

CASE REPORT

CHRONIC DIARRHEA AND ABNORMAL SERUM IMMUNOGLOBULIN LEVELS: A CASE REPORT

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Abstract. A 15-year-old Thai boy with multiple episodes of chronic diarrhea caused by giardiasis with hypogammaglobulin M and IgG₄ subclass deficiency (but normal antibody response to rabies vaccine) is reported. Immune status follow-up is necessary for a definite diagnosis and proper management.

CASE REPORT

A 15-year-old Thai boy was referred to the Hospital for Tropical Diseases with a history of diarrhea, dyspepsia and intermittent weight loss for 2 years. Previous investigations revealed *Giardia lamblia* cysts in the stool, but were negative for other intestinal parasites by stool concentration and modified acid-fast staining. Since his father's chest X ray revealed an old tuberculous lesion in his left upper lung, he was investigated for tuberculosis and hilar adenopathy was suspected on the chest film but the tuberculin test was negative. An upper GI evaluation and colonoscopic biopsies were performed and duodenitis was suspected but the colon and rectum were unremarkable. The patient improved with several courses of metronidazole and tinidazole, however, the symptoms recurred concurrently with

the reappearance of *Giardia* cysts.

At the Hospital for Tropical Diseases, physical examination detected no abnormalities with a weight 50 kg and a height 153 cm. Stool examination revealed *Giardia lamblia* cysts/trophozoites. Gastroduodenoscopy revealed multiple small, pink mucosal nodules in the pyloric region containing chronic microscopic superficial ulcers and one cluster of *Giardia* trophozoites in a superficial mucosal ulcer (Fig 1). A tuberculin skin test was positive with 15 mm induration. Polymerase chain reaction of a pyloric ulcer was negative for *M. tuberculosis*. Because of the tuberculin conversion and suspected symptoms, he was started on and responded well to an antituberculous regimen, with cessation of diarrhea, weight gain, and the disappearance of *G. lamblia* in the stool during the first 3 months of treatment. However, the above symptoms recurred.

An immunoglobulin assay revealed a normal IgA (161 mg/dl, normal 100-490 mg/dl) and total IgG levels (812 mg/dl, normal 800-1,700 mg/dl), but decreased IgG₄ (4.48 mg/dl, normal 8-140 mg/dl). Interestingly, IgM was

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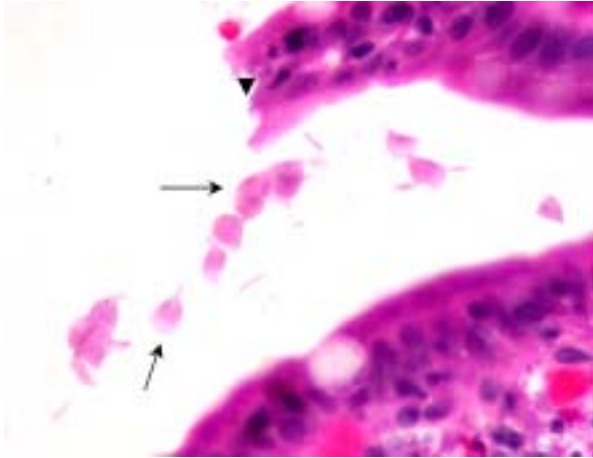


Fig 1—Chronic superficial ulcer in the pyloric region, shown by arrowhead. Arrows indicate *Giardia* trophozoites (Hematoxylin and eosin-stained), 400 x.

< 16.5 mg/dl (normal 50-320 mg/dl). The absolute B-cell count was 681 cell/mm³ (normal 140-660 cell/mm³) with 21.4% B-cells (normal 7.7-25.4%). A rabies vaccination with an intramuscular purified chick embryo cell rabies vaccine on D0 and D7 resulted in a rabies neutralizing antibody titer on D28 post-vaccination of 8.57 IU/ml.

DISCUSSION

Selective IgM deficiency is an uncommon disease. It has been reported in a 9-year-old boy with chronic diarrhea, failure to thrive, recurrent respiratory tract infections and *G. lamblia* in the stool (De La Concha *et al*, 1982). IgG subclass deficiencies are being increasingly recognized, especially in association with infection (Nettagul *et al*, 2003). Isolated IgG₄ subclass deficiency appears to be associated with impaired respiratory tract defenses, suggesting a physiologic defense role for mucosal IgG₄. The normal levels of IgG, IgA and IgM in Thai children aged 6-13 years demonstrated by Vichayanond *et al* (1996) were found to be higher than the respective normals in Cauca-

sian children. The IgG subclasses have been shown preferentially to recognize either protein or carbohydrate antigens. Antibodies to protein antigens tend to be T-cell dependent and are usually IgG₁ and/or IgG₃, while antibodies to carbohydrate antigens and polysaccharides, including bacterial capsules, tend to be T-cell independent and are usually IgG₂. IgG₄ appears to be univalent (Walker *et al*, 1983). The IgG₄ subclass is simply a marker of antigen exposure and chronic inflammation. Parasitic infection is often associated with elevated IgG₄ levels. The normal levels of IgG₁, IgG₃ and IgG₄ in Thai children were not different from those of Caucasian children, whereas the normal IgG₂ level in Thai children was higher than in Caucasian children (Shur, 1987).

In this patient, B- and T-cell functions were investigated. The positive tuberculin test, normal B-cell count and normal antibody response to rabies vaccination supported the belief that his T- and B-cell functions were not significantly impaired. During 18 months follow-up, he had intermittent diarrhea, dyspepsia and fluctuation in body weight between 43 and 50 kg and *Giardia* was persistently found without other infections. *G. lamblia* resistant to 5-nitroimidazole and low IgM and IgG₄ subclass levels may be the cause of his persistent giardiasis. We attempted to obtain trophozoites from the small bowel for drug sensitivities but were not successful. Regarding the immunodeficiency, a follow-up for immunological assay will need to be performed. With adequate T- and B-cell functions, we expect the patient will not have any serious infections.

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REFERENCES

- De La Concha EG, Garcia-Rodriguez MC, Zabay JM, *et al*. Functional assessment of T and B lymphocytes in patients with selective IgM deficiency. *Clin Exp Immunol* 1982; 49: 670-6.
- Nettagul R, Visitsunthorn N, Vichayanond P. A case of IgG subclass deficiency with the initial presentation of transient hypogammaglobulinemia of infancy and a review of IgG subclass deficiency. *J Med Assoc Thai* 2003; 86: 686-92.
- Shur PH. IgG subclasses-a review. *Ann Allergy* 1987; 58: 89-99.
- Vichayanond P, Petranand S, Senawong S, Banchuen N, Assateerawat A, Tuchinda M. Normal IgG subclass and immunoglobulin levels in Thai school children. *Thai J Pediatr* 1996; 35: 233-9.
- Walker L, Johnson GD, Mac Lennan IC. The IgG subclass response of human lymphocytes to B-cell activators. *Immunology* 1983; 50: 269-72.