Contact Dermatitis, 1994, 30, 7–11
Printed in Denmark . All rights reserved

Copyright © Munksgaard 1994

CONTACT DERMATITIS
ISSN 0105-1873

21346

Combined allergy to human seminal plasma and latex: case report and review of the literature

B. KINT, H. DEGREEF AND AN DOOMS-GOOSSENS
Department of Medical Research (Dermatology), University Hospital, Katholieke Universiteit Leuven, Belgium

The case is reported of a young atopic woman with combined Type I and possible Type IV allergy to human seminal plasma, as well as Type-I allergy to latex. Clinical symptoms were swelling and a burning sensation on the vulva and in the vulvovaginal area during or after coitus, followed by vesiculation, lichenification and the development of generalized eczema. Diagnosis was confirmed by investigation (RAST, prick testing, histology). Literature on the subject is reviewed.

Key words: contact urticaria; latex; human seminal plasma; protein contact dermatitis; atopy; gynecological differential diagnosis; vulvovaginitis; respiratory effect. © Munksgaard, 1994.

Accepted for publication 2 February 1993

Human seminal plasma (HSP) allergy is a rarely diagnosed disease that gives a variety of clinical pictures in response to antigenic glycoproteins in seminal plasma. In most cases, only vulvovaginal symptoms are elicited, which are often chronic and for which no cause is readily apparent. These occur during or after coitus and are sometimes associated with systemic symptoms. Mild local reactions may precede by months and even years the development of systemic reactions. The disease is generally allergic and Type I mediated, but Type III and IV reactions have also been reported. Here we report the case of a patient with combined Type I and possible Type IV allergy to HSP, known as protein contact dermatitis (1), as well as Type I allergy to latex.

Case Report

A 32-year-old atopic woman, known to our department since 1988, had mild flexural eczema as a child. Her father has hay fever, and her grandfather asthma. She herself became short of breath when near a cat. For 6 years, her eczema had worsened, for which she had repeatedly been treated with corticosteroid- and tar-containing topical medicaments, as well as oral antibiotics, and for which, on one occasion, she had been hospitalized.

She reported a clear relationship between her eczema and sexual intercourse: immediately after coitus, with or without a condom, she would experience vulvovaginal swelling and a burning sensation, and, after 6 to 24 h, she would break out in generalized eczema. Sometimes, the vulvovaginal mucosa became erosive. She used there no topical medicaments or lubricants.

Clinical examination of the entire skin revealed excoriations and dry squamous vesicular plaques, mainly on the limbs. In the vulva and perivulval area, the skin was dry and eczematous with vesiculation and lichenification. The vaginal mucosa was lesion-free.

Her investigations comprised patch tests, radioallergosorbent tests, prick tests, total immunoglobulin E, vaginal candida culture, and biopsy of perivulval skin.

Results

(a) *Patch tests*

- European standard series (Trolab-Hermal, Germany): negative, except for a pustular reaction to nickel sulfate (history revealed no hypersensitivity to metals).
- Rubber series (Trolab-Hermal, Germany): negative
- Corticosteroid series (2): negative
- Atopenes (housedust mite, grass pollen, *Artemisia vulgaris*, flour mixture, *Penicillium* (mixture), *Candida albicans*, dairy products (Hal, The Netherlands): negative
- Own products (topcial medicaments): negative

(b) *Radio-allergosorbent tests* for grasses, spices, trees, animal epithelia, fungi, housedust mite, fish

and other seafoods, grains, and foodstuffs were negative, but positive for cat epithelia (++), human sperm (++), and latex (+).

(c) *Prick test* for latex: + (wheal and flare reaction after 10′); for whole sperm: erythema and very slight induration after 10′.

(d) *Total IgE:* 265 IU/ml.

(e) *Vaginal candida culture:* negative.

(f) *Biopsy of the perivulval skin*

- Epidermis: hyperplasia with rather irregular acanthosis. No spongiosis.
- Cutis: predominantly perivascular inflammatory infiltrate in the superficial cutis; accumulation of Langerhans cells in a hair follicle.

