

TABLE I. IgE levels in serum and CSF

Subject	Total IgE serum	Total IgE CSF	Latex IgE serum	Latex IgE CSF	SX 1 Serum	SX1 CSF	fx 5 Serum	fx 5 CSF
E.T.	2.7	<2.0	<0.35	<0.35	<0.35	<0.35	<0.35	<0.35
F.S.	203.0	2.9	<0.35	<0.35	Pos.	<0.35	<0.35	<0.35
S.A.	34.6	<2.0	<0.35	<0.35	<0.35	<0.35	<0.35	<0.35
M.P.	119.0	<2.0	<0.35	<0.35	Pos.	<0.35	<0.35	<0.35
W.J.	169.0	<2.0	0.76	<0.35	Pos.	<0.35	<0.35	<0.35
H.M.	84.9	<2.0	12.5	<0.35	Pos.	<0.35	Pos.	<0.35
G.B.	961.0	87.4	95.1	73.0	Pos.	<0.35	Pos.	<0.35

All data are given in kilounits per liter: <0.35 kU/L = below detection limit for specific IgE; <2.0 kU/L = below detection limit for total IgE. SX 1, IgE screening test for eight inhalant allergens; fx 5, IgE screening test for six nutritional allergens; Pos., positive.

patient showed a CSF eosinophilia—including the two patients sensitized to latex in serum.

Our results indicate that IgE detected in CSF is not the consequence of a leaky hemato-encephalic barrier but has been synthesized locally. IgE may be produced by plasma cells in CSF deriving from lymphocytes, which we were able to detect in the differential cytologic specimens.

The source of latex leading to sensitization was probably not the shunt system because since 1989 these have been latex-free. We therefore suspect that repeated contact with glove powder containing latex during multiple operations established a long-term allergen depot as the probable cause.

In conclusion, this is the first report pointing to a local specific IgE production in CSF leading to a local men-

ingeal allergic reaction in the form of an eosinophilia. It should be considered that eosinophilia in CSF may be linked to latex allergy.

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Apnea as a manifestation of mast cell activation in an infant with mastocytosis

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Apnea in infancy is often associated with serious illnesses such as sepsis, neurologic disorders, or metabolic disturbances. Apnea may also occur in premature infants in the absence of identifiable disease. We describe a 5-month-old infant with recurrent episodes of

apnea preceding the onset of cutaneous lesions of mastocytosis. Elevation of the serum β -tryptase level after an episode of apnea suggests that mast cell activation may have been involved in the development of apnea in this patient.

CASE REPORT

The patient is a black male infant born at 36 weeks of gestational age. He experienced recurrent episodes of apnea commencing at 3 days of age, for which he was repeatedly evaluated in the local emergency department without a clear diagnosis and without any treatment instituted. At 5 months of age he had a generalized skin rash and demonstrated increased irritability. Three weeks later, he was admitted to a local

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hospital after an episode of apnea with perioral cyanosis had occurred at home. On physical examination the infant was noted to have bullous skin lesions, as well as dark macules over the trunk and extremities, with a positive Darier's sign. There was hepatomegaly with a total liver span of 9 cm. The results of the rest of the physical examination were normal, including results of a complete neurologic examination. While hospitalized, the patient had an episode of apnea with bradycardia (heart rate of 52 beats/min), which responded to tactile stimulation. The lungs remained clear on auscultation. An allergy and immunology consult was requested.

A biopsy of a cutaneous lesion was performed, which revealed characteristic findings of urticaria pigmentosa with diffuse mast cell infiltration of the dermis. Abdominal ultrasonography confirmed the presence of hepatomegaly. To assess the possible role of mast cell activation in our patient's symptoms, serum tryptase levels were obtained approximately 3 hours after the episode of apnea, which revealed a marked elevation of α -protryptase and a moderate elevation of β -tryptase (Table I), as determined by analysis of the results from the G5- and B12-tryptase immunoassays.¹⁻³ Results of a bone marrow biopsy were normal, without mast cell infiltration. A skeletal survey showed two radiolucent lesions, one in each humerus. The infant was treated with a combination of H₁ and H₂ antihistamines and was placed on an apnea monitor.

Repeat serum tryptase determinations were obtained over the next 10 months, which showed minimal to absent β -tryptase and gradually declining α -protryptase levels. However, levels of α -protryptase have remained persistently elevated throughout the follow-up period. Clinically, the infant did not experience further episodes of apnea, and the extent of the skin lesions has decreased progressively over time. A repeat abdominal ultrasound performed 9 months after the initial study showed persistent hepatomegaly. Repeat radiographs of the humeri were normal.

DISCUSSION

Our group has previously demonstrated that the G5 immunoassay is specific for β -tryptase, whereas the B12 immunoassay detects total tryptase (α -protryptase and β -tryptase).¹ Levels of α -protryptase can then be estimated by subtraction. Because β -tryptase is stored in secretory granules of mast cells and is released only on mast cell activation, serum levels of β -tryptase are normally undetectable and increase as a result of mast cell activation, as seen in systemic anaphylaxis.^{1,2} On the other hand, α -protryptase, which remains in an inactive proenzyme form, is constitutively released. Normal serum levels of α -protryptase average 1 to 10 ng/ml.^{1,3} Elevation of the total tryptase level in the absence of elevated β -tryptase indicates an increase in α -protryptase, reflecting an increase in total mast cell numbers, as seen in systemic mastocytosis.¹ Because the G5 monoclonal antibody used to detect β -tryptase weakly cross-reacts with α -protryptase, high levels of α -protryptase result in low apparent levels of β -tryptase. This seems to be the case in our patient in whom β -tryptase levels of 1 to 1.7 ng/ml persisted after the acute episode.

Our patient exhibited an increase in serum levels of α -protryptase, suggesting that systemic mastocytosis was present in addition to the visible lesions of cutaneous mastocytosis. Indeed, further workup revealed hepatomeg-

TABLE I. Serum tryptase levels

Date	β -Tryptase	α -protryptase + β -tryptase
	G5 immunoassay (NL <1 ng/ml)	B12 immunoassay (NL 1 to 10 ng/ml)
3-11-96	9*	92*
3-25-96	1.7	90
4-19-96	1.5	33
9-6-96	1	38
11-4-96	<1	26
1-20-96	<1	20

NL, Normal.

*Three hours after apneic episode.

ally and skeletal involvement, with a normal bone marrow biopsy result. An unusual feature of this case is the presentation of recurrent apnea before onset of skin lesions of mastocytosis. Thus measurement of tryptase levels in infants with apnea of unknown etiology may be useful.

This case provides new insight into the pathogenesis of apnea. The increase in serum levels of β -tryptase in association with an episode of apnea in our patient indicates the occurrence of mast cell-dependent anaphylaxis and suggests that anaphylaxis in some infants may be first seen as apnea. A review of the literature revealed only one other reported case of apnea in association with anaphylactic shock, which occurred in a 32-year-old patient with previously undiagnosed diffuse cutaneous mastocytosis.⁴ In this latter case, apnea was associated with cardiovascular shock. In our patient the episodes of apnea responded to stimulation alone, suggesting central nervous system suppression of respiration. Whether any of the mediators secreted by mast cells cause such central nervous system suppression is unclear.

We have previously reported elevated β -tryptase levels in postmortem sera from a subset of the victims of sudden infant death syndrome.⁵ This case raises the possibility that anaphylaxis with resulting apnea may be involved, although the stimulus for mast cell activation remains unknown.

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