Deficiency of the seventh component of complement in an eight-year-old girl

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ABSTRACT

Complement defects are uncommon. The late components of complement deficiency is associated with recurrent and invasive meningococcal infections especially meningitis. We report the case of an eight-year-old girl with no prior family or personal history of recurrent infections who was admitted twice in the paediatric department within four months for meningococcal meningitis. A complement system test revealed a seventh component of the complement deficiency.

keywords : Meningitis; Neisseria meningitidis; Complement component 7 deficiency

RESUME

Les déficits en un composant du système du complément sont des situations relativement rares. Elles s'associent à une prédisposition à des pathologies d'une grande diversité clinique. Le déficit des composants tardifs du complément est associé à des infections récurrentes et invasives, notamment à Neisseria. Nous rapportons le cas d'une fille âgée de huit ans sans antécédents familiaux ou personnels d'infections récurrentes qui a été admise à deux reprises dans le service de pédiatrie à quatre mois d'intervalle, pour méningite à méningocoque. Une exploration du système du complément a mis en évidence un déficit en C7.

INTRODUCTION

Complement deficiency account for less than 1% of primary immunodeficiency cases [1]. The late components of complement (C5 to C9) deficiency is associated with recurrent meningococcal infections especially meningitis. We are reporting the case of an eight-year-old girl who was diagnosed with C7 complement component deficiency after the second episode of Neisseria meningitidis meningitis.

CASE REPORT

An eight-year-old girl with no prior family or personal history of recurrent infections was admitted twice to paediatric department within four months for meningococcal meningitis. The table I summarize these two episodes.

A screening for an underlying cause of recurrent invasive meningococcal infection was indicated. An abdomen ultrasound showed the presence of a normal spleen. Immunoglobulin levels were in the normal range for the patient's age (IgA=1,55g/L, IgG=8,85g/L, IgM=0,67g/L).

Functional activity of the classical and the alternative pathway of complement (CH50 and AP50 respectively) were measured according to standards procedures. Serum concentration of C3 and C4 were determined by nephelometry.

Complement tests revealed low CH50 (<10%) and AP50 (< 25%), normal C3 and C4 (1,384 and 0,292 g/l), suggesting terminal pathway deficiency. Hemolytic tests supplementation with known C5, C6, C7 and C8 deficient plasmas were performed and showed undetectable haemolytic activity upon addition of C7 deficient plasma and the restoration of hemolytic activity with the remaining deficient plasmas. These data suggest C7 deficiency which confirmed by a homemade double-ligand ELISA with a C7 value of 0.2% (Normal range: 70-130%). Antibiotic prophylaxis, with phenoxymethylpenicillin 1000000UI/day was started.

The patient was vaccinated with the MENCEVAX ACWY vaccine (Meningococcus A, C, Y, W-135, tetravalent purified polysaccharide antigen). After six months of follow up, the infant was in a good general condition with normal neurological exam.

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Table 1 : clinical presentation, biology findings and treatment of the two episodes of meningitis.

		1st episode	2nd episode
Fever		Yes	Yes
Headache		Yes	Yes
Vomiting		Yes	Yes
Stiff neck		Yes	Yes
Kerning		No	Yes
Brudzinski		No	Yes
Petechiae		Yes	Yes
Hemodynamic instability		Yes	No
WBC/µl		22910 (94 % Neutrophils)	27330 (94 % Neutrophils)
CRP (mg/L)		91,4	91,8
Lumbar puncture	Appearance	Turbid	Turbid
	Leucocytes	1470	100
	Protein (g/L)	0,69	0,98
	Glucose: CSF/serum ratio	0,5	0,02
	Culture	*Neisseria meningitidis*	*Neisseria meningitidis*
Antibiotic	Molecule	Cefotaxime	Cefotaxime
	Dose	200 mg/kg/day	200 mg/kg/day
	Duration	7 days	7 days
Vasoactive drugs		Yes	No
Outcome		Favourable outcome with no complications	

WBC: white blood cells, CRP: C-reactive protein

DISCUSSION

Deficiencies in terminal complement components, such as the 7th component, predispose patients to an increased risk of recurrent meningococcal infections. A prospective Tunisian study evaluated the prevalence of complement deficiency in patients presenting with community acquired purulent meningitis within 122 patients. Fifteen patients presented with a complement deficiency (12.3 %), three with the seventh component deficiency (2.5 %) [2]. All children presenting with a second episode of bacterial meningitis should be screened for congenital immunoglobulin or complement deficiencies. Serological testing for HIV infection is requested if the parents have risk factors. For children who are at risk for development of splenic dysfunction or congenital asplenia, splenic function should be evaluated.

Some studies suggest complement system test should be considered even after one episode of invasive meningococcal infection because the prevalence of complement deficiencies could reach 20 to 28 % among patients with history of a meningococcal disease [3].

Some criteria could limit the systematic complement system test after one infection due to Neisseria meningitidis. The test is requested if the patient presents with family history of meningococcal infections, recurrent infections, infection due to rare serogroups of the bacteria often isolated in patients with complement deficiencies, fulminant meningitis and age less than 6 months or more than 5 years. Densen and al[4] made a study about 250 cases of terminal complement components deficiency and showed that 93 % of these patients had their first meningococcal infection before the age of 6 months and after the age of 5 years.

For our patient, since she was eight, we could have screened for complement components deficiency after the first meningococcal meningitis. Preventive treatment could have prevented the second episode of Neisseria meningitidis meningitis.

The deficiency of the terminal components of the complement is to consider if, C3 and C4 are normal with very low CH50 and AP50 (< 10 %). The dosage of 5th to 9th components is needed to identify the type of deficiency [5].

Preventive treatment to reduce recurrences is indicated once the diagnosis of terminal components of the complement is made. First step is to educate the patient and his family about early signs of meningitis to avoid the delay diagnosis. The Center for Disease Control in the United States recommends tetravalent meningococcal vaccine for complement-deficient individuals [6].

Administration of prophylactic penicillin is effective in areas highly endemic for meningococcal infection; its efficacy remains controversial in non-endemic areas. Replacement therapy with C7 could theoretically correct the immune deficiency but it is not clinically practice [7].

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