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Allergy and Sexual Behaviours: an Update

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Abstract The exact prevalence of hypersensitivity reactions related to sexual behaviours is not known; however, they heavily impact on the quality of life and of sex life of affected patients. In fact, not only common respiratory and skin allergies, such as asthma, rhinitis, urticaria and atopic dermatitis, but also food and drug allergy have been found to negatively affect the quality of sex life. Allergic diseases impact on the sexual function in both physical and psychological ways, representing one of the main complaints of a considerable proportion of patients. Sexual behaviours may act as the triggers of allergic reactions or as the carriers of allergens. Food and drug allergens can be carried through human organic fluids, like saliva and semen. Latex in condoms and numerous substances in lubricants, spermicides, topical medications and cosmetics can cause allergic reactions or contact dermatitis. Sexual activity itself is also a potential trigger of symptoms in patients affected by respiratory allergies, like honeymoon asthma and rhinitis. In seminal plasma hypersensitivity, seminal fluid proteins are the culprit allergens. The present review aims at summarizing the state of the art about allergy and sexual behaviours. In clinical practice, the influence of common allergic diseases on the sexual quality of life should be taken carefully into account. Sexual behaviours need to be accounted in the differential diagnosis of hypersensitivity reactions, and awareness on those exposure routes should be raised between different specialists and general practitioners.

Keywords Sex and allergy · Kiss-induced allergy · Seminal plasma hypersensitivity · Quality of life · Respiratory sex allergies · Genital contact dermatitis

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Introduction

Allergy is a typical systemic disease, although clinical manifestations usually regard a single target organ, such as nose, bronchi or skin. However, the reaction can potentially involve more than one organ at the same time, that is the case of the anaphylactic reaction [1]. Allergy onset may occur at any time in life and has a potential impact on different aspects of daily life, such as sleep, study or work, as well as on intimate behaviours [2]. In fact, very frequently allergic diseases such as rhinitis and asthma have been described as conditions that could affect the quality of sexual life of affected patients [3, 4]. Few data are available on this topic, but both patients and doctors should be aware of such implication, which also represents an additional motivation for a proper treatment and management of those diseases [5].

On the other side, hypersensitivity reactions can be strictly linked to sexual behaviours, and albeit being rare, they deserve to be included in the clinical and diagnostic evaluation. In fact, they may represent an atypical presentation of a more frequent allergic disease, due to an unusual way of exposure to the culprit allergen through human organic fluids. Sexual behaviours can also cause allergic reactions due to allergens and routes of exposure typical of that situation [5]. Anyway, sex-related allergies have a definitely negative impact on patients' quality of life (QoL) and especially on sexual life [3, 4, 6, 7]. Symptoms could be poorly specific and not immediately related to a hypersensitivity mechanism, so that different specialists, especially in the field of sexual medicine, as well as general practitioners, could be involved in the recognition and management of such diseases.

The present review aims at summarizing the current knowledge about allergy and sexual behaviours through a very practical approach, in order to spread the awareness and the basic know-how in the field of sexual-related allergies.

Search Strategy

For this systematic review, a selective search on PubMed and Medline (keywords: allergy and sexual intercourse, consort contact dermatitis, genital contact allergy, honeymoon asthma, honeymoon rhinitis, kiss-induced allergy, latex allergy, post-coital asthma, post-coital rhinitis, semen allergy, seminal plasma hypersensitivity, sexual dysfunction and allergy, sexual dysfunction and asthma, sexual dysfunction atopic dermatitis, sexual dysfunction and rhinitis, sexual dysfunction and urticarial, sperm allergy) was carried out, including papers published up to July 2016. Any type of article relevant to the topic and published up to July 2016 was considered for the review.

Allergic Diseases and Quality of Sex Life

The quality of sex life of patients affected by allergic diseases has been a scarcely studied topic by the medical community until recent years. Although the presence of sexual dysfunctions in asthmatic patients had already been speculated in an article published in 1992 [8], the first epidemiological data can be found 1 year later in a survey conducted among the members of the United Kingdom's National Eczema Society [9], in which 19% of patients reported that their sex lives had been affected by eczema. This data, however, passed neglected for nearly 10 years, when in 2002, an American study revealed the impact of asthma on patients' sexual functioning [10]. Since then, the sexual life of allergic patients has been the primary or co-primary object of few studies that demonstrated that allergic diseases do impact on the sexual functioning of a considerable proportion of patients and that both physical and psychological facets of sex life are involved.