Discussion

This picture concurs with that of a chronic dermatitis. On the basis of the history, clinical symptoms and investigations, we made the diagnosis of combined Type I allergy to both HSP and latex. In view of the delayed eczematous reaction after contact with sperm, we think it possible that there was also an additional Type IV reaction to HSP, as encountered in protein contact dermatitis (1). A patch test with sperm or a lymphocyte transformation test were, however, not performed, so this diagnosis cannot be confirmed. An analogous case has been described by Schimkat et al. (3): this patient had a positive vulvovaginal provocation test with sperm and a positive lymphocyte transformation test for specific HSP fractions, but a patch test with sperm remained negative. It is noteworthy that our patient has since become pregnant, which indicates that an allergy to HSP does not necessarily imply infertility.

Allergic reactions to antigens in HSP

(a) *Systemic reactions*

Severe anaphylactic reactions may occur either during or after coitus: urticaria, mucous membrane swelling, generalized itching, dyspnea, bronchospasm (postcoital asthma may easily be overlooked by respiratory physicians because of their own lack of awareness of its possibility and the embarrassment of the patient (4)), lower abdominal pain, hypotension, and shock. They occur together with local vulvovaginal symptoms.

To our knowledge, HSP allergy was first reported in 1958 by Specken (5), who described the case of a 65-year-old woman who, after coitus, would have a generalized urticarial skin reaction, sometimes accompanied by asthma attacks, which would disappear after some 3 h. Scratch tests and prick tests with HSP were positive but negative in controls. There was no reaction to animal semen.

In 1967, Halpern et al. (6) described the case of a 29-year-old atopic woman who, after her first contact with HSP, developed an anaphylactic reaction with giant urticaria, asthma, swelling of the mucous membranes, and cardiovascular collapse. Scratch and intradermal tests were positive for HSP and for whole sperm. The Prausnitz-Kustner test was positive for dilutions to 1/100. Chromatography was used to demonstrate that protein fractions were responsible. Desensitization with completely undiluted HSP was not successful.

In a review article, Presti & Druce (7) described 32 cases of HSP hypersensitivity. In 18 of the 32, the condition developed between the ages of 20 and 30 years, and in the others sometimes much later and even after the menopause.

The most frequently observed reactions were dermatitis, urticaria, and pruritus (27/32), edema (15/32), and local pain (18/32). Dyspnea (7/32) and life-threatening anaphylactic reactions (7/32) also occurred. 2/3 of the patients were atopic. The condition occurred with monoandry as well as polyandry.

Freeman (8) has described a woman who suffered severe itching and flushing after coitus or other physical contact with her husband. She reacted positively to an intradermal test with HSP and sweat from her husband, to sweat from her 2 sons, and to pooled donor sperm.

Mike et al. (9) described a Type III reaction to sperm: a woman developed post-coital arthritis, hemorrhagic proctitis, and a rash. A scratch test with HSP gave no reaction, but an intradermal test gave an induration after 8 h, which was accompanied by general symptoms. Treatment with H1 and H2 antihistamines was not successful, but tranexamic acid cleared up the lesions, and the patient remained symptom-free after cessation of therapy.

Best et al. (10) described a patient who developed a bullous fixed drug eruption on the vagina, vulva, fingers, ears, breasts, and hips after coitus. The lesions recurred after coitus in exactly the same places and were not associated with general symptoms. Over a period of 2 years, the interval between coitus and the eruption evolved from 2 days to 2 h. Initially, there were hyperpigmented macules, which later became vesiculobullous and resulted in hyperpigmentation. Histological examination of a bullous lesion showed a subepidermal bulla consistent with a bullous fixed drug eruption.

A female patient reported by Blair & Parish (11) manifested asthma, urticaria, and angioedema due to HSP hypersensitivity. Prick tests and RAST were positive. There was antigen-induced histamine release from leukocytes (LHR+) and a delayed hypersensitivity reaction to the same antigen,

which was demonstrated by a skin test and lymphocyte transformation tests.

(b) *Localized reactions*

Local reactions can occur together with systemic reactions or can be present as a chronically recurring condition.

The clinical characteristics of the allergic vulvovaginitis are generally nonspecific: itching, stinging and burning, and edema. The symptoms are related to coitus, last for a few hours or days and do not occur during sexual abstinence or when a condom is used. There seems to be an inherited predisposition (12). Indeed, a hereditary form of vulvovaginitis after contact with sperm has been described in a mother and her 3 daughters (13).

