

# Bovine serum albumin contained in culture medium used in artificial insemination is an important anaphylaxis risk factor

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**Objective:** To analyze the cause of the anaphylactic reaction after a standard artificial insemination process in a patient diagnosed with asthma.

**Design:** Case report.

**Setting:** Residencia Sanitaria Virgen de la Arrixaca (Murcia, Spain) and University of the Basque Country (Vitoria, Spain).

**Patient(s):** A 30-year-old woman with a previous medical history compatible with respiratory allergy who suffered an anaphylactic reaction after an artificial insemination with spermatozooids in capable medium (Upgraded B2 INRA medium; Laboratories CCD, Paris, France).

**Intervention(s):** Cutaneous tests and specific IgE levels to inhalant allergens, grass and *Olea* pollens, and insemination medium were performed.

**Main Outcome Measure(s):** Specific IgE levels to mammal epithelia and bovine serum albumin (BSA).

**Result(s):** Skin prick tests were positive for inhalant allergens such as mites, cat, dog, horse, and rabbit epithelia, grasses and *Olea* pollens, and the insemination medium. The  $\beta$ -lactamic tests were negative. The determination of specific IgE demonstrated positive values to mammal epithelia and mammal serum albumins including BSA.

**Conclusion(s):** We report a case of an anaphylactic reaction to the BSA included in the insemination culture medium induced by a subclinical sensitivity to serum albumins of mammal epithelia. A previous testing with the medium is recommended and specific testing might be needed in women who have a history of animal epithelium allergies. (Fertil Steril® 2008; ■: ■–■. ©2008 by American Society for Reproductive Medicine.)

**Key Words:** Allergy, anaphylaxis, insemination, bovine serum albumin, epithelium

Some components included in the artificial insemination culture medium, such as penicillin, streptomycin, or bovine serum albumin (BSA), can cause severe allergic reactions (1–4).

Bovine serum albumin is a well-known 68-kDa protein implicated in some cases of food hypersensitivity reactions and it is considered responsible for the cross-reactivity between different types of mammal products such as milk, epithelia, and meat (4–9).

Here we report an anaphylactic reaction after a standard process of artificial insemination caused by the BSA contained in the insemination medium and induced by a subclinical sensitivity to serum albumins of mammal epithelia.

## CASE REPORT

A 30-year-old woman with a previous medical history compatible with respiratory allergy (asthma/rhinitis) to mites,

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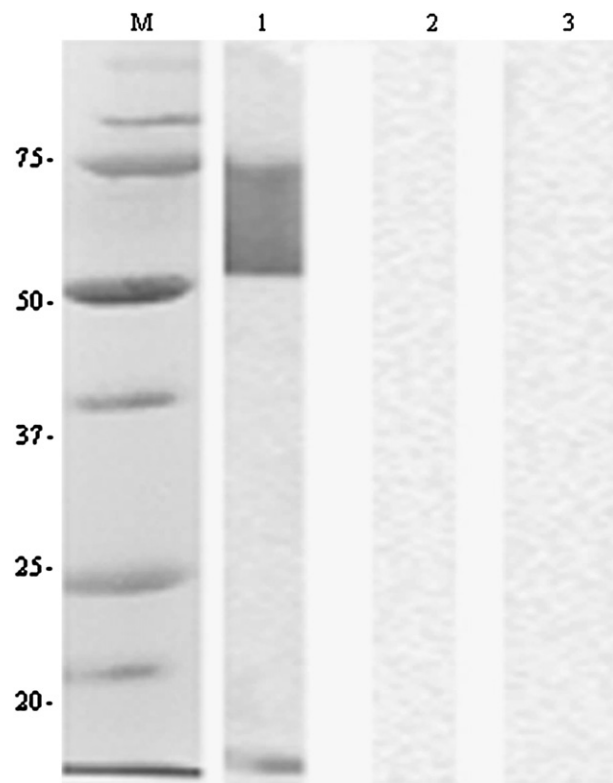
epithelia, and grass pollens was referred for artificial insemination in October 2006. She was inseminated with spermatozooids in capable medium (Upgraded B2 INRA medium; Laboratories CCD, Paris, France), which contains amino acids, lipids, vitamins, BSA (10g/L), penicillin, and streptomycin, in addition to inorganic salts. One hour after insemination she developed a severe anaphylactic reaction with generalized urticaria, angioedema, dyspnea, pharynx oppression, and dysphonia. She was admitted to hospital and treated with systemic steroids and antihistamines. She recovered the following day without further complications.

