

although there are two plausible hypotheses: an immune-mediated reaction or direct lung injury by biologically active lipids generated during the storage of the blood product.¹⁰ Classically it has been attributed to the presence of antileukocyte antibodies in the patient's or donor's serum, which are found in less than 50% of cases with specific tests.¹² In 90% of these cases the antibodies are, however, found in the donor's serum,¹¹ unlike our case. Previously described antigranulocyte antibodies have shown specificities for the NB and 5b antigens.^{4,6,8} Other antibodies implicated have been anti-HLA class I antibodies,¹¹ anti-HLA A2⁴ and B35-specific antibodies.⁶ Currently the role of these antibodies in the pathogenesis of TRALI is controversial, since anti-HLA antibodies are found in 1-2% of the general population.² Recently, Silliman *et al.* suggested that TRALI may be mediated by biologically active lipids generated during the storage of blood products, particularly when transfused to patients with certain predisposing factors, leading to a *syndrome of neutrophil overactivation* with endogenous cytokine release, indiscriminate endothelial neutrophil adhesion and activation.¹⁰ Although unproven, the concept of a multifactorial pathogenic mechanism, including the effect of specific antigranulocyte antibodies, active lipids and other as yet undefined factors, emerges as a more rational explanation of this complex syndrome.

Key words

Transfusion-related injuries, antigranulocyte antibodies

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Plasma and urinary endothelin-1 titers and plasma von Willebrand activity in *Pseudo-xanthoma Elasticum*

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We found high endothelin-1 and von Willebrand factor plasma titers not only in two individuals (daughter and father) affected with *Pseudoxanthoma elasticum* but also in a young unaffected relative. These findings raise the possibility that these molecules could be the first biochemical fingerprints of this, still not clinically evident, rare inherited disorder of elastic tissue.

Pseudoxanthoma elasticum (PXE) is a rare inherited disorder of elastic tissue characterized by progressive calcification of the elastic fibers in the skin, retina and cardiovascular system;¹ the estimated prevalence of this disease is 1 in 70,000-100,000. A more common autosomal recessive and a less common autosomal dominant pattern of inheritance, with high penetrance, have been described. Recently, an area on the long arm of chromosome 16 (16p13.1) was identified as the single gene that accounts for both the recessive and dominant forms of PXE.² The most characteristic clinical manifestations of PXE are yellowish grouped papules and plaques on the skin of flexure areas, angioid streaks in Bruch's membrane of the retina, calcified cardiovascular lesions, and severe hemorrhagic diatheses.¹ Diagnosis of PXE is based on clinical evaluation, histologic demonstration of abnormal, calcified elastic fibers in skin biopsy, and fundoscopic examination showing the presence of the typical angioid streaks.¹

We recently cared for a 41-year-old woman affect-

Table 1. Plasma and urinary ET-1 levels, and plasma vWF activity in two relatives affected by PXE and in three other unaffected relatives. Plasma vWF activity was expressed as percentages of normal pooled plasma, the antigen levels of which were defined as 100%.

	Father (affected)	Patient (affected)	Sister (unaffected)	Brother (unaffected)	Son (unaffected)
Plasma ET-1 (n.v. 0.5-1.2 pg/mL)	2.78	2.98	0.98	0.67	2.66
Urinary ET-1 (n.v. 0.3-1.2 µg/h)	1.5	3.34	0.58	0.68	4.56
Plasma vWF activity	212%	188%	100%	98%	176%

ed by PXE, who, besides presenting all the required diagnostic criteria, also developed, as a rare complication of her disease, an atrial septal aneurysm. Both the patient's father and one of her brothers, who had died of acute myocardial infarction, had been diagnosed as having PXE, and her paternal grandfather was also supposed to have had it. Neither her mother nor any other relative from the maternal lineage showed signs of the disease, thus suggesting a dominant autosomal inheritance. Two of the patient's brothers and her 15 year-old son do not present clinical evidence of PXE.

Endothelin-1 (ET-1), a potent vasoconstrictor, and von Willebrand factor (vWF), have been demonstrated to be markedly increased when the vascular endothelium is damaged.³ Furthermore, some authors have suggested that both ET-1 and vWF could contribute to the progression of vascular lesions in patients with PXE.⁴ Plasma and urinary ET-1 titers, and vWF plasma activity were titrated in the two PXE patients and in their three clinically unaffected relatives using a commercial sandwich immunoassay technique (R&D Systems, Minneapolis, MN, USA),⁵ and an enzyme-linked immunosorbent assay method, respectively (Boehringer-Mannheim Co., Milan, Italy).⁴ The results we obtained (Table 1) showed a marked increase in ET-1 plasma and urinary titers and in vWF plasma activity not only in the affected individuals, but also in the patient's healthy son, despite his lack of clinical signs of PXE.

Although we cannot predict whether this boy will develop PXE during his lifetime, the increase in ET-1 and vWF titers might be the first biochemical fingerprint, of this still not clinically evident disease.

However, the central question still remains unanswered; as a matter of fact, if the patient does go on to develop PXE, we do not know whether the observed early increase in ET-1 and vWF is the primary insult leading to overt PXE or simply the first sign of a still subclinical disease.

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Severe immune thrombocytopenia during formestane treatment

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Formestane is a new aromatase inhibitor used as second-line endocrine treatment for postmenopausal women with advanced breast cancer. The most frequent side effects are local reactions. Here we report the development of immune thrombocytopenia coinciding with administration of this drug.

Formestane (4-hydroxyandrostenedione) is a new competitive, irreversible, steroidal aromatase inhibitor, 30 to 60 times more potent than aminoglutethimide.¹ Aromatase is the enzyme responsible for the conversion of non-aromatic androgens, particularly androstenedione and testosterone, to aromatic estrogens: estrone and estradiol. In postmenopausal women androstenedione is converted to estrogens by aromatase in the skin, muscles, liver and fat tissue. Aromatase is also present in breast tumor tissue. Thus, formestane decreases both circulating and tumour estrogen levels and is a successful second-line endocrine treatment for postmenopausal women with advanced breast cancer in whom previous therapy with tamoxifen has failed.¹⁻³

The most frequent side effects are local and transient reactions at the site of injection (gluteal pain,