Asthma and Rhinitis

The first study assessing sexual functioning limitations in patients affected by asthma is the above-mentioned US study [10]. In a cohort of 365 patients (228 women and 137 men) referring to an emergency department, 58% of them reported limitations in sexual functioning caused by asthma. This study also identified risk factors for sexual dysfunctions, such as moderate or severe asthma (OR 2.5; 95% confidence interval (CI) = 1.5, 4.2), female gender (OR 1.6; 95% CI = 1.0, 2.7), age above 40 years old (OR 2.7; 95% CI = 1.6, 4.3), lower income (OR 2.0; 95% CI = 1.1, 3.6) and indoor exposure to mould (OR 3.6; 95% CI = 1.7, 7.5; OR = 1.8) and mice (OR 1.895% CI = 1.1, 3.0). Interestingly, when the patients were asked to identify their five most important limiting activities, sexual limitation was the third most prevalent complaint after climbing stairs and doing housework. Another study conducted in the Netherlands in 2008 [4] compared sexual evaluation scores of 30 patients affected by asthma and 25 patients affected by COPD with the healthy population, by means of the Intimate Physical Contact Scales and the Respiratory Experiences with Sexuality Profile. It was shown that sexual quality of life scores in asthmatic patients were better than in COPD patients, but worse than the healthy control group. The disease affected sexual desire in both sexes and satisfaction from orgasm and self esteem in the female population but not in males.

Two studies addressed the problem focusing exclusively on the female asthmatic population. An American study conducted in 2007 [11] on 808 female asthmatic patients reported that 15.1% of patients in the control group and 22.9% in the intervention group reported to be bothered by asthma during sexual activities. The complaint was more prevalent in women with persistent asthma than in women with intermittent symptoms and improved after a year of self-regulation intervention. Another study conducted in Poland in the same year [12] on 31 asthmatic females evaluated the sexual function by means of the Female Sexual Function Index and reported a prevalence of sexual dysfunctions of 25.8% in asthmatic women compared to 17.1% of controls, with a statistically significant worse sexual functioning that correlated with the duration of bronchial asthma. Differently from the study conducted in the Netherlands, sexual drive of women was not reduced, but a decrease in sexual arousal, lubrication, orgasm, sexual satisfaction and pain domain was reported.

As far as allergic rhino-conjunctivitis (ARC) is concerned, a Turkish study conducted in 2005 [13] on 43 patients reported a significantly lower Female Sexual Function Index and International Index of Erectile Function in symptomatic ARC than in treated ARC and controls. The improvement in

conjunctival and nasal symptoms after therapy led to a rise in all sexual function indexes in males; in females, it led to an increase in sexual desire, arousal and orgasmic function but not in lubrication, intercourse satisfaction and pain relief. A subsequent American study conducted in 2009 on 320 patients affected by ARC [3] confirmed the interference of ARC on patients' sexual life using a RSDI score including one question about sexuality, showing that 55.9% of patients reported that at least sometimes their illness influenced their sexual life. This percentage was higher in ARC patients than in patients affected by non-allergic rhinitis and controls.

Atopic Dermatitis and Chronic Idiopathic Urticaria

As previously mentioned, the first data on eczema are dated 1993 [9]. Among a population of 1972 adults, 19% of patients reported an impaction of eczema on their sexual lives. A subsequent study conducted in France on 266 patients [14] reported a referred decrease in sexual desire due to the disease in 57.5% of patients. Among them, 55.4% of patients reported effects on their sex life due to the appearance of atopic dermatitis (AD) and 46.8% due to the treatment of the disease. Moreover, this study revealed an impact on the partner's sexual desire due to the appearance of AD in 32% of couples, with 15.3% of partners expressing the fear that the illness might be contagious. Finally, a population-based study in Taiwan [6] on 3997 patients with ED found a 1.6-fold higher risk in patients affected by erectile dysfunction of having been previously diagnosed with atopic dermatitis in comparison with controls.

