Lactation anaphylaxis: report of a rare case with recurrent postpartum anaphylaxis

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Abstract

Lactation anaphylaxis is extremely rare and has been scarcely reported in the literature. Breast feeding and/or milk expression immediately induces life-threatening anaphylactic reactions, including generalized urticaria, angioedema, respiratory symptoms, and hypotension. Six English-language case reports have described the clinical course in detail. The present report describes a case involving a 24-year-old woman with no history of allergic reactions or anaphylaxis who experienced anaphylactic reactions three times immediately after milk expression. Lactation anaphylaxis was suspected when a detailed medical history revealed lactation-related recurrent anaphylactic symptoms. The authors prescribed bromocriptine to stop lactation and switched her to formula feeding, which resulted in no further anaphylactic episodes. Based on a review of the relevant literature, this report describes the characteristics of lactation anaphylaxis and possible management strategies. The pathogenesis of lactation anaphylaxis has been inferred from various experimental results.

Keywords: breastfeeding, lactation anaphylaxis, mast cell, mammary gland, tryptase

Introduction

Lactation anaphylaxis (LA), also known as breastfeeding anaphylaxis, is an extremely rare phenomenon and has been rarely reported. Lactation, including breastfeeding and milk expression, precipitates life-threatening anaphylactic reactions, such as generalized urticaria, angioedema, respiratory symptoms, and hypotension. One characteristic of LA is that attacks often occur immediately after lactation and appear to be related to it; however, attacks do not always occur despite continued lactation.

We report a patient who experienced an anaphylactic reaction during milk expression after delivering her two children. However, the mechanism of action of LA is yet to be elucidated. To the best of our knowledge, only six English-language case reports have described the clinical course in detail [1-6]. We summarized and compared these case reports to identify the salient characteristics of LA. Although life-threatening events occurred in all cases, no deaths have reported to date.

Case Synopsis

A 24-year-old woman (gravida 1, para 1) presented to the emergency department four months after delivery. The patient experienced breast engorgement and expressed milk using an electric pump. She almost immediately noticed wheals on the anterior chest and developed generalized urticaria with vomiting and shortness of breath. She could not identify any obvious triggers or causes and denied any previous history of allergic diseases such as atopic dermatitis, urticaria, asthma, or allergic

reactions to food or drugs. The patient was diagnosed with anaphylaxis and treated with intra-muscular epinephrine and intravenous fluid, with a good response. The patient was observed overnight and was discharged with an epinephrine auto-injector as a precautionary measure. At the next appointment, the patient underwent skin -prick testing for a reaction to the silicone part of the breast pump that contacted the skin. However, the test results were negative. An electric breast pump was used and no symptoms were observed. She continued to breastfeed and express milk without any problems. However, three months later, she manually expressed a relatively large amount of milk and developed the same symptoms, including generalized urticaria. Lactation anaphylaxis was suspected on the basis of a literature search of case reports describing patients with similar symptoms. Therefore, we recommended the cessation of breastfeeding.

During follow-up, the patient reported no further anaphylactic reactions after transitioning to formula feeding. Fifteen months later, she gave birth to a second baby girl. After consultation with the patient, she resumed breast feeding. Postpartum days one and two were unremarkable and breastfeeding was performed without difficulty. Three days after delivery, the patient noticed wheals on the anterior chest while expressing milk and developed generalized urticaria (**Figure 1**). The patient was immediately administered with intra-muscular epinephrine (0.5mg), intravenous d-chlorpheniramine (5mg), intravenous betamethasone valerate (2mg), and oral levocetirizine hydrochloride (5mg); her symptoms resolved. Twelve hours later, the patient had expressed milk and did not develop any wheals or other symptoms. Serum tryptase and histamine levels were measured before and after milk expression, but no significant increases were observed. This may have been related to the effects of the systemic corticosteroids and antihistamines administered or to the depletion of chemical mediators in mast cells from the previous attack. Basophil histamine release assay was performed using the patient's milk and serum immediately after birth and showed no positive reactions compared with healthy subjects. Furthermore, no changes in the basophil reactivity to various stimuli (immunoglobulin E, C5a, or calcium ionophores) were observed before or after birth. In addition, a prick test for the patient's serum and milk was performed and no clear positive findings were obtained compared with the positive control histamine. The patient was asked to discontinue breastfeeding. Bromocriptine (a dopamine agonist) was prescribed to stop lactation and she was switched to formula feeding. At the three-month follow -up, the patient reported no further episodes of anaphylactic reactions.

Case Discussion

Lactation anaphylaxis is characterized by symptoms that range from generalized urticaria to respiratory symptoms and hypotension, that are closely associated with lactation. The first case of LA was reported by Mullins et al. in 1991 [1]. Since then, only a few cases have been reported, with six English-language case reports describing the clinical course in detail (**Table 1**), [1-6]. Seven mothers, including our patient, gave birth to fourteen children. Every episode was triggered immediately after breastfeeding or expression of milk. In all patients with LA, skin eruptions appeared as an initial symptom that progressed to generalized urticaria. In addition to urticaria, many respiratory symptoms are observed, such as choking, coughing, and wheezing. Two cases of life-threatening hypotension have been reported [1,6]. However, to date, no deaths related to LA have been reported to the best of our knowledge. Anaphylactic reactions often occur on the third day after birth and, in most cases, attacks occurred within four days after delivery. However, in one case the