As already mentioned, Schimkat et al. (3), who described a patient with contact dermatitis that occurred 15 h after coitus, obtained positive results with local provocation tests with sperm. Patch tests and RAST for HSP were negative. The total IgE was not mentioned. Histological examination of the affected skin showed spongiosis, exocytosis of lymphocytes in the basal and spinous layers, together with perivascular lymphocytic infiltration and edema in the cutis. Lymphocyte transformation tests for specific fractions of HSP were positive. Treatment with 0.06 g diphenhydramine 30 min before sexual relations, a spermicidal cream, and a vaginal douche after coitus made her lesion-free.

(c) *Differential diagnosis*

Differential diagnosis from the medicament allergens transferred by semen is also important. It is known that penicillin (14), vinblastine (15), and thioridazine (16) can be transferred via HSP and cause generalized reactions in allergic persons.

In addition, a post-coital allergic reactions has been described in a woman who was allergic to walnuts and whose husband had been eating them. Walnut fractions were found in the HSP (17).

Pathogenesis

Specken (5) and Halpern et al. (6) have both suggested a circulating reagin as the cause of HSP intolerance. The latter have demonstrated that the sensitizing allergens from HSP is associated with a glycoprotein that is strongly PAS-positive and contains a great deal of sialic acid. The Prausnitz and Kustner reaction was also positive.

Most patients with HSP hypersensitivity have circulating IgE antibodies to HSP (7, 11, 18, 19).

Levine et al. (20) demonstrated in 1973 that HSP hypersensitivity was Type I mediated and isolated from HSP a protein fraction of 20,000–30,000 daltons that was presumed to be responsible for the allergic reaction.

Schulz et al. (21) reported that the causative proteins have a molecular weight of 14,000–18,000 Daltons, presumed to be from the prostate gland; Ohman et al. (22), however, found a protein with a molecular weight of 12,000 to 75,000 Daltons.

Blair & Parish (11) described a patient with a Type I reaction combined with delayed hypersensitivity to HSP. The allergen fraction for seminal plasma had about 5 components in the range of 20,000 to 40,000 Daltons molecular weight.

Some patients, however, manifest no circulating specific IgE (6), although they are not always thus tested (3, 10), and/or have negative prick tests to HSP. Generally, their reactions after contact with HSP are less serious and largely local (7). Other reaction types have also been described: Mike et al. (9) described a patient with a Type III reaction, while immunoglobulin levels, including IgE, were within the normal range; Best et al. (10) reported a patient who developed a bullous fixed drug eruption; and, finally, Schimkat et al. (3) reported a contact dermatitis from HSP in which patch tests and RAST were negative, but local provocation was positive, and, moreover, lymphocyte transformation tests were positive for specific HSP fractions.

A number of theories have been proposed to explain the allergic phenomenon.

(i) Sensitization to an unknown substance that cross-reacts with an HSP protein. Some cases, indeed, manifest a generalized reaction from the very first coitus onwards, so that cross-sensitization must be presumed (6, 7, 23).

(ii) The presence of immunosuppressive factors in HSP has been demonstrated by different authors (24, 25). In men, they are necessary to protect the spermatozoa from immunological damage, and, in women, to prevent sensitization to antigens of the HSP. Vasectomy, chronic illness, and infections could suppress the immunosuppressive characteristics of HSP and so give rise to hypersensitivity (7) or a change in the immunogenicity of the seminal plasma (12).

(iii) Disruption of normal immunomodulation in the female reproductive tract: pregnancy, infection, gynaecological surgery or the insertion of an intrauterine device (7, 12, 26).

(iv) A high degree of HLA sharing between affected partners as a causal factor has also been suggested (25).

Therapy

(i) *Barriers (condom).* Many people have objections to this form of therapy. Since most condoms

are made of latex, they can only be used by patients who are not latex-sensitive. We suggested that our patient use Lambskin® condoms (made from processed sheep's intestine) or Tactylon® synthetic condoms. The latter belong to the category of thermoplastic elastomers, which are also called block copolymers. The Tactylon® condom is made of polystyrene-poly(ethylene-butylene)-polystyrene (27), which is not a known allergen, though one study reported an allergic patch test reaction to it (28). Our patient was free of symptoms when her partner used Tactylon® condoms.