The sexual function of patients affected by chronic urticaria has been evaluated by a single study conducted in Turkey in 2007 [7]. It compared ASEX scores of 50 patients affected by chronic urticaria with patients affected by vitiligo and controls, showing more difficulties in sexual drive and arousal, lubrication, reaching orgasm and satisfaction from orgasm in affected women than in controls. A less satisfaction from orgasm in the male patients group was also described, resulting in an overall prevalence of 58% of sexual dysfunction in the chronic urticaria group; it regarded 70.5% of women and 31.2% of male patients, being significantly higher than both the vitiligo patients group and the controls.

Sexual Behaviours as a Carrier of Allergy

Organic fluids, particularly saliva and semen, can act as carrier of allergenic proteins. They represent an unusual way of exposure to the culprit allergen, but able as well to cause a hypersensitivity reaction in the context of an intimate situation. The frequency of this phenomenon is difficult to establish, since it is probably underestimated by physicians and under-reported by patients.

Kissing and Saliva as a Carrier of Food Allergy

Patients with food or drug allergy may have an allergic reaction after kissing someone who has taken the culprit food or drug. Allergic reactions have been described after passionate or platonic kisses and are generally mild or moderate, with local angioedema and/or hives being the most frequent symptoms [15]. Such particular allergic manifestation has been described in the last 20 years; in fact, the first case report has been published in 1997 [16].

As regard to food allergens transfer through saliva, only two studies assessed its frequency among patients with a suspect of food allergy. Hallet et al. [15] reported a prevalence of 5.3% among 379 patients with a history compatible with an immediate hypersensitivity reaction to nuts or seeds. However, the prevalence has been probably underestimated in this case; in fact, it was based on spontaneous declarations (information regarding allergic reactions after a kiss was not specifically requested in the administered questionnaire). The time interval between the intake of food and the kiss varied from less than 1 min to 6 h.

The second study was conducted by Eriksson et al. [17]. A questionnaire to assess the possible social inconveniences of food allergy (e.g. allergic reactions after kissing) was administered to 1139 patients, with a self-reported diagnosis of food allergy. Twelve percent of them reported symptoms compatible with an IgE-mediated reaction after kissing someone who had eaten a food, related to a previous hypersensitivity reaction.

Some case reports described allergic reactions to food after a passionate kiss. In patients with pollen-fruit allergy syndrome, symptoms are mild [15, 18], while patients with severe food allergy can manifest mild to moderate reactions requiring only oral anti-histamines [19, 20] or potentially life-threatening reactions [21]. Patients with a history of severe food allergy who describe symptoms also if exposed to vapours or very low amount of allergen are supposed to have a greater risk to react after kissing a person who has eaten the culprit food. Only one potentially fatal kiss has been reported in literature: a young girl allergic to shellfish developed an anaphylactic reaction after kissing her boyfriend who had eaten some shrimps less than 1 h before. This girl worked as a waitress in a seafood restaurant and reported urticaria on her arms during her work shifts [21].

Allergic reactions after platonic kisses are generally mild, characterized by local wheals or angioedema [15, 19], even if severe reactions are reported in children [15].

Diagnosis

The diagnosis of kiss-induced allergic reactions is mainly a clinical diagnosis and a pivotal role is played by clinical history. This unusual way of allergen exposure should be always

taken into consideration, especially as an explanation of apparently "idiopathic" reactions (Fig. 1).

In vivo testing with the partner's saliva has been also described in literature [18]. A young girl with a kiss-induced oral allergy syndrome to kiwi underwent skin prick tests with the partner's saliva, before and after he had eaten a kiwi. The tests were positive up to 5 min after fruit ingestion.

