

Pork-cat syndrome revealed after surgery: Anaphylaxis to bovine serum albumin tissue adhesive



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Clinical Implications

- Sensitization to cat serum albumin (SA) cross-reacted to other mammalian SAs and led to anaphylaxis to bovine serum albumin (BSA) tissue adhesive use. In cat-allergic patients, preoperative measurement of the cat SA IgE level could be useful to potentially avoid BSA tissue adhesive if positive.

TO THE EDITOR:

Pork-cat syndrome is a food allergy characterized by mammalian serum albumin (SA) cross-reactivity.¹ We report a singular case of bovine SA (BSA) anaphylaxis after BSA tissue

adhesive use. Primary sensitization was due to cat SA leading to unsuspected pork-cat syndrome.

A 53-year-old man was scheduled for celiac aneurysm surgical repair. Anesthetics and antimicrobial prophylaxis were uneventfully administered. After aneurysm resection and prosthetic grafting, a BSA-glutaraldehyde tissue adhesive (BioGlue; Cryolife, Kennesaw, Ga) was applied to seal the suture line of the anastomosis on the supraceliac aorta and achieve hemostasis. Shortly after aortic unclamping, a life-threatening hypotension and severe bronchospasm occurred. Colloid, epinephrine, and several attempted supraceliac unclamping/clamping partially corrected the cardiovascular disturbances while ventilation became easier. Epinephrine infusion was initiated because of a persistent vasoplegic state. As hemodynamics were restored, a thoracic erythema appeared. The patient was admitted to the intensive care unit where supportive epinephrine was weaned. Further outcome was uneventful. Plasma histamine and tryptase concentrations were measured and skin testing was performed subsequently (Table I). IgE-mediated BSA allergy was proven on the timing between tissue adhesive application and the onset of symptoms, the clinical presentation, tryptase levels, and results of skin tests.²

On further clinical review, the patient did report experiencing rhinoconjunctivitis associated with cat exposure (he kept a cat at

TABLE I. Biological, skin testing, and ImmunoCAP inhibition results

Plasma histamine and tryptase			
	T0 + 1 h	T0 + 3 h	T0 + 24 h
Histamine (normal < 10 nmol/L)	>100	61	ND
Tryptase (normal < 11.4 μg/L)	32	60	3.1
Skin prick tests*		Specific serum IgE	
Controls/cutoff	Positive (histamine 10 mg/mL): 4/8 mm Negative (saline): 0/0 mm	ImmunoCAP Phadia (normal < 0.1 kU/L)	
BSA-glutaraldehyde tissue adhesive	BSA (neat): 10/14 mm Glutaraldehyde (neat): neg	Glutaraldehyde: NA	
Cat	Dander: 8/12 mm	Dander: 11 Uteroglobulin (rFel d 1): 2.29 Serum albumin (nFel d 2): 22.8 Lipocalin (rFel d 4) < 0.1	
Pork	Raw meat: 3/7 mm Cooked meat: neg	Serum albumin (nSus s PSAS): 0.52 Meat (<i>Sus spp</i>): 0.42	
Beef	Raw meat: 3/5 mm Cooked meat: neg	Serum albumin (nBos d 6) < 0.1 Meat (<i>Bos spp.</i>) < 0.1	
Lamb	Raw and cooked meats: neg	Meat (<i>Ovis spp.</i>): 0.19	
α-Gal	ND	nGal-alpha-1,3-Gal (thyroglobulin, bovine) < 0.1	
IgE inhibitions using cat and pork SAs†			
IgE (kU/L)	Control	Serum preincubation with cat-SA	Serum preincubation with pork-SA
IgE to pork-SA	0.26	0.19	0.16
IgE to cat-SA	16.2	7.03	18.2

BSA, Bovine serum albumin; NA, not available; ND, not done; neg, negative; SA, serum albumin.

*Prick tests results given in wheal/erythema (mm).

†Serum preincubation was performed with the relevant coated albumin cat (e220) or pork (e222) or uncoated (ImmunoCAP). Serum was then assayed for IgE to cat SA (e220) and pork SA (e222) using ImmunoCAP.

