Letter to the Editor

Yersiniosis in a patient with selective immunoglobulin A deficiency: an unusual combination

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Yersinia Enterocolitica is an important gram-negative intestinal pathogen that can cause a variety of clinical situations ranging from gastroenteritis to ileitis and colitis. While it is primarily a gastrointestinal tract pathogen it may produce extraintestinal infections in hosts with underlying predisposing factors. It comprises both pathogenic and nonpathogenic species. Routes of acquisition include oral and blood transfusion. Major animal reservoirs so far identified include mainly pigs and other animals.[1-5]

Selective Immunoglobulin A (IgA) deficiency is a relatively rare disorder predisposing to gastrointestinal and other types of infection. In this situation, IgA antibodies to a variety of antigenic stimulants are not produced and therefore are absent from the serum.[6,7]

We describe a patient with selective IgA deficiency who developed Yersinia enterocolitica infection. As a result, IgA antibodies against Yop proteins of Yersinia were not detected in the serum. This is the first report describing such a combination in the literature.

Case report: A woman, aged 35, was admitted to our department on April 2001 complaining mostly of diarrhea, and mild abdominal pain. Past history: a) four years earlier, she had mentioned a severe episode of pneumonia, which lasted for 3 weeks and was settled with systematic administration of antibiotics. b) Since the age of 25 she had experienced episodes of diarrhea, especially when traveling abroad, accompanied by borborygms, and mild, diffuse, abdominal pain. Present illness: Five weeks before admission she had started having 3 to 4 liquid bowel movements per day, accompanied by diffuse abdominal pain, tendency to vomite and abdominal bloating. At that time she also mentioned an episode of "arthritis" involving the large joints. Over the next two or three weeks, the "arthritis" improved gradually by the use of non-steroidal-antiinflammatory drugs. One week after the onset of diarrhea she had undergone elsewhere a colonoscopy, the description of which was: "mildly inflamed mucosa of the terminal ileum with some aphthous-like ulcers. The endoscopic picture is compatible with inflammatory bowel disease (Crohn's disease)". Histology from the small bowel showed "infiltration of the mucosa by lymphocytes, plasmatocytes and polymorphonuclear leucocytes. In some sites the inflammatory infiltration is quite dense, extending into the submucosa". With the possible diagnosis of Crohn's disease involving the terminal ileum, she started on mesalazine, ciprofloxacine and metronidazole with gradual improvement of the symptoms.

On admission to our department, which aimed to confirm or exclude the possible diagnosis of Crohn's disease, she was almost asymptomatic. Physical examination revealed a slight tenderness on the palpation of the right lower part of the abdomen. Laboratory investigation showed hematocrite 43.2, hemoglobin 13.7, WBC 5140 (ND), MCV 89.3, MCH 28.3, Platelets 171000, ESR 15mm, cholesterol 166 mg/dl, HDL 62 mg/dl, LDL 86.8 mg/dl, total lipids 582 mg/dl, uric acid 3.2 mg/dl, albumin 4.8 g%, globulins 2.7 g%, glucose 81, renal and liver function test normal, serum amylase 78, calcium 9.3, phosphorus 3.9, C3:0.9 g/l, C4 0.2 g/l, CRP <3.4 mg/l, a1-acid-glycoprotein 0.6 g/l, Anti-ds DNA 3.6 U/ml, negative antinuclear antibodies, Helicobacter pylori IgG antibodies 16, gastrin 33 pg/ml, ferritine 22 μg/ml, vitamin B12 687 pg/ml, folic acid >24 ng/ml, IF bAb nega-