Treatment

The gold standard for treatment is prevention. In other words, partners of allergic subjects should avoid eating the culprit food before intimate situations. Even if all kinds of food can be involved, the persistence of allergens in saliva has been demonstrated for peanuts in particular, probably because of their frequent involvement in allergic reactions, especially in the USA. A group of American researchers calculated that salivary Ara h1 concentration reaches its peak 5 min after the ingestion of a peanut butter meal and slowly decreases reaching undetectable levels after an hour, even if in some individuals, Ara h1 is still detectable after some hours [22]. A huge variability is also observed in Ara h1 salivary concentration among individuals (from undetectable levels to 1.110.000 ng/ml). No immediate intervention is effective in reducing Ara h1 to undetectable levels (<20 ng/ml) in saliva. This result can be reached in 90% of people only by waiting several hours after consumption. Thus, the gold standard remains avoiding the food if the partner has a severe allergy [22].

Kissing and Saliva as a Carrier of Drug Allergy

As regard to kiss-induced allergic reactions to drugs, the prevalence is unknown and only a few case reports pertaining to penicillin-derived antibiotics are available. Some of them reported mild allergic reactions in women: urticaria and oropharyngeal angioedema occurred some minutes after kissing the boyfriend, who had taken amoxicillin a few minutes before [23]; angioedema and mild labial itching occurred after kissing the husband who had taken bacampicillin 2 h before [24] and itching and edema of the lips and some wheals occurred on the face and neck, followed by an eczematous perioral dermatitis, after kissing on the lips the son who had taken amoxicillin some minutes before [25]. Grims et al. [26], instead, described a systemic reaction in a woman after kissing her husband, who had taken a penicillin tablet 30 min before.

Diagnosis

Similarly to kiss-induced food allergic reactions, the diagnosis of kiss-induced allergic reactions to drugs primarily relies on clinical history. However, it has to be supported by specific diagnostic tests to confirm the culprit drug when possible (Fig. 1). Liccardi et al. [24] performed a "placebo-controlled kiss drug challenge": the couple involved in the allergic reaction was convened and the husband had to take placebo or 120, 360 and 520 mg of bacampicillin on different days. His wife had to kiss him 2 h after he had taken the drug. The woman reacted after her husband had taken the 360 mg dose,

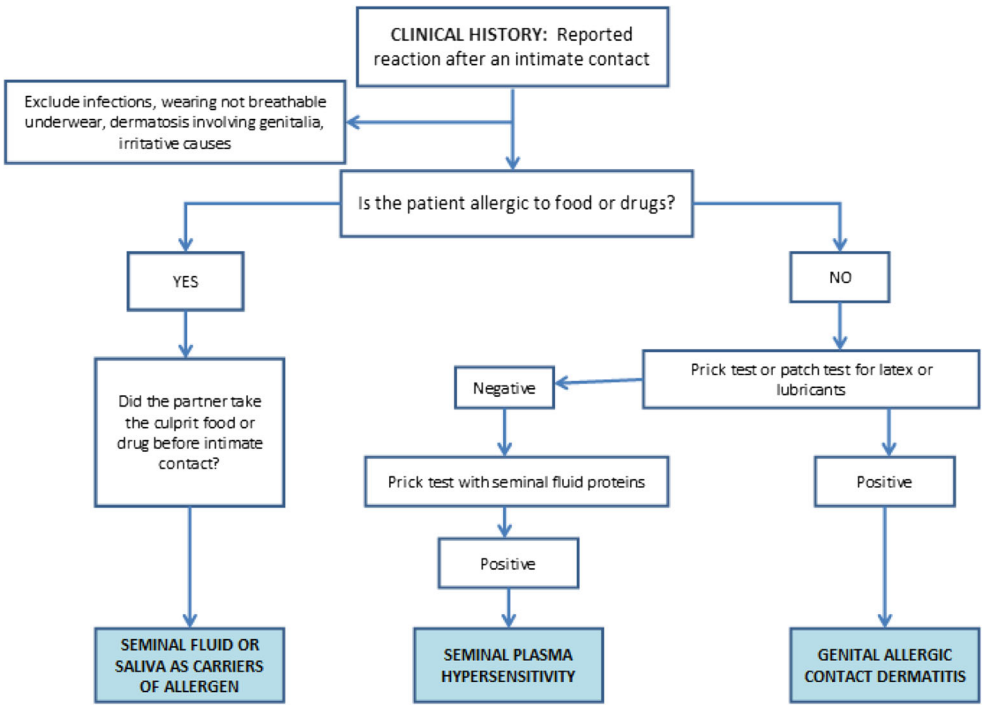

Fig. 1 Pragmatic diagnostic approach to suspected sexual behaviour-related hypersensitivity reactions

manifesting mild oral itching and urticaria on the face and arms and therefore reproducing the allergic reaction occurred at home.