The use of condoms or local allergy treatment may be suspended from time to time, say every 6 months, in an attempt to capitalize on the unpredictable natural history of the disease. Sometimes a period of treatment may be followed by an extended or permanent remission of symptoms (12).

(ii) *Antihistamines.* Antihistamines alleviate the symptoms in most patients (12), particularly in mild cases. Our patient reported less local itching after taking diphenhydramine (50 mg 1 h before planned coitus and for the following 3 days), but the eczematous rash was not impeded by it.

(iii) *Immunotherapy.* Halpern et al. (6) first tried desensitization with whole HSP but was not successful. Mathias et al. (26) reduced the anaphylactic reactions of a female patient to mild urticaria by means of immunotherapy with whole HSP (11).

Bernstein et al. (18) treated 3 women with specific allergenic fractions of HSP, which were obtained by means of gel-exclusion chromatography. This therapy was successful in 2 women, and they propose it as a standard therapy. They used it because of the possible immunosuppressive effect of whole HSP and the assumed greater specificity of selective immunotherapy with only the allergenic fractions of HSP. Other successful desensitizations have also been reported (29).

Ohman et al. (22), by means of immunotherapy with a sephadex fraction of HSP, were able to reduce the IgE antibodies with respect to HSP and to raise the IgG antibodies, which was expressed clinically as better tolerance to HSP.

(iv) Other forms of therapy have also been described in isolated cases. To be noted are tranexamic acid (9), mephenamic acid (10), and benzalkonium chloride cream (spermicide) in association with diphenhydramine and vaginal douching (3). Some patients may benefit from the use of intravaginal 8% cromolyn cream (12, 14).

Conclusions

HSP hypersensitivity is a little-known immunologically-mediated disorder, which occurs mainly in younger atopic women. This allergic reaction elicits local (vulvovaginal) and systemic (anaphylactic) symptoms. The disease occurs more frequently than is generally supposed. It should always be considered in chronic non-specific vulvovaginitis, in some cases associated with systemic symptoms, that is being treated unsuccessfully for candidiasis or other gynecological diseases, particularly when the patient is atopic. The diagnosis is established by scratch tests with whole sperm or HSP and is confirmed with a RAST. The case of this 32-year-old woman with combined Type I and apparently also Type IV allergy to HSP (presenting clinically as an urticarial reaction followed by the development of eczema) as well as contact urticaria to latex is, as far as we know, unique in the literature.

References

1. Hjorth N H, Roed-Petersen J. Occupational protein contact dermatitis in food handlers. *Contact Dermatitis* 1976: *2:* 28–42.
2. Dooms-Goossens A, Morren M. Results of routine patch testing with a corticosteroid series in 2073 patients. *Contact Dermatitis* 1992: *26:* 182–191.
3. Schimkat H G, Andary M, Clot J, Humeau C, Descomps B, Dieng A, Previero B, Sultan C, Robinet-Levy M, Barneon G, Meynadier J M, Meynadier J. Contact urticaria and allergic contact dermatitis to constituents of human seminal fluid. In: Frosch P, Dooms-Goossens A, Lachapelle J-M, Rycroft R J G, Scheper R J (eds). *Current topics in contact dermatitis.* Berlin-Heidelberg, Springer Verlag 1989.
4. Shah A, Agasnol M K. Human seminal plasma allergy as a cause of postcoital asthma. *Eur Respir J* 1988: *1:* 972.
5. Specken J L H. Een merkwaardig geval van allergie in de gynecologie. *Nederlands Tijdschrift voor Verloskunde* 1958: *38:* 314–319.
6. Halpern B N, Ky T, Robert B. Clinical and immunological study of an exceptional case of reaginic type sensitization to human seminal fluid. *Immunology* 1967: *12:* 247–258.
7. Presti M E, Druce H M. Hypersensitivity reactions to human seminal plasma. *Annals of Allergy* 1989: *63:* 477–482.
8. Freeman S. Woman allergic to husband's sweat and semen. *Contact Dermatitis* 1986: *14:* 110–112.
9. Mike N, Bird G, Asquith P. A new manifestation of seminal fluid hypersensitivity. *Quarterly Journal of Medicine* (New Series) 1990: *75,* no. 276: 371–376.
10. Best C L, Walters C, Adelman D C. Fixed cutaneous eruptions to seminal plasma challenge: a case report. *Fertil Steril* 1988: *50:* 532–534.
11. Blair H, Parish W E. Asthma and urticaria induced by seminal plasma in a woman with IgE antibody and T lymphocyte responsiveness to a seminal plasma antigen. *Clin Allergy* 1985: *15:* 117–130.
12. Jones W R. Allergy to coitus. *Aust NZ J Obstet Gynaecol* 1991: *31:* 137–141.
13. Chang Te Wen. Familial allergic seminal vulvovaginitis. *Am J Obstet Gynecol* 1976: *126:* 442–444.
14. Green R L, Green M A. Postcoital urticaria in a penicillin-sensitive patient: Possible seminal transfer of penicillin. *J Am Med Assoc* 1985: *254:* 531.
15. Paladine W J, Cunningham T J, Donovan M A. Possible sensitivity to vinblastine in prostatic or seminal fluid. *N Engl J Med* 1975: *29:* 52.
16. Sell M B. Sensitization to thioridazine through sexual intercourse. *Am J Psychiat* 1985: *142:* 271–272.