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tive, CEA 1.7ng/ml, CA 125 25 U/ml, CA 19-9 9U/ml, CA 15-3 26U/ml, CA 50 8U/ml, a-feto-P 2.2 ng/ml, SCC 0.5ng/ml, CA 72-4 <3.2 U/ml, TPA 19 U/L, CMV:IgG >250 U/ml, IgM negative, and antibodies against entamoeda histolytica: IgG 1:128 (+), 1:256 (±), 1:512 (-). Colonoscopy was unremarkable. Upper GI endoscopy showed mild gastritis involving the antrum. Histology of the small and large bowel and abdominal computed tomography showed no abnormalities. A transdermal ultrasound revealed normal terminal ileum thickness. The enteroclysis was also normal. On the fifth day of hospitalization the results concerning the serum levels of immunoglobulins were available revealing an IgG level of 19.1 g/l, IgA <0.056g/l, and IgM 3.3 g/l, a picture compatible with selective deficiency of IgA. Immunohistochemical study of the biopsies obtained from the small bowel showed plasmacytes negative for a-heavy chains, a small number containing γ-heavy chains, while the majority of them were positive for μ-chains. The infiltration by plasmacytes, however, was polyclonal. The immunohistochemical findings were compatible with the diagnosis of IgA immunodeficiency. On the seventh day the results of serum estimation of antibodies against Yersinia enterocolitica (western blot) showed the picture seen on table 1. The patient was advised about the concurrent diagnosis of Yersiniosis and selective IgA deficiency and no Crohn's disease. Twenty months later she is completely asymptomatic. Yop D and N antigens, which previously were positive, are now negative.

COMMENT

To the best of our knowledge this is the first description of Yersinia enterocolitica infection appearing in a patient with selective IgA deficiency. The diagnosis of Yersiniosis was based on the positive results for the presence of specific monoclonal IgG antibodies directed against outer membrane proteins (Yop proteins) and the compatible history including the recent episode of arthritis. The diagnosis of selective IgA deficiency was made on the basis of the almost complete absence of serum IgA, and confirmed histologically by the complete absence of IgA producing plasmacytes in the lamina propria of the small bowel. The episodes of diarrhea and severe upper respiratory infection in the past, were also compatible with the diagnosis of selective IgA deficiency.

In this patient we confronted diagnostic difficulties as the initial endoscopic picture and the histology of small bowel suggested the existence of inflammatory bowel disease. However, the presence of specific IgG Yop antibodies and the compatible clinical picture, made the diagnosis of Yersiniosis most probable. The absence of Yop IgA antibodies from the serum, (which are necessary to confirm the diagnosis of Yersinia infection), can easily be explained by the absence of IgA from the serum. Moreover, the absence of any kind of symptoms during the follow-up period of almost two years, is in favour of the diagnosis of Yersiniosis.

Yersinia spp are widely disseminated in birds, pets and poultry. It can be transmitted from person to person through food, animal contact, and contaminated blood products.[1] However, in our patient, no obvious source of infection could be identified. Patients with iron excess are at a higher risk for serious Yersinia infection. It is clear now, that a putative role of chromosomal and plasmid-encoded virulence factors is involved in the pathogenesis of the disease.

Selective IgA deficiency is the most common primary immunodeficiency of humans. In most cases this defect is not associated with any kind of illness. The frequency of IgA deficiency differs, depending on the ethnic origin and the presence of symptoms. In a relevant study, a frequency of 0.24% of selective IgA deficiency in healthy blood donors, was found.[6] However, the prevalence was increased both in children (1.5%), adults with a history of frequent respiratory infection (0.9%) and first-degree relatives of patients with IgA deficiency (6%). In Greece, the estimated incidence of selective IgA deficiency is 0.17%.[7] In severely ill patients or when symptoms per-

Table 1. Serum antibodies against Yersinia enterocolitica (western blot) in the patient with selective IgA deficiency

Antibodies against proteins	Size of proteins	IgG antibodies	IgA antibodies
Yop M (2a)	58kd	(-)	(-)
Yop H (2b)	46kd	(-)	(-)
Yop B (3)	38kd	(-)	(-)
Yop D (4a)	36kd	(Positive)	(-)
Yop N (4b)	34kd	(Positive)	(-)
Yop E (5)	25kd	(-)	(-)

sist, treatment with antibiotics should be started[8]. Yersinia is sensitive to a wide range of antibiotics including tetracycline, and cotrimoxazole. Quinolones and ciprofloxacin are increasingly used on patients with Yersiniosis with promising results.[9,10] Our patient responded well to previous administration of antibiotics (ciprofloxacin and metronidazole).

From the description of this patient we can conclude that Yersiniosis can appear in patients with selective IgA deficiency. The estimation of serum immunoglobulins is indicated in all cases with a history of episodes of diarrhea accompanied by arthralgias and/or respiratory system infections. Gastroenterologists and clinicians must include the diagnosis of Yersiniosis in all cases with endoscopic and histological pictures compatible with inflammatory bowel disease. The results of serum estimation of Yop proteins must not be considered as negative, until the results of serum estimation of immunoglobulins are available.

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