Semen as a Carrier of Food and Drug Allergy

Semen is another possible vehicle of transmission of food and drug allergens. Only a few case reports are available on this topic. As regard to food allergy, Basal et al. [27] described an unusual allergic reaction to Brazil nuts: a woman manifested itching and swelling of the vulva and vagina after a sexual intercourse. Her boyfriend had eaten 4–5 Brazil nuts about 2–3 h before and had brushed his teeth and washed his hands, as he knew that the girl was allergic to this kind of food. Condom had not been used and transmission of nut proteins through saliva was ruled out because no local symptoms (e.g. labial itching and/or swelling) appeared. Semen allergy was also ruled out, as the girl subsequently had other sexual intercourses without any problems. Secretion of allergens in seminal fluid was demonstrated by skin prick tests performed utilizing the boyfriend's semen, collected before eating 4 brazil nuts and 2 h and a half afterwards. The first skin prick test was negative, while the second was positive (7 mm).

In 1978, Haddad [28] described a case of a severe allergic reaction in a woman after sexual intercourse with her husband, who had eaten walnuts before. The woman was allergic to walnuts and walnut proteins were subsequently detected in her husband's seminal fluid.

Other case reports described allergic reactions to drugs, as penicillin [29], vinblastine [30], thioridazine [31] and azathioprine [32].

Diagnostic work-up and treatment/prevention indications are shared with kiss-induced allergic reactions to food and drugs (see above).

Sexual Behaviours as a Cause of Allergy

Respiratory Sex Allergies

Sexual activity itself has been known to be a potential trigger of symptoms in patients affected by respiratory allergies. In 1976, Symington and Kerr [33] coined the term "sexercise-induced asthma" to describe dyspnoea and wheezing provoked by sexual activity in patients with exercise-induced asthma. In more recent years, the hypothesis that post-coital asthma and rhinitis (also called honeymoon asthma and honeymoon rhinitis) may have a mechanism different from exercise-induced asthma [34] was formulated. In fact, post-coital bronchial or nasal symptom [35] exacerbation was described in patients asymptomatic after walking up two flights of stairs (the exertional equivalent of sexual intercourse) [34] or even in patients without history of asthma or rhinitis [36]. Autonomic imbalance and high levels of cholinergic activity, possibly linked to physiological and/or emotional sequelae of sexual activity, might account for that specific phenotype of respiratory allergy. Timing of symptom onset is very variable, ranging from pre-coital stimulation to up to 6 h after coitus, and symptoms severity can range from self-limiting episodes to extremely severe exacerbations requiring mechanical ventilation. Prophylactic use of inhaled beta-2 agonists, eventually coupled with inhaled corticosteroids or nasal cromolyn, has shown to be effective in the prevention of symptoms.

Seminal Plasma Hypersensitivity

Allergy to seminal fluids, generally known as seminal plasma hypersensitivity (SPH), is a well-described allergic phenomenon, first reported by J. L. H. Specken in 1958 [37]. Its prevalence is unknown, as this condition is probably under-recognized and under-reported. Data extrapolated by questionnaires in which women self-reported that they thought they were affected by SPH indicated that it might be not so rare as previously estimated [38].

SPH is characterized by immediate local or systemic post-coital symptoms following mucosal exposure to seminal fluid. Systemic SPH (SSPH) is a classical type I, immediate, IgE-mediated hypersensitivity reaction. Pruritus, acute urticaria, angioedema, chest tightness, wheezing and dizziness are part of its typical clinical presentation, in some cases, leading up to hypotension and overt anaphylactic shock.

