339 Unusual Infections in a Mother and Son With G6PD and a Defective Oxidative Burst

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INTRODUCTION: Glucose-6-Phosphate Deficiency is one of the most common enzyme deficiencies in the world. Typically, patients develop a hemolytic anemia in response to oxidative stress. The defect results in the failure of the hexose monophosphate shunt pathway to produce NADPH. NADPH is an important catalyst for the respiratory burst in neutrophils. Certain patients with G6PD have been found to have an impaired respiratory burst in their neutrophils, resulting in increased susceptibility to infections.

CASE: Our patient is a 4 year old boy who presented to the hospital with a left knee abscess. The knee abscess responded slowly to antibiotics. Culture grew *Pseudomonas fluorescens.* The patient's mother had no past medical history until age 33, when after a week of URI symptoms, she developed worsening fever and cough, leading to lobar pneumonia, sepsis, and respiratory and renal failure. She developed an empyema that grew resistant staphylococcus treated with Vancomycin. When she failed to improve, biopsy of her lungs revealed aspergillus, managed with both Amphotericin and steroids. After a four month hospitalization, she improved, but remains in renal failure, receiving dialysis 3 days a week. DCF on both the patient and his mom indicated a severely impaired respiratory burst. The patient's G6PD assay was low at 3.7%.

CONCLUSION: G6PD is a very common enzymopathy, typically causing hemolytic anemia. In rare cases, it may be associated with increased risk of severe infections similar to those seen in CGD. This case highlights the difficulty in defining the cause of a defective respiratory burst.

340 Sarcoid, Infectious Disease, or Immunodeficiency?

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RATIONALE: The pathologic hallmark of sarcoid is non-caseating granulomas. Other causes of non-caseating granulomas include infection with weakly pathogenic mycobacteria due to acquired or congenital immunodeficiency. One congenital cause is Mendelian susceptibility to mycobacterial disease (MSMD) (MIM 209950) which can be caused by genes in the IL-12/IL-23/IFN-γ pathways. We report a case that illustrates the difficulty of diagnosing this rare disease.

CASE DESCRIPTION: An 11-yr-old female presented with enlarged abdominal lymph nodes, bilateral renal masses and chylous ascites. Biopsy of lesions showed non-caseating granulomas. There was no history of opportunistic infections. Examination for micro-organisms and HIV were negative. Sarcoid was diagnosed and corticosteroids started. A peritoneal catheter was inserted to relieve the chylous ascites. She developed bacterial peritonitis and increased size of her lesions. Urine culture showed *Mycobacterium avium* complex. Treatment was instituted with Isoniazid, Ethambutol, Rifampin, Clarithromycin, and Bactrim. Corticosteroids were stopped. IFN-γ was undetectable in her plasma, but blood leukocytes produced IFN-γ after stimulation with heat killed *Pseudomonas aeruginosa*. An antibody recognizing the p40 subunit of IL-12 indicated it was present after stimulation of blood leukocytes. Her age and lack of plasma IFN-γ indicate that if she has MSMD, it is a partial defect. IFN-γ was added to her treatment regimen with stabilization of her disease, but with continued chylous ascites.

CONCLUSIONS: The combination of non-caseating granulomas, decreased blood T-lymphocytes secondary to drainage of chylous ascites, and infection with *Mycobacterium avium* complex created difficulty in diagnosing and proper treatment. Definitive diagnosis will require sequencing of several genes in the relevant pathways.

341 The Prevalence of Selective IgA Deficiency in Patients With IgE Hypogammaglobulinemia

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RATIONALE: Selective IgA deficiency had been associated with atopy and high serum IgE levels, but previous studies in small numbers of patients demonstrated its association also with IgE hypogammaglobulinemia in (6.4%-32%). The present study examines this association in a large cohort of patients.

METHODS: The database of the Clinical Immunology Laboratory for 2001-2003 was searched for test results of serum IgE level <10 IU/ml and serum IgA levels <6.6 mg/dl and normal IgG and IgM levels.

For patients with IgE-IgA deficiency, data were collected on age, gender, clinical diagnosis and serum IgG subclass levels.

RESULTS: Serum IgE levels <10 IU/ml were found in 532 of the 3287 patients tested (16%). Selective IgA deficiency was detected in 6 of them (age range 4-30 years, serum IgE levels 0-3 IU/ml). Four of these patients also had low serum IgG2 and IgG4 levels. Two had bronchial asthma and four had recurrent upper and lower respiratory tract infections, with bronchiectasis in one of them.

CONCLUSIONS: The prevalence of selective IgA deficiency in patients with IgE hypogammaglobulinemia is 1.12%, lower than reported in previous studies. The presence of IgG2-IgG4 deficiency in two-thirds of the patients with combined IgA-IgE deficiency points to the possibility of genetic background such as deletions of immunoglobulin heavy chain constant region genes.

342 Transient Deficiency of Complement Factor D Function in Infancy

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INTRODUCTION

Complement factor D (FD) is an alternate pathway (AP) serine esterase (1-2 mcg/ml), required for C3b-bound factor B cleavage to C3bBb. Sera lacking FD have normal classical pathway (CH50) activity, but little or no AP (AH50) function, associated with lifelong increased risk of bacterial infection. We describe an infant with a previously undocumented transient form of FD deficiency or dysfunction.

CASE REPORT

A 9-wk-old African-American male presented with meningococcal meningitis. He was a healthy term infant, but developed respiratory syncitial virus infection at age 3 wk, diarrhea at 6 wk and hypomagnesemia and seizures at age 8 wk. The meningitis cleared with antibiotics, and he was well thereafter. Immunologic studies including serum CH50 and C4 were normal, but C3 was decreased. AH50 was <5U/ml, but 100% normal after addition of purified FD (1 mcg) in vitro. FD protein was demonstrable by Western immunoblot and presumably dysfunctional. AH50 was still <5U/ml at age 6 mos, but normal (23 U/ml) at age 1.3 yr.

LITERATURE REVIEW

Previous reports of FD deficiency involved adults from 3 unrelated Dutch kindreds and one other African-American male infant. The inheritance of FD deficiency was autosomal recessive in one family or not determined.

CONCLUSIONS

This unique patient inexplicably had no serum FD or AP function before age 0.6 yr, even though FD protein was detectable, and normal AP function when retested 10 mos later. The rarity with which FD deficiency is diagnosed worldwide emphasizes the importance of measuring AH50, as well as CH50, when complement deficiency is suspected.

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