

Elevated serum leptin in AEDS

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• IgE-associated atopic eczema/ dermatitis syndrome (AEDS) is a chronic inflammatory skin disease associated with pruritis and enhanced production of IgE and IgG4 (1). I have previously reported that children with IgE-associated AEDS often had fatty liver (2). Here, fasting serum leptin levels in young children (1–6 years old) with IgE-associated AEDS with or without fatty liver was studied by ELISA (TECHNE Corporation, MN, USA).

Age-matched 25 nonatopic controls, 25 patients with IgE-associated AEDS but without fatty liver, and 25 patients with IgE-associated AEDS with mild to moderate fatty liver were included after informed consent was obtained. All were male and none of them were obese as determined by body mass index (BMI) (Table 1). Levels of serum GOT and GPT were within normal range in all of the subjects, although patients with IgE-associated AEDS with fatty liver had elevated levels of serum total cholesterol (>220 mg/dL) and/or LDL-cholesterol (>120 mg/dL).

Serum leptin levels were significantly elevated in patients with IgE-associated AEDS, and the elevation was further augmented in patients with IgE-associated AEDS with fatty liver (Table 1). Similar results were obtained in female patients aged 1–6 years with IgE-associated AEDS with or without fatty liver (data not shown).

The effect of leptin on *in vitro* Ig production was then studied. Peripheral blood mononuclear cells (MNC) were

cultured ($2 \times 10^5/0.2$ ml/well) with medium or with 250 ng/ml of recombinant leptin (Pepro Tech, Inc., NJ, USA) for 12 days (1). While MNC from controls failed to produce IgE or IgG4, MNC from IgE-associated AEDS spontaneously produced IgE and IgG4, and levels of those Ig production were augmented in IgE-associated AEDS with fatty liver. Leptin inhibited *in vitro* IgE and IgG4 production in both groups, and the inhibition was reversed by antileptin mAb (Pepro Tech). This inhibition is most likely owing to increasing Th1 and suppressing Th2 cytokine production (3). This is currently under investigation.

Serum leptin levels were elevated in patients with steatohepatitis, and this may be related to hyperlipidemia (4). In patients with IgE-associated AEDS, hyperlipidemia and fatty liver are frequently observed, and fatty acid dysregulation may be involved in the pathogenesis of AEDS (5). It is tempting to speculate that hyperlipidemia may elevate serum leptin, which in turn may facilitate fatty liver. On the other hand, the fact that leptin decreased IgE and IgG4 production may indicate negative regulatory system in IgE and IgG4 production by leptin.

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Table 1. Leptin and IgE and IgG4 production in patients with IgE-associated atopiceczema/ dermatitis syndrome (AEDS) with fatty liver

	Controls	AEDS	AEDS and fatty liver
Total number	25	25	25
Range of age (years)	1.0–6.0	1.1–5.8	1.0–6.0
Serum leptin (ng/ml)	1.1 ± 0.6	1.8 ± 0.6*	3.4 ± 1.1**
BMI	20.1 ± 3.4	19.9 ± 3.6	20.4 ± 3.7
IgE production (ng/ml)			
Medium	<0.3	1.0 ± 0.5	1.7 ± 0.9**
Leptin	<0.3	0.6 ± 0.3	0.7 ± 0.4
Leptin + Anti-leptin mAb	<0.3	0.9 ± 0.5	1.6 ± 0.8**
IgG4 production (ng/ml)			
Medium	<0.3	8.2 ± 3.6	17.8 ± 3.5**
Leptin	<0.3	4.2 ± 1.4	5.2 ± 2.1
Leptin + Anti-leptin mAb	<0.3	7.9 ± 3.5	16.9 ± 4.2**

* . $P < 0.01$ vs. controls

** . $P < 0.01$ vs. AEDS without fatty liver