Localized SPH (LSPH) can cause vaginal pain, local burning, swelling and/or pruritus. In this case, the immunologic mechanisms are not so clear. Both IgE-mediated and type IV hypersensitivity mechanisms have been suggested, but also direct inflammation, seminal fluid prostaglandins and epithelial barrier disruption by proteases in the seminal fluid may explain the reaction [39, 40]. Localized SPH has been also described as a mucosal form of contact dermatitis, which is caused by the contact with high-molecular weight proteins from foods or animal fluids [41]. A different pathological mechanism of SSPH and LSHP may account for the different timing in symptoms onset. In fact, they generally occur in few minutes in SSPH, while in LSPH, the manifestations might appear after a few hours. Symptom duration is variable upon type of presentation, generally limited to less than 24 h in systemic forms and up to several days in localized ones.

Around half of patients develop symptoms after their first unprotected intercourse. In this case, a role of naturally occurring anti-sperm antibodies, possibly produced by cross-reacting pathogens, has been described. It was also proposed that a prior sensitization to a cross-reactive allergen could be responsible for the reactions. The prostate-specific antigen (PSA), a 33–34-kD glycoprotein, better known for its use in monitoring prostate cancer in men, was in fact identified as a major allergen in human seminal fluids. It was found that PSA

carries high homology to the canine prostatic kallikrein, which was identified as Can f 5. The clinical relevance of this cross-reactivity was confirmed in a few cases, and investigators have hypothesized that patients who experienced SPH after their first unprotected intercourse could have been sensitized by previous exposure to dogs [42, 43].

In some cases, SPH occurred after resuming intercourse after a gap of time, or in coincidence of events concerning the reproductive life of the patient, like pregnancies, menopause, insertion of intrauterine devices or hysterectomy [44]. Occurrence of SPH is usually persistent after every intercourse; it was described to occur sometimes with multiple partners as well as to be partner specific [44].

The only consistent association with SPH is an atopic background, which was reported in around 84% of the patients. Family or personal history of asthma, allergic rhino-conjunctivitis, atopic dermatitis, eczema, urticarial and food and/or drug reactions is very common [44].

It was frequently reported that infertility was an issue with those patients; however, there is no data confirming a cause-effect link, except from the obvious need to manage post-coital symptoms. In fact, a number of successful pregnancies, spontaneous, after therapy or with assisted reproduction techniques, have been reported. A failure to conceive after a successful management should prompt the research for other causes for infertility [45].

A rare form of seminal fluid hypersensitivity is the so-called post-orgasm illness syndrome (POIS), firstly reported and named by Waldinger and Schweitzer in 2002 [46]. It is characterised by the onset of a post-ejaculation complex of local and systemic symptoms, which occur within seconds to hours after ejaculation. Affected males may experience flu-like manifestations, myalgia, fatigue, burning eyes and nasal congestion, rarely associated with genital local reactions [47]. Little is known about its epidemiology and aetiology, although an auto-reactive immunogenic mechanism has been proposed [47]. According to this hypothesis, autologous seminal peptides or peptides released from the damaged urethral lining cells become exposed to the inner mucosal urethral epithelium. Semen antigens are then recognized and taken up by epithelial dendritic cells and sensitization occurs. However, the absence of specific serum IgE has been recently described in a Chinese man affected by POIS [48], suggesting that IgE-mediated hypersensitivity could not be the potential mechanism of POIS.

Diagnosis

Clinical history collection is the most relevant step. A high level of suspicion is needed to make a presumptive diagnosis of SPH (Fig. 1). The main clues are a post-coital presentation and the disappearance of the symptoms with the use of condoms throughout the intercourse.

Once the potential transfer of allergens, especially food and drugs, through the partner's organic fluids, is excluded, as described above, the diagnosis can be confirmed by in vivo and in vitro tests. Skin prick test should be performed with seminal fluid proteins. In order to obtain this "extract", a sample of fresh whole seminal fluid from the partner has to be stored at room temperature for half an hour. Once liquefied, 10-min centrifugation at 5000*g* allows separating the supernatant containing the seminal fluid proteins, so that it can be used for skin prick testing.