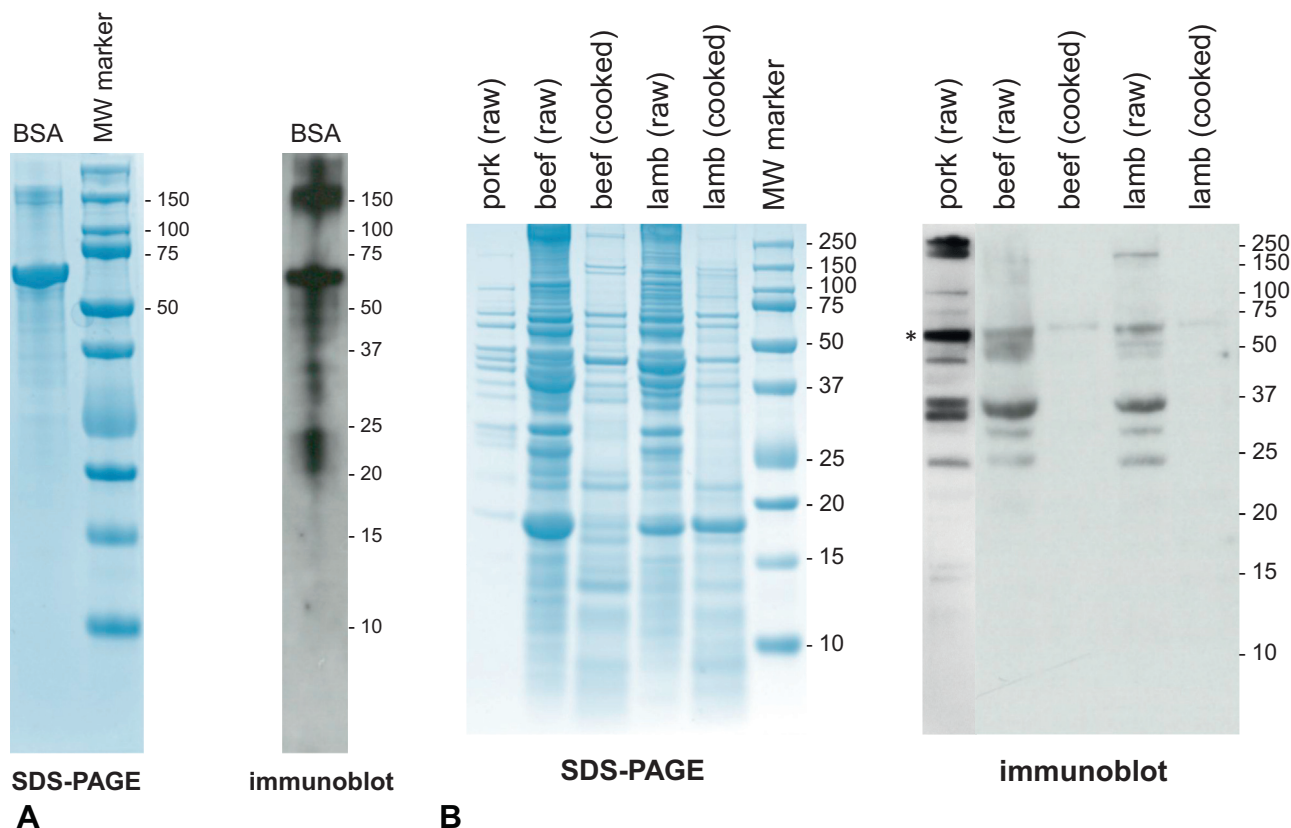


FIGURE 1. IgE sensitization to bovine serum albumin (BSA) and mammalian meats. **A**, SDS-PAGE using BSA from tissue adhesive shows monomeric (66 kDa) and dimeric (≈ 140 kDa) proteins. IgE immunoblotting with the patient's serum reveals IgE reactivity to BSA. **B**, SDS-PAGE using raw and cooked meats shows proteins ranging from less than 10 kDa to greater than 250 kDa. IgE immunoblotting with the patient's serum shows IgE-reactive proteins ranging between 14 and 426 kDa in raw in contrast to cooked meats. One 66 kDa band might be consistent with SA (marked with an asterisk). *MW marker*, molecular weight marker (kDa).

home for years). Abdominal bloating and diarrhea also occurred 2 to 3 times a month, within 2 to 3 hours after lamb or pork meat consumption, and would resolve within 24 to 48 hours. Very well-done beef meat was tolerated without clinical features; however, he seldom ate such food (approximately once a month). Conversely, he had an aversion to raw or rare meat leading to avoidance for years. Recently, he ate a hamburger whose meat was raw, and this triggered abdominal cramps and diarrhea without oral symptoms, within 2 to 4 hours of consumption. Meat avoidance was suggested over a 2-week period to prove that the digestive symptoms were related to meat consumption. No symptoms were reported during this time frame. In addition, our patient has an aversion to milk and reported to never drink milk.

