OCCURRENCE OF ATYPICAL HEMOLYTIC UREMIC SYNDROME FOLLOWING INFLUENZA B INFECTION

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Background

Hemolytic uremic syndrome (HUS)

= Thrombotic microangiopathy with triad of non-immune hemolytic anemia, thrombocytopenia and renal impairment

Etiology of HUS:

1. Typical HUS (90%) versus atypical HUS (aHUS)
2. Etiologically, aHUS is a heterogeneous group with the primary hereditary forms as the largest group. Many genetically forms of aHUS pathology are known, only about 50% of carriers develop the disease. The reason remains unclear, and triggering events like intercurrent infections have been postulated.
3. In rare cases, influenza A is the known trigger of aHUS, however no cases of influenza B have been reported. We described, to our knowledge, for the first time a series of three patients who presented with a first episode or or recurrence of aHUS triggered by influenza B virus infection.

Materials and methods

-3 patients with a known primary hereditary complement disorder present with first episode or or recurrence of aHUS triggered by influenza B virus infection within the same flu season 2012- 2013

-Retrospective evaluation based on patients notes

Casus 1

10 year old boy

-Flu like symptoms for 3 days without history of diarrhea

-Developing jaundice and macroscopic hematuria

-Family history: maternal grandmother and her sister were known with ESRD due to an undefined genetically forms of aHUS with low C3

Physical examination:

-BP: 123/79 mmHg (P95: 121/81 mmHg)

-Petechiae on the lower limbs and jaundice

-Mild peripheral edema

-Investigations are revealed below

Therapy:

-Supportive treatment (fluid, furosemide infusion and packed cell transfusion)

-No need of antihypertensive drugs or dialysis or plasma exchange

Casus 2

15 year old boy

-Flu like symptoms for 2 days without history of diarrhea

-He was known with a primary hereditary complement disorder

-Previous 2episodes of aHUS (without known triggers) at the age of 4 and 5, with the need for plasma exchanges and hemodialysis

Physical examination:

-BP: 135/90 mmHg (P95: 133/84 mmHg)

-Oliguric

-Moderate orbital and peripheral edema

-Investigations are revealed below

Therapy:

-Supportive treatment (fluid, furosemide infusion and packed cell transfusion)

-Plasma exchanges (6 times) with improvement renal function. There was no need of dialysis.

Casus 3

9 year old boy

-Flu like symptoms for 3 days without history of diarrhea

-Developing epistaxis and macroscopic hematuria

-Previous 1 episode of aHUS after a Salmonella typhimurium infection at the age of 5 years, with spontaneous recovery

Physical examination:

-BP: 114/67 mmHg (P95: 118/79 mmHg)

-Normal diuresis

-Euvolemic

-Investigations are revealed below

Therapy:

-Supportive treatment (fluid, furosemide infusion and packed cell transfusion)

-Plasma exchanges (6 times) with improvement renal function. There was no need of dialysis.

Extensive examination was negative for:

-EHEC bacteria or Shigella dysenteriae type 1 in stool, blood or urine samples. No Strep pneumoniae

-Viruses such as EBV, CMV and hepatitis A, B or C, ...

-TTP (nl Von Willebrand factor cleaving protease)

-Secondary aHUS due to autoimmune disease

-Normal homocysteine and the absence of methylmalonic acidemia ruled out a cobalamine deficiency

-Other triggers: example medication use

Genetic examination was positive for:

-Primary hereditary complement disorder (see table)

All three patients (within the same flu season 2012-2013) were infected with the same B-strain, from the B/Yamagata lineage as determined by sequencing of the hemaglutinin gene.

Results	Patient 1	Patient 2	Patient 3
1. Blood results			
Hemoglobin (g/dl)	11.3	13	10.4
Schistocytosis (/1000 RBC)	12-17	30-40	12-17
Platelet count (x10³/µl)	25	20	22
Creatinine level (mg/dl)	1.53	4.1	1.01
Urea nitrogen level (mg/dl)	77	136	105
Haptoglobine (g/L)	0.35	0.19	0.13
LDH (U/L)	2920	5218	2700
Total/direct bilirubin (mg/dl)	1.46/<0.18	3.8/1.1	1.73/0.27
AST (U/L)	189	211	107
ALT (U/L)	33	68	14
2. Urine result			
RBC (/µL)	52	106	Massive hematuria
Protein/creat ratio (gr/gr creat)	12.58	4.08	4.76
3. Nasopharyngeal swab			
Influenza B	Positive	Positive	Positive
4. Cause aHUS			
Primary hereditary complement disorder	Mutation C3	Mutation clusterin + MCP	Mutation MCP

Follow-up

The next year we were confronted by the issue to vaccination these patients with aHUS.

We decide to vaccinate our patients because of the lack of literature and because vaccination is the only available mean to prevent influenza infection, and therefore possible relapse. Also, the likelihood of influenza infection causing a recurrence of aHUS was perceived to be far greater than the possibility of the inactivated trivalent vaccine.

Our three patients were vaccinated prior to the 2013-2014 influenza season. We followed them very carefully and they did not relapse.

Conclusion

Influenza viruses are an uncommon trigger of aHUS. Influenza A viruses have been recognized as a trigger for aHUS in the past. We suggest that the influenza B strain is also capable of triggering aHUS in children with a genetic predisposition. We also showed that immunization these children with an inactivated trivalent vaccine appears to be save. We also showed that immunization these children with an inactivated trivalent vaccine appears to be save.

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