The use of anti-histamines drugs and a dilutional effect by non-allergenic proteins in whole seminal fluid may account for false negative results. The partner should be tested together with a negative control in order to exclude false positive results due to the presence of an irritant [49]. Subcutaneous testing is not recommended because of the high rate of false positive results, probably caused by the prostaglandins contained in seminal fluid. In fact, it was shown that healthy controls develop a wheal and flare reaction after subcutaneous injection of seminal fluid, and that this reaction is reduced by premedication with non-steroidal anti-inflammatory drugs [40]. Seminal plasma can be also separated by column fractionation, in order to isolate protein fractions that are less irritant, and can therefore be used for subcutaneous testing and immunotherapy [43]. Serum seminal fluid specific IgE (sIgE) can be evaluated through commercial assays or home-made tests; however, there are no clear negative or positive predictive values for those tests. Component-resolved diagnosis is strictly experimental at the moment, and the relevance of Can f 5 sIgE positivity is unknown.

In the case of suspected POIS, together with a careful clinical history, intradermal test has been proposed for the diagnosis [47]. The diagnostic extract is prepared with defrosted of frozen semen diluted with 0.9% NaCl to a concentration of 1:40,000. The response is evaluated 15 min after the injection of 0.05 ml of the diluted auto-semen. The test has not yet been validated.

Treatment

Although condom use completely prevents the symptoms, it might be an unacceptable treatment for some couples or for those willing to conceive. Premedication approaches, mainly based on local cromolyn gels and anti-histamines, have been tried with controversial results. In few cases of LSPH, anti-inflammatory non-steroidal drugs have been successfully used, hinting at the role of prostanoids in local reactions. However, in systemic, IgE related, SPH, the most effective approaches have been immunotherapy and desensitization protocols. Successful local desensitization protocols by intravaginal graded challenge (IVGC) have been described. Usually, whole seminal fluid serial dilutions starting at 1:10.000 or 1:100.000 are instilled in the vagina

with 20–60 min intervals. Whole seminal plasma subcutaneous desensitization has not been reported as effective. However, rapid immunotherapy protocols with specific seminal plasma proteins obtained by column fractioning following standard subcutaneous allergic immunotherapy protocols have been reported to be very effective. A total amount of 60–100 μl of protein is administered, throughout a series of injections. After this treatment, the patient is able to experience unprotected intercourses. After the procedures, regardless of the method used, regular unprotected intercourse is necessary in order to maintain the achieved tolerance, usually at a recommended rate of 2–3 times weekly [43]. Successful spontaneous pregnancies have been reported after IVGC, and due to its simple, cheap and not invasive nature, it is usually recommended as the first line approach, before the more risky subcutaneous immunotherapy [49].

A hypo-sensitization protocol has been proposed for POIS as well [50]. Multiple escalating doses of autologous semen are administered via subcutaneous injections every 2/52 weeks for the first year and then every 4/52 weeks in the second and third year. Progressive semen dilutions from 1:40,000 to 1:20 are used. So far, the protocol has been performed in very few patients. It was successful and well tolerated but further research is needed.

Differential Diagnosis of Sexual Behaviour-Related Allergic Reactions

A careful differential diagnosis algorithm should be designed in order to exclude common potential causes of localized or systemic symptoms, other than hypersensitivity reactions (Fig. 1).

Genitourinary infections should be ruled out, both viral and bacterial, including sexually transmitted diseases; also, chronic vaginal candidiasis could trigger a *Candida* hypersensitivity vulvo-vaginitis, mimicking a local allergic reaction [51].

Physical factors may also play a role in the onset of local reactions such as redness, swelling and pruritus; it is the case of small introituses or the use of sex tools triggering vibratory urticaria or exacerbating a pre-existing congenital or acquired angioedema [51].

As far as hypersensitivity reactions are concerned, latex allergy and genital allergic contact dermatitis should be taken into consideration firstly, as they are much more common than the above described reactions.

Latex Allergy

Latex allergy may be responsible for local or even systemic reactions after sexual intercourse, when condom is used.