The study was performed in compliance with the Declaration of Helsinki (2001) (10) and the informed consent from the patient was obtained.

The cutaneous tests, performed 1 week after the anaphylactic reaction by the Allergy Service of the Hospital in accordance with the European Society of Allergy and Clinical Immunology procedures (11), showed positive results (>3 mm wheal diameter) to mites, grasses and *Olea* pollens, cat, dog, horse, and rabbit epithelia, and Upgraded B2 INRA medium. The specific IgE (ImmunoCAP; Phadia, Uppsala, Sweden) measurements showed positive levels (>0.35 kU/L) for cat, dog, and rabbit epithelium (41.4, 26, and 1.1 kU/L, respectively); cat, dog, pig, and bovine serum albumins

**FIGURE 1**

Immunoblotting and immunoblotting-inhibition using bovine serum albumin (BSA) in the solid phase. *Lane M*, molecular weight marker (kDa); *lane 1*, patient's serum; *lane 2*, control serum (pool from nonatopic subjects' serum); *lane 3*, immunoblotting-inhibition with BSA.



Pagán. Anaphylaxis during artificial insemination. *Fertil Steril* 2008.

(25.1, 15.2, 1.2, and 0.7 kU/L, respectively); horse serum proteins (10.5 kU/L), and Fel d 1 (12.1 kU/L). The  $\beta$ -lactamic tests (12) were negative.

The sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) immunoblotting (13, 14) carried out using BSA (Sigma-Aldrich Inc., St. Louis, MO) in the solid phase, revealed an IgE-binding component ranging from 60–68 kDa (Fig. 1). The SDS-PAGE IgE immunoblotting inhibition (15) demonstrated that the IgE antibodies were specific for BSA (Fig. 1). Inhibition assays (16) were carried out using four different BSA concentrations (100, 10, 1, and 0.1 mg/mL) and cat, dog, and rabbit epithelia proteins in the solid phase. Results showed a 90% inhibition when rabbit epithelium was used in the solid phase, and 56% and 50% inhibition when cat and dog epithelium were used in the solid phase.

## DISCUSSION

Although BSA has been described as a cause of anaphylactic reactions after standard insemination processes (2, 3) only

one other case has been reported, demonstrating the relationship between sensitization to mammal epithelia and the anaphylactic reaction to BSA (4). The BSA is a well-known 68-kDa protein implicated in some cases of food hypersensitivity reactions and it is considered responsible for the cross-reactivity between different types of mammal products such as milk, epithelia, and meat (5–9).

In the present case, the skin prick test revealed immediate positive reactions to insemination medium and mammal epithelium proteins, suggesting the presence of a specific IgE to the BSA present in the medium and a possible relationship with albumins contained in mammal epithelia.

Cutaneous tests and IgE results by means of specific IgE ImmunoCAP and SDS-PAGE IgE immunoblotting strongly support the implication of BSA in the allergic reaction after artificial insemination. Inhibition studies demonstrate the close relationship between serum albumins contained in mammal epithelia extracts and the BSA contained in the insemination medium. The reported data strongly suggest that the patient was subclinically sensitized to mammal epithelium and that the cross-reactivity with BSA in the medium could be the origin of the anaphylaxis reaction. These results are very similar to those reported by Orta et al. (4), where they also described the same sensitization profile. These investigators also suggest that the cat albumin could be the most likely sensitizing agent. The previous sensitization to serum albumin of mammal epithelia may be an important risk factor to be taken into account during artificial insemination using culture medium containing BSA. A preoperative testing with the medium is definitively recommended and specific testing might be needed in women who have a history of allergy to animal epithelia.

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