17. Hadded Z H. Clearer picture of food allergies is still needed. *Perspect Allergy* 1978: *1:* 2–3.
18. Bernstein I L, Gallagher J S, Friedman S A, Marcus Z H. Standardized immunotherapy protocol for IgG mediated anaphylaxis to human seminal plasma. *Contr Gynec Obstet* 1985: *14:* 151–159.
19. Moulik S, Ranga G, Mehersi P K, Shahani S K. Detection of immunosuppressive activity in human seminal plasma by an immunobioassay. *Int J of Andrology* 1989: *12:* 131–138.
20. Levine B B, Siraganion R P, Schenkein I. Allergy to human seminal plasma. *N Engl J Med* 1973: *288:* 894–896.
21. Schulz K H, Schirren C, Kueppers F. Allergy to seminal fluid. *N Engl J Med* 1974: *290:* 916.
22. Ohman J L Jr, Malkiel S, Lewis S, Lorusso J R. Allergy to human seminal fluid. Characterization of the allergen and experience with immunotherapy. *J Allergy Clin Immunol* 1990: *85:* 103–107.
23. Boppana S B, German D F, Frick O L. Chronic vulvovaginitis in a 30-year-old woman. *Annals of Allergy* 1991: *66:* 381–384.
24. Hern Ku Lee, Tai You Ha. Human seminal plasma suppresses delayed type hypersensitivity response to intravaginally deposited sheep red blood cells and sperm: separation of immunosuppressive factors. *Int Arch Allergy Appl Immunol* 1989: *88:* 412–419.
25. Bernstein I L, Englander B F, Gallagher J S, Nat Jan P, Marcus H. Localized and systemic hypersensitivity reactions to human seminal fluid. *Ann Internal Medicine* 1981: *94* (Part 1): 459–465.
26. Mathias C G T, Frick O L, Coldwell T M, Yunginger J W, Maibach H I. Immediate hypersensitivity to seminal fluid and atopic dermatitis. *Arch Dermatol* 1980: *116:* 209–212.
27. Lahti A, Turjanmaa K. Prick and use tests with 6 glove brands in patients with immediate allergy to rubber proteins. *Contact Dermatitis* 1992: *26:* 259–262.
28. Lahti A, Camarasa J G, Ducombs G, Lachapelle J M, Maibach H I, Menné T, Niinimäki A, Wahlberg J E, Wilkinson J D, Wrangsjö K. Patch tests with Tactylon™ in patients wit contact allergy to rubber. *Contact Dermatitis* 1992: *27:* 188.
29. Mittman R J, Bernstein D I, Adler T R, Korbee L, Nath V, Gallagher J S, Bernstein I L. Selective desensitization to seminal plasma protein fractions after immunotherapy for postcoital anaphylaxis. *J Allergy Clin Immunol* 1990: *86:* 954–960.

Address:

An Dooms-Goossens
Department of Medical Research (Dermatology)
University Hospital
Katholieke Universiteit Leuven
Belgium