Table 1 Possible causes of genital contact dermatitis

Items described in literature	Possible substances involved
Condoms	Accelerator chemicals, natural rubber latex, local anaesthetics…
Lubricants	Propylene glycol
Spermicides	Benzocaine, monophenoxypolyethoxy derivatives, hexylresorcinol, chloramine, quinine, fragrances, nonoxynol-9…
Topical medications	Steroids, imidazoles, acyclovir…
Bubble baths and scented soaps	Perfumes, e.g. balsam of Perù
Hygiene sprays	Perfumes, e.g. balsam of Perù
Cosmetics (nail polish)	Methacrilate
Newsprint	Paraphenylenediamine
Pleasure enhancers	Butyl nitrate
Sperm	?
Rosin for violin strings	Colophony

Exposure to latex can lead to an IgE-mediated allergic reaction (from contact urticaria to anaphylaxis) [52] and, more often, to a type IV allergic reaction (more frequently related to accelerator chemicals) [53]. Diagnosis is based on positivity of skin prick test and specific and recombinant IgE in the case of a clinical history suggestive for an immediate allergic reaction. In the case of a type IV reaction, positive patch tests to latex and/or accelerator chemicals support the diagnosis. Notably, people affected by type I allergy to latex can react when exposed to fruits like avocado, banana, kiwi, chestnut and other fruits [54].

Genital Allergic Contact Dermatitis

In the case of genital dermatitis, the most common causes (infections, wearing not breathable underwear, dermatosis involving genitalia, irritative causes, e.g. urine...) should be ruled out, without neglecting contact allergy. Genital allergic contact dermatitis can be related to the use of underwear (e.g. colourants) or sanitary or self-adhesive pads (containing fragrances and disinfecting agents like CuII-acetyl acetonate and acetyl acetonate). Contact hypersensitivity can also be triggered during the sexual intercourse by the use of condoms, lubricants, spermicides and cosmetic products [51]. Table 1 summarizes possible causes of contact allergic reactions after sexual intercourse.

Conclusions

The exact prevalence of hypersensitivity reactions related to intimate behaviours is not known. The intimate nature of those conditions and the scarce awareness of that kind of allergy

may account for it. For the same reasons, we can expect that the problem is underestimated and under-reported but, however, rare. Nevertheless, sexual behaviour-related allergic reactions deserve to be taken carefully into consideration in the clinical practice for two main reasons. (1) Both common respiratory and skin allergies, such as asthma, rhinitis and atopic dermatitis, but also food and drug allergy, may potentially affect the quality of sex life. As it is an extremely relevant component of the overall QoL, it should be carefully investigated in the assessment and management of allergic patients. (2) The link between sexual behaviours and allergy may account for unusual or unexplained hypersensitivity reactions. Human organic fluids may act as carrier of known or potential culprit food or drug allergens or may contain specific allergens responsible for the allergic reaction. All these aspects should be explored, besides the more common latex allergy and genital allergic contact dermatitis.

In terms of gender-related predisposing determinants, females affected by respiratory allergies (rhinitis and asthma) are more at risk of sexual QoL impairment due to their disease, although treated, in comparison with male [4, 10, 13]. A similar trend can be observed in the case of patients affected by urticaria [7]. In the context of sexual behaviours as carrier or cause of allergy, gender cannot be considered a real risk factor; published epidemiological data are surely not enough to support such hypothesis, as they mostly come from case reports or case series. Nevertheless, a slight prevalence of female gender can be observed among the published case reports. The overall trend of allergic diseases, affecting more female than male gender [55, 56], may account for it. Furthermore, for obvious reasons, semen, as carrier or cause itself of hypersensitivity reactions, represents a risk factor for female gender only, with the exception of POIS. No cases of vaginal fluids as cause or carriers of allergy have been described so far. Although no evidence is available in scientific literature, from a theoretical point of view, homosexual intercourses and intimate behaviours do not present any specific differences with heterosexual situations, and seminal fluid may trigger hypersensitivity reactions in the anal area as well.

Thus, female gender could be overall considered more at risk of sexual behaviour-related allergies.

As circumstances and symptoms may suggest different diseases, including infectious diseases, identifying a potential sexual behaviour-related allergic reaction, particularly a local one, on the basis of patient history and clinical examination may be tricky, for both physicians and patients. In fact, different specialists could be consulted by the affected patients, including ob-gyns, allergy specialists, dermatologists and specialists active in the field of sexual medicine, as well as general practitioners. Thus, a differential diagnosis algorithm including sexual behaviour-related allergic reactions should be shared as a common background for the proper management of diseases affecting intimate behaviours.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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