Disseminated gonococcal infection associated with deficiency of the second component of complement

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Summary: A case of C2 deficiency presenting with disseminated gonococcal infection is described. The predisposition of C2-deficient individuals to infection in addition to the commoner problem of immune complex diseases is noted. Attention is drawn to the absence of documented cases of gonococcal infection associated with C2 deficiency. No other homozygous C2 deficient family members were identified. Lifelong penicillin prophylaxis was recommended for the patient.

Introduction

Deficiency of the second component of complement (C2) is an autosomal recessive disorder often associated with systemic lupus erythematosus (SLE) like syndromes, but also frequently associated with recurrent sepsis. The most commonly implicated organisms are meningococci, pneumococci and Haemophilus influenzae. The association of terminal complement deficiency (particularly C8) with disseminated gonococcal infection (DGI) is well documented, but C2 deficiency has not been noted to be associated with gonococcaemia. We report a case of subcute gonococcal septicemia associated with C2 deficiency.

Case report

A 22 year old single male presented with a 6 day history of sore throat and a migrating arthropathy of knees and wrists associated with a skin rash. While on holiday in Spain 2 months prior to admission he had a similar episode of self limiting arthropathy, associated with diarrhoea but no skin rash. He had mild asthma, and gave a history of an episode of bronchitis and two episodes of pleurisy. His only medications were a salbutamol inhaler and, just prior to admission, indomethacin. He had recent unprotected sexual contact with a known female partner, but denied any other contacts.

Apart from a single temperature spike of 38°C he remained apyrexial. He had marked painful limitation of movement in his wrists, knees and ankles but no synovial effusion. Sparse cutaneous lesions – small erythematous macules, tiny pustules and crusted lesions – were noted. After admission a few more pustules developed. Otherwise examination was unremarkable. Routine biochemical and haematological investigations were normal except for an erythrocyte sedimentation rate of 49 and a C-reactive protein of 21 mg/l (normal range < 6). His ASO titre was less than 200 Todd units. A throat swab grew group C beta haemolytic streptococci. No organisms were grown from the skin lesions. Blood cultures grew Neisseria gonorrhoeae serogroup WI (genetic serovar: Aedghik, Pharmacia serovar: Arost), which was sensitive to less than 0.015 mg/l penicillin. Tests for antinuclear factor, rheumatoid factor, anti-Ro, anti-La, anti-Sm and anti-RNP were all negative. Viral serological screens were negative as was serology for meningococci, yersinia, syphilis and Borreilla burgdorferi. Details of complement levels are shown in Table I.

He was treated with benzyl penicillin and made a rapid and complete recovery. There was no evidence of other sexually transmitted disease. His immediate family all have normal levels of C2. Lifelong prophylaxis with phenoxymethyl penicillin has been recommended.

Discussion

C2 deficiency appears to present most frequently with immune complex diseases. However, in a series of 38 cases of which 36 had presented with a connective tissue disorder, many had a history of...
significant bacterial infections. In another series of 77 individuals with C2 deficiency, 32 had had significant bacterial infections, including 11 individuals with pneumococcal sepsis on one or more occasion and 3 each of meningococci, H. influenzae and tuberculosis, but no cases of DGI. The absence of cases of DGI in both of these series and other published cases is striking, implying either that C2 deficiency does not predispose to gonococcal sepsis or that there has been a failure to diagnose C2 deficiency in infected patients. Alternatively, cases may not have been reported due to the mistaken assumption that the well documented association of C2 deficiency with neisserial sepsis includes DGI. As DGI is a less spectacular infection there may be a tendency for cases not to be investigated. It has also been suggested that as aerial transmission is important for meningococci they have greater opportunities for spread to susceptible individuals than gonococci. In view of the susceptibility of C2-deficient individuals to infections by capsulated bacteria it would be surprising if this case represented the coincidence of two independent conditions. Furthermore it has been shown that in vitro killing of N. gonorrhoeae is slowed when C2 deficient plasma is used. 

The organism isolated in this case is a serum-resistant strain typical of those associated with DGI. Even these do not usually cause systemic disease, and individuals who develop DGI may have defective host defence mechanisms. Additionally gonococci not usually associated with dissemination may cause invasive disease in such patients.

C2 deficiency is the most common complement deficiency with a prevalence of 1:10,000. It has already been suggested that gonococcal septicaemia is an indication to screen for complement deficiencies, and this case adds further weight to that suggestion. Measurement of the CH50 is a convenient and readily available screening test which will prompt further investigation where appropriate. Diagnosis of the defect has important implications for the long term prophylaxis of individuals who are prone to infections (a subgroup of C2 deficient individuals). As the most commonly diagnosed pathogen is S. pneumoniae, oral penicillin is an appropriate antibiotic. Pneumococcal vaccine may not be effective. The predisposition to infections may only become apparent when individuals (as in this case) are aged over 20 years, and family members should be screened, so primary prophylaxis may be offered where appropriate.

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References

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