

Anaphylactic sensitivity to human seminal fluid

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Summary

A patient is described who had generalized allergic symptoms due to a specific allergy to her second husband's seminal fluid. The woman's serum contained a heat labile reaginic IgE antibody that conferred anaphylactic sensitivity on human and monkey skin. The antigen is a glycoprotein of the seminal plasma.

Introduction

Allergy to human semen must occur very rarely and in the four cases known to one author (Frankland, 1973) the diagnosis was first made by the patient and not by the doctors who had not considered or known that a wife could be allergic to her husband's semen. In Halpern, Ky & Robert's (1967) patient, urticaria developed immediately after coitus and this was followed by asthma and loss of consciousness. In the patient described by Levine and his colleagues (1973) symptoms started 5 min after coitus. The symptoms were nasal obstruction, sneezing, periorbital swelling, diffuse urticaria, perivaginal swelling and a sensation of throat swelling. Yet in another patient (Blair & Parish, in preparation), there is no local vaginal urticaria but a generalized urticaria with asthma occurring 1–2 hr after coitus. Brief reference has already been made (Frankland, 1973) to a patient allergic to her husband's seminal fluid, which when first discussed in 1972 was referred to as the second recorded example of a wife being allergic to her husband's seminal fluid. The reaginic antibody IgE had not been characterized when Halpern described the immunology of the antibody concerned in the reaction. The following case report is presented with immunological data.

Case report

A 32-year-old married woman who had three children by a previous husband, was first seen in April 1971. There was no previous history of any atopic disease, nor was there a family history of atopy. She complained that intercourse with her new husband was causing her a great deal of vaginal irritation, and when various local applications had been used without success, she volunteered the information that she had noticed

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that her husband's semen had caused a similar acute irritation on her skin. She believed that she was allergic to her husband's semen. On closer questioning she stated that within 5 min of intercourse she noted intense vulval and vaginal irritation, usually followed by a generalized irritation of the body particularly involving the palms of her hands and her feet. Sometimes the irritation became a generalized urticaria. She also had pelvic pain and had experienced difficulty in breathing, but no actual cough or wheeze. She had noted that when a condom or coitus interruptus had been employed during sexual intercourse, she usually had no untoward symptoms. It was found that a specimen of her husband's semen rubbed on to the mucosa of the vulva produced in 5 min local oedema and redness with irritation. Although this patient has been shown to be ovulating, her main complaint is that she remains sterile.

Immunological studies

Materials and methods

Sera and semen. The sera and semen were stored at -25°C , except the glycoprotein fraction which was obtained from a fresh sample, and was used immediately after preparation, any overnight storage being at 4°C .

P.K. test. The modification of challenge by the prick test (Augustin & Hayward, 1960) was used by injecting 0.1 ml of the patient's serum intracutaneously into the forearm of a human subject. The following day the husband's semen was pricked through a sensitized site as well as an unsensitized site.

Skin tests. Using the prick method, the patient was tested with many common allergens as well as with an aqueous extract (w/v, 1–10) of her husband's shavings, his undiluted saliva and his serum. Histamine 1% was used as a positive control.

Monkey passive cutaneous anaphylaxis. Two baboons were sensitized by intradermal injections of 0.1 ml sera undiluted, or diluted in saline, unheated, or after heating at 56°C for 1 hr. Sera from women with IgG antibodies to seminal plasma, from two women with 'non-antibody agglutinating substance for seminal plasma coated particles' and from three normal (no antibody to seminal plasma) women were tested concomitantly. Intravenous challenge was made at 22 hr with 1 ml containing 30 mg seminal plasma and Evans blue dye, and the results read at 15 min.

Agglutinins for seminal plasma and spermatozoa. Agglutinins to seminal plasma were examined by the tanned cell agglutination test, and to spermatozoa by agglutination of suspensions of washed spermatozoa, living or dead: both techniques according to Jeffery & Parish (1972).

Immunofluorescence. After the agglutination tests, the suspensions of spermatozoa were washed and tested with fluorescein labelled monospecific anti-IgG, -IgA, -IgM (Jeffery & Parish, 1972).

Radio-immunodiffusion precipitation in gels. The technique of Heiner & Rose (1970) was used to detect the immunoglobulin classes of antiseminal plasma antibodies. Precipitates were formed by testing monospecific anti-IgG, -A, -M or -E, against the serum of the patient, with a purified preparation of the immunoglobulin, as appropriate, in one well to confirm the identity of the precipitated immunoglobulin. The plates containing the precipitates were washed free of unbound protein. Then whole seminal plasma, or a fraction thereof, labelled with ^{125}I , were added to the wells to detect any antibodies in the precipitates of the patient's immunoglobulins that bound the seminal antigens.

The antigens tested were whole seminal plasma, and a polysaccharide-rich fraction prepared by precipitation in ethanol (Mann & Rottenberg, 1966). Five millilitres of seminal plasma were precipitated with 25 ml of redistilled ethanol, and the precipitate washed twice with 5:1 (v/v) ethanol:water. Details of the antigenic and chemical composition of this fraction are to be published separately.