As BSA allergy is uncommon, we hypothesized that the route of BSA sensitization would be likely via cat SA sensitization.¹ To assess cat SA allergy and potential mammalian cross-reactivity of SAs, we performed prick tests (PTs) to cat dander extract (Stalergenes Greer, Antony, France) and native raw and cooked meats (pork, beef, lamb).^{3,4} Specific IgEs (cat, pork, beef, lamb, α -gal) were determined (ImmunoCAP; ThermoFisher Scientific, Saint-Quentin-en-Yvelines, France) (Table 1). Cat allergy was proven on the clinical history, IgE levels (dander, SA, Fel d 1), and results of PTs along with cross-reactivity to pork and beef.

To identify and characterize the IgE-binding proteins, protein extracts of raw and cooked meats (pork, beef, lamb) were prepared by homogenization in phosphate buffered saline (pH 7.4) and the supernatant protein concentrations were determined using the Bradford assay (Bio-Rad, Marnes-la-Coquette, France). Native BSA (5 μ g) from tissue adhesive and raw or cooked meat protein extracts (15 μ g) were separated by Coomassie-stained SDS-PAGE or immunoblotted as previously reported.⁵ SDS-PAGE using BSA shows monomeric (66 kDa) and dimeric (≈ 140 kDa) proteins (Figure 1, A). IgE reactivity to BSA on immunoblot proves BSA sensitization (Figure 1, A) supporting evidence for BSA allergy.

SDS-PAGE using meats shows proteins ranging from <10 to >250 kDa (Figure 1, B). Immunoblot analysis reveals IgE-reactive proteins ranging between 14 and 426 kDa in raw meats in contrast to cooked meats, where IgE-reactive proteins remained almost undetectable. One 66 kDa band might be consistent with BSA (Figure 1, B). Pork meat allergy extended to beef and lamb was thus proven on the clinical history and PTs and/or immunoblot results.

To identify the route of BSA sensitization, we investigated cross-reactivity between pork and cat SAs. The patient's serum was depleted from specific IgE to one SA and used to measure residual

specific IgE to the same SA or the other one. Briefly, undiluted serum was incubated at 37°C for 1 hour with cat SA, pork SA, or control (ImmunoCAP). Serum was harvested and incubated at 37°C for an additional hour with a second ImmunoCAP of the same reference. Serum was then assayed using ImmunoCAP for specific IgE to cat and pork SAs as described above. Both SAs were efficient to inhibit specific IgE binding to pork SA (Table I). Conversely, the IgE response to cat SA was reduced by preincubation with cat SA, whereas pork SA did not show inhibition of the cat SA response. These findings suggest that the primary sensitization was linked to cat SA, also called Fel d 2.¹

The properties of BioGlue (45% BSA, 10% glutaraldehyde) are based on glutaraldehyde molecules that covalently cross-link BSA molecules to each other leading to polymerized BSA without degradation/resorption for months. As no subsequent BSA-induced clinical reaction occurred after initial resuscitation although the BSA tissue adhesive remained in place, the chemical modifications induced by glutaraldehyde might have irreversibly modified BSA structures and hidden epitopes recognized by specific IgE to native BSA. A few cases of IgE-mediated allergy to BSA contained in artificial insemination or bone marrow preparation or to inhaled BSA powder have been reported, the clinical presentation being determined by the route of BSA administration.⁶ Here, BSA allergy typically reproduced the clinical pattern of perioperative drug-induced anaphylaxis with cardiovascular disturbances as a key feature.²

We showed that anti-cat SA IgE reactivity completely contained IgE reactivity to pork SA, whereas the reverse was untrue. This finding suggests that sensitization to cat SA in dander via the respiratory route was the primary event in the development of the cross-reactive IgEs.¹ Pork meat allergy extended to beef and lamb, the so-called pork-cat syndrome, may be explained by cross-reactivity of SAs and other unidentified proteins, whereas the role of the oligosaccharide α -gal⁷ and lipocalins, another group of mammalian inhalant allergens,⁸ was excluded.

Meat allergy is rare and SAs belong to known major allergens.⁷ The differences in skin reactivity and immunoblot results to rare or well-cooked meats and the tolerance to well-cooked meats may be explained by SA thermal denaturation. Interestingly, our patient had an aversion to red and/or rare/raw meats leading to its avoidance, a likely “self-protection.” Finally, the pork SA IgE level was lower than cat SA in correlation with the intensity of response to PTs. This may be linked to infrequent pork-meat consumption and continued cat exposure.¹ Conversely, the BSA IgE level remained undetectable, its sensitivity being low.⁹

In conclusion, this report highlights the critical role of cat SA sensitization in IgE-mediated allergy induced by nonhuman SA. Cat allergy is a growing public health concern, whereas BSA tissue adhesive is widely used. As cat SA sensitization may predict cross-reactivity to other mammalian SAs, measuring preoperatively cat SA IgE level before the use of BSA tissue adhesive in cat-allergic patients could be meaningful to avoid BSA tissue adhesive if positive, because other sealants are available.

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