Letters to the Editor

Endocrine disorders and antiphospholipid antibodies

Sir,

Autoimmune mechanisms have been suggested as a pathogenesis of endocrine disorders (1). The presence of antiphospholipid antibody (aPL) has also been reported to induce certain endocrine disorders, although there have not been many cases reported (2). To date, adrenal insufficiency (Addison's disease), hyperthyroidism (Graves' disease), and primary and secondary hypopituitarisms have been reported as aPL-related endocrine disorders (3-9) (Table I). Asherson *et al.* reported a case of Addison's disease associated with primary antiphospholipid syndrome (APS) (3, 4). Árnason *et al*. summarized 27 cases of adrenal insufficiency associated with APS and/or the presence of aPL (5). Of these patients, half showed several thrombotic symptoms such as deep vein thromboses, pulmonary thromboses, and cerebral embolisms. In addition, approximately 20% of these patients had systemic lupus erythematosus (SLE) as an underlying disease. Furthermore, there are 2 case reports suggesting a closer link between Graves' disease and extensive thromboses resulting from APS at their onset (6, 7). These cases may indicate the important role of aPL in the induction of Graves' disease.

With regard to hypopituitarism, there are 2 reported cases associated with primary APS (8, 9). The first case (a 48-year-old woman) involved secondary hypopituitarism revealed by hormonal dysfunctions of suprasellar origin and an abnormal magnetic resonance imaging (MRI) finding - atrophy of the left thalamus (8). She showed multiple thrombotic events affecting the deep veins and coronary arteries before the development of the endocrine disorder. The second case (a 62-year-old woman) showed primary hypopituitarism associated with APS (9). On MRI, the pituitary gland disclosed "empty sella" of the hypophysis, which is a neuroradiologic finding of pituitary necrosis (10). This case also showed several severe thrombotic events such as cerebral embolism and cardiomyopathy before the appearance of hormonal abnormalities, similar to the first case.

In addition, we recently encountered an interesting case of primary hypopituitarism. After giving birth, a patient complained of fatigue, failure to lactate and failure to resume menses. Hormonal examinations revealed low levels of ACTH and prolactin, and MRI indicated "empty sella" of the pituitary gland. Furthermore, she showed thrombocytopenia related to the presence of aPL [lupus anticoagulant 85.7 sec., normal values (nv) < 55.5] and anticardiolipin antibodies [IgG 1.4, nv < 0.8; IgM 1.4, nv < 1.0, β2-glycoprotein I 1.2, nv < 3.53] detected using the methods recently recommended by Wilson *et al*. (11). Thorough investigations allowed us to exclude other connective tissue diseases such as SLE. The patient was therefore thought to have Sheehan's syndrome associated with the presence of aPL. She has not yet developed any thrombotic events affecting the deep veins or arteries such as myocardial and/or cerebral infarctions.

It is difficult to directly prove the relationship between "empty sella" and thromboses of the pituitary vessels, although the pituitary gland is rich in blood vessels. This case suggests that endocrine disorders can occur in association with the presence of aPL, even in patients without severe thromboses as observed in other cases (Table I). Although Sheehan's syndrome is thought to be induced by ischemic hypophyseal necrosis caused by extensive blood loss related to delivery (12), blood loss in this patient was not severe. APS and/or the presence of aPL may play an important role in the occurrence of such postpartum hypopituitarisms. Recent reports have indicated that aPL are related to clinical manifestations such as cardiac valve lesions and hemolytic anemia, in addition to the major clinical features of APS such as thromboses, thrombocytopenia, and recurrent fetal loss. Regarding endocrine diseases, the aPL-related onset of these diseases may be more frequent than is generally appreciated.

Table I. Endocrine disorders and antiphospholipid antibodies.

Adrenal insufficiency (Addison's disease)							Refs. 3, 4, 5	
Hyperthyroidism (Graves' disease)							Refs. 6, 7	
Hypopituitarism								
Case	Sex	Age	aPL				Thrombotic symptoms	Refs.
			LAC*	IgG	IgM	β_2GP1$^+$		
1	F	48	+	+	ND†	ND	Myocardial infarction Deep vein thrombosis	8
2	F	62	+	-	-	-	Cerebral infarction Cardiomyopathy	9
3	F	39	+	+	+	-	-	Our pt.

*Lupus anticoagulant; $^+\beta_2$glycoprotein 1; †Not described.

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