Results

Skin tests

Skin tests gave no immediate, late or delayed responses to the common allergens. Skin tests were not made in the patient with the husband's semen. The histamine positive control gave a normal response maximal at 15 min with a weal 7 mm in diameter and flare 15 mm in diameter.

P.K. test using patient's semen

A positive weal (4 mm) and flare (12 mm) was produced by the husband's semen only and not by his saliva or shavings.

Laboratory investigations of anti-seminal plasma antibodies

IgE reaginic anti-seminal plasma antibody was also detected by monkey passive cutaneous anaphylaxis. In the first test, a weak but definite (6×7 mm) reaction was observed at the site sensitized with undiluted serum, and no reaction at a similar site injected with the serum previously heated at 56°C for 1 hr. In a second test, a diffuse reaction occurred at the site injected with undiluted serum, and no response at sites injected with the serum diluted at 1/5 or when heated. There was no reaction at control sites injected with other sera, or with another serum also containing IgE anti-seminal plasma antibody. The total IgE on sample April 1971 was 471 u/ml and on sample January 1972 was 400 u/ml.

In the Heiner & Rose (1970) technique of immunodiffusion precipitation, precipitates were obtained in gels when the patient's serum was tested against monospecific anti-IgG, -IgM, -IgA and -IgE. The washed precipitates were then treated with ^{125}I -labelled seminal plasma. The IgE precipitate clearly bound the antigen, showing that some of the IgE was anti-seminal plasma antibody. The IgG precipitate also bound some antigen, but very weakly, indicating the presence of a small amount of IgG antibody. When the tests were repeated with the polysaccharide-rich fraction of seminal plasma, the IgE precipitates bound more of the antigen, but the IgG appeared to bind no more than that in the tests with native, unfractionated, seminal plasma. The IgM precipitates also bound a small amount of the polysaccharide-rich fraction, but this was probably non-specific, because the binding could not be blocked by previous treatment of the precipitate with unlabelled native seminal plasma or the polysaccharide-rich fraction.

No antibody to seminal plasma was detected by the tanned cell agglutination test, using the seminal plasma of the husband, or of a group A nonsecretor, or a pool from group O donors.

No agglutinating antibody for suspensions of washed spermatozoa was found using the dead spermatozoa of the husband, or the living or dead spermatozoa of a group O donor. After the agglutination tests the spermatozoa were washed, and samples treated with fluorescein labelled monospecific anti-IgG, -IgM and -IgA. There

was weak overall staining of the cells with anti-IgM which was not considered to be significant, and no reaction with the anti-IgG or -IgA.

Discussion

Though agglutination tests have been widely used to detect antibodies to spermatozoa or to seminal plasma, the immunoglobulin class of the agglutinins has seldom been reported. Parish & Ward (1968) found cytotoxic anti-spermatozoal head antibodies to be IgG and anti-seminal plasma antibodies to be IgM, in sera of infertile women, and similar antibodies together with IgA were present in the cervical mucus. In further tests to compare the ability of five different techniques to detect anti-seminal antibodies, IgG and/or IgM antibodies were found in thirteen of twenty female sera (Jeffery & Parish, 1972).

Though IgG and IgM antibodies are not uncommonly, and IgA is occasionally, formed by women against seminal plasma, it appears that IgE, manifested by anaphylaxis, is very rarely formed. Halpern *et al.* (1967) described a woman who had reaginic antibody and anaphylactic sensitivity to seminal plasma. The case reported above, also with anaphylactic sensitivity and IgE reaginic anti-seminal antibodies, is the second (Frankland, 1973). A third woman who is extremely anaphylactically sensitive, with severe asthma after coitus, has IgE anti-seminal plasma antibodies, and also a weak delayed hypersensitivity response detected *in vitro* (Blair & Parish, unpublished).

The case of Halpern *et al.* (1967) is particularly interesting because the wife was spontaneously sensitized and anaphylactic signs occurred on first exposure to the seminal antigen. The presence of reagins was shown by passive transfer of cutaneous sensitivity to man and monkey by antibodies susceptible to heating at 56°C.

In our case, the woman's serum contained a heat-labile antibody that conferred anaphylactic sensitivity on human and monkey skin. Techniques, not available at the time of Halpern's investigation, further showed that the reagin was IgE. It is particularly interesting that the seminal plasma antigen in this case, like that of Halpern, is a glycoprotein, or is associated with a glycoprotein-rich fraction of seminal plasma. Moreover, no agglutinating antibodies to seminal plasma, or to spermatozoa were formed by their patient or ours, and were also absent from the serum of the patient of Blair & Parish (in preparation).

The reaction of the patient to the seminal antigen is very specific. She complains more of the concomitant sterility than the immediate unpleasant symptoms following coitus.

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