum Ig values, the child was given 1.6 ml/kg gammaglobulin im. On the thirteenth day of hospitalization, antibiotics were stopped and the patient was discharged with a treatment schedule of monthly gammaglobulin injections in dosages of 0.8 ml/kg to be given in the hospital.

Discussion

Primary immunodeficiency disorders are among the predisposing factors of recurrent purulent meningitis. Untreated humoral immunodeficiency diseases and particularly late complement component deficiencies may be associated with recurrent meningitis[1,5]. Thus immunological evaluation must be made in children with recurrent bacterial infections as well as meningitis. The presented case, who suffered from recurrent meningitis and chronic otitis media, had low immunoglobulin levels (below 100 mg/dl), very few circulating B cells, an absence of palpable lymph nodes and invisible tonsils. These findings are compatible with the diagnosis of X-linked hypogammaglobulinemia.

Humoral immunodeficiency diseases are the most common type of immunodeficiencies. The incidence of these diseases in Turkey is not known, but estimates in the United Kingdom suggest an overall incidence of one case per 100,000 population. Male infants with these disorders usually become symptomatic following the natural decay of transplacentally acquired maternal immunoglobulins at about the first five or six months of life. The loss of maternal immunoglobulin is usually associated with recurrent bacterial infections, such as otitis media, bronchitis, pneumonia, and skin infections. Many infections respond promptly to antibiotic therapy and this response occasionally delays the diagnosis of hypogammaglobulinemia, as in the case presented[6-9].

Summary

A five-year-old boy with Bruton's disease and recurrent pyogenic meningitis is presented, and the importance of the evaluation of patients with recurrent meningitis for immunodeficiency diseases is emphasized.

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