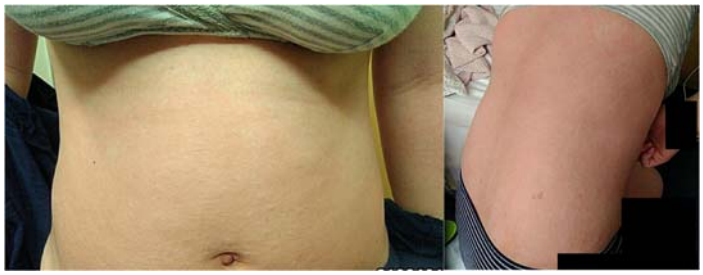

Figure 1. *Clinical images of diffuse urticarial reaction on the trunk.*

Table 1. *Reported cases of lactation anaphylaxis.*

Case	Age	BN	Time of first onset after the delivery	Inducement	Symptoms	cNSAID	Disease outcome	Ref
1	29	1	First brestfeeding	Breast-feeding, expression of milk	GU, RS, Angioedema, Hypotention	Aspirin, Acetaminophen	Stopping lactation with bromocriptine	[1]
		2	48 hours	Breast-feeding	GU, RS, Angioedema, Hypotention	Not used	Stopping lactation with bromocriptine	
2	30	1	3 days	Breast-feeding, expression of milk	GU, RS	Ibuprofen	Continuing breast-feeding without incident	[2]
3	32	1	4 days	Breast-feeding	GU, RS	Ibuprofen	Continuing breast-feeding using anti-histamine	[3]
4	34	1	No anaphylactic reaction					[4]
		2	First brestfeeding	Breast-feeding, expression of milk	GU, RS, Angioedema	Ibuprofen	Stopping lactation	
		3	ND	Breast-feeding	GU, Angioedema	Ibuprofen	Continuing breast-feeding using cetirizine	
5	35	1	3 days	Breast-feeding	GU, RS, Angioedema	ND	ND	[5]
		2	3 days	Breast-feeding	GU, RS	ND	ND	
		3	3 days	Breast-feeding	GU, RS	ND	ND	
		4	3 days	Breast-feeding	GU, RS, Angioedema	Ibuprofen, Acetaminophen	Continuing breast-feeding without incident	
6	38	1	1 week	Breast-feeding	GU, RS, Hypotension	ND	Stopping lactation	[6]
7	23	1	4 months	Expression of milk	GU, RS	Not used	Stopping lactation	Current case
		2	3 days	Expression of milk	GU	Not used	Stopping lactation with bromocriptine	

BN, baby number; cNSAID, concomitant non-steroidal anti-inflammatory drugs; GU, generalized urticarial; RS, respiratory symptoms; ND, not described.

patient did not develop an anaphylactic reaction with the first child [4]. In our case, the attacks after the birth of the first child occurred four and 7 months after delivery. We considered the possibility that attacks may be delayed in primiparous women. Standard treatments for LA, including epinephrine, glucocorticoids, and antihistamines, were administered in all cases. Durgakeri et al. reported the utility of antihistamines to control symptoms [3]. Nonsteroidal anti-inflammatory drugs (NSAIDs) are an important contributing factor in predisposing patients to anaphylactic reactions, probably because of their inhibitory effects on cyclooxygenases. NSAIDs were administered in five of the six cases in which the use of NSAIDs was recorded. Although symptoms persisted in one case even after discontinuing NSAIDs [5]. Considering the pharmacological effects of NSAIDs, we believe that NSAIDs should be discontinued in patients with LA. We did not use NSAIDs in this patient. Regarding the course of LA, attacks disappeared in four of the seven cases, while lactation continued. In three patients in

whom lactation was discontinued, the attacks disappeared immediately. The best method for managing LA is stopping breastfeeding, and mild expression.

However, the exact pathogenesis of LA remains unclear. Experiments in mice have shown that the number of mast cells in the mammary glands increases during pregnancy and decreases after childbirth [7]. Durgakeri et al. reported elevated levels of serum tryptase, a relatively specific chemical mediator of mast cells [8], during LA [3]. According to this patient, all three post-milk expression attacks occurred at times of significant breast swelling and when a large amount of milk was expressed. During the attack, wheals appeared on the anterior chest and spread throughout the entire body. We hypothesized that mammary mast cells that increase during pregnancy and normally decrease after childbirth, do not decrease in patients with LA, and that anaphylactic reactions develop when mechanical stimulation exceeds a specific threshold. The unique feature of this case is that the attacks were not induced by breastfeeding but only during milk expression. We speculated that the mechanical stimulus threshold in this patient was higher than that in other cases. We measured serum tryptase levels 12h after the third LA attack and found no significant increase. Tryptase levels are elevated between 15min and three hours after an anaphylactic reaction [3]. In this case, we speculated that tryptase levels might have been elevated immediately after the attack. The basophil histamine release assay for various stimuli did not detect significant changes before or after delivery; therefore, basophils are unlikely to be involved in LA pathology. The skin prick test for milk was negative and the patient did not experience any symptoms, such as wheals, even when milk contacts her skin. Therefore, we ruled out the possibility of milk-induced contact anaphylaxis. Lactation anaphylaxis is extremely rare, and its pathogenesis has not yet been fully elucidated. Determining the pathophysiology of LA is important for developing measures to suppress attacks other than stopping lactation.

Conclusion

Lactation anaphylaxis is an extremely rare condition. Given that the first symptom is general urticaria and the condition is life-threatening, dermatologists should recognize this entity. If an anaphylactic reaction of undetermined cause is encountered in a postpartum woman, its temporal relationship with lactation must be addressed. The exact pathogenesis of LA has not yet been clarified and the role of lactation in its development requires further investigation.

Potential conflicts of interest

The authors declare no conflicts of interest.

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