

## SHORT REPORT

## Idiopathic intracranial hypertension and anticardiolipin antibodies

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### Abstract

**The association of idiopathic intracranial hypertension (IIH) or pseudotumour cerebri (PTC) with anticardiolipin antibodies (aCL-Abs) has been only acknowledged recently. However, its true incidence is as yet unknown.**

**In this retrospective study, the co-occurrence of IIH and aCL-Abs was looked for among a relatively large group of patients diagnosed with IIH or PTC in the neuro-ophthalmology clinic during the years of 1992–8. All patients underwent routine blood tests and the presence of activated protein C resistance and protein S and protein C deficiency were recorded. ACL-Abs were determined in all patients. The co-occurrence of IIH and aCL-Abs was found in three out of 37 patients (8.1%), which is higher than the incidence of aCL-Abs in the general population but considerably lower than that reported in two previously published studies. The aCL-Ab positive patients in our series were significantly older and thinner than those in whom antibodies were undetected. In conclusion, it seems that patients with this association should be considered as a unique subgroup of IIH.**

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Idiopathic intracranial hypertension (IIH), also known as pseudotumour cerebri (PTC) is the term used to describe the occurrence of raised intracranial pressure which is not due to mass lesions, obstruction of CSF flow, or focal structural abnormalities, in alert and oriented patients. Headaches, transient visual obscurations, and tinnitus are common complaints and the neurological examination is usually normal. The term “idiopathic” requires the exclusion of intracranial venous sinus thrombosis.

Circulating anticardiolipin autoantibodies (aCL-Abs) may be associated with recurrent abortions, deep vein thrombosis, systemic lupus erythematosus, and cerebrovascular accidents.<sup>1–3</sup> Idiopathic intracranial hypertension has been reported only anecdotally in association with the presence of anticardiolipin antibodies.<sup>4,5</sup> However, 3%–5% of healthy

people may have circulating antiphospholipid antibodies without having an increased risk for thromboembolism.<sup>6</sup>

The purpose of this study was to determine the prevalence of aCL-Abs in a group of patients with IIH.

### Patients and methods

The medical records of all patients diagnosed with IIH or PTC between the years 1992 and 1998 were reviewed. There were 41 patients in whom aCL-Abs were determined. Four of these (two with aCL-Abs) had cerebral sinus thrombosis and were excluded. Thus the study population consisted of 37 patients in whom the association of IIH and aCL-Abs was looked for. All reported at least one of the following symptoms: headaches, transient visual obscurations, tinnitus, and horizontal diplopia. Relevant cerebral sinus thrombosis and intracranial mass lesions or obstruction of the ventricular system were excluded in all patients using contrast enhanced brain CT and MRI. No patient underwent angiography as all had a typical clinical picture of IIH. The laboratory investigation included complete blood count, routine biochemical profile (SMA 16), determination of activated protein C resistance (APCR), protein C activity, protein S antigen (free) concentration and activity, and antithrombin activity.

Activated protein C resistance was determined using a partial thromboplastin time (PTT) based test in which the results of the PTT test were compared before and after the addition of activated protein C to the test reaction (Chromogenix, Sweden). Protein C activity was measured using a chromogenic assay (Dade, USA). Protein S activity was measured using protein S deficient plasma with the addition of Ca<sup>2+</sup> (Biopool, USA). Protein S free antigen was determined by enzyme linked immunosorbent assay (ELISA; Stago, France). Antithrombin III activity was measured using a chromogenic assay (Chromogenix, Sweden). Anticardiolipin IgG and IgM antibodies were determined by a semiquantitative ELISA assay (Reads, USA).

When aCL-Abs were detected, the test was repeated after 6 weeks. A patient was regarded as aCL-Ab positive if he had at least two positive tests.

Obesity was defined as a body mass index >30 kg/m<sup>2</sup>.<sup>7,8</sup>

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Table 1 Demographic, clinical, and laboratory data on 37 patients with IIH

	aCL-Ab Positive	aCL-Ab Negative	p Value
Number of patients	3	34	
Mean age (SD) y	43.33 (6.3)	32.23 (8.5)	<0.035
No of women (%)	3 (100)	32 (94.1)	
Overweight (%)	None	28 (82.35)	
Use of tetracyclines	None	4	
Polycystic ovaries	None	2	
APCR	1	1	
Essential thrombocytosis	None	1	

APCR=activated protein C resistance.

Table 2 aCL-Ab titres in three "positive" patients

Patient	Age (y)	aCL-Ab titre	
		IgG units	IgM units
1	47	81.7; 48	<11
2	47	37.6; 41.2	<11
3	36	30.4; 30.3	<11

Normal values: IgG <23; IgM 11.0

## Results

Of the 37 patients, 35 were women (94.5%) and two were men (5.5%). The mean age of the group at diagnosis was 33.78 (SD 7.8) years (range:19–48). The mean age of the women was 33.71 (SD 7.17) years and the men 23 (SD 5.6) years. In all patients, papilloedema was evident. The neurological examination was normal except for transient abducens palsy in those with horizontal diplopia.

Demographic, clinical, and laboratory data are shown in table 1.

Three women were aCL-Ab. positive; one of them also had an APCR of 1.6 (normal>2). The aCL-Ab were of the IgG type whereas IgM type antibodies were undetected (table 2). Of the 34 aCL-Ab negative patients, one woman had an APCR of 1.8 (normal>2) and another essential thrombocytosis. Known risk factors for IIH were present only in the aCL-Ab negative patients. These included use of tetracyclines in four, polycystic ovaries in two, and use of growth hormone (hGH) in one. Thirty of the 34 "negative" patients were significantly overweight (88.23 %) whereas all three "positives" had a normal body mass index.

Israeli prevalence of anticardiolipin antibodies was 3%–5%; APCR 5%–8%; protein C deficiency <1%; protein S deficiency <1%, among the normal general population from which these study patients were taken.

The aCL-Ab positive patients were significantly older than the negatives (43.33 (SD 6.3) v 32.23 (SD 8.5) years, (p<0.035). All patients, regardless of the presence of aCL-Ab, were treated with daily acetazolamide, with no patient receiving anticoagulants. All experienced a rapid subjective improvement in headaches. During the long term follow up the papilloedema resolved and no permanent visual loss was encountered.

## Discussion

In this retrospective study of a relatively large group of patients, the incidence of the association of IIH and IgG type aCL-Ab was

lower than previously reported. Leker *et al* found this association in six out of 14 patients with IIH (42.85%).<sup>1</sup> However, known risk factors for IIH such as thyroid disorders, Cushing's syndrome, systemic lupus erythematosus, and anticardiolipin syndrome were found in four patients, only half of these patients were obese.

Sussman *et al* reported on 11 out 38 patients (29%); however, only four had aCL-Ab without other "prothrombotic risk factors" or evidence of sinus thrombosis.<sup>9</sup> Thus the corrected rate in this study is 10.52%, which is similar to our findings of 8.1%. Although none of our patients underwent cerebral angiography, we were able to diagnose venous sinus thrombosis by CT and MRI in four patients, two with aCL-Ab, who were excluded from the study. Our patients did not have overt sinus thrombosis. However, occult thrombosis cannot be ruled out. Based on the present results, we are able to define two subgroups of patients with IIH: the aCL-Ab negative group consisting of 82.35% obese and relatively young women and three aCL-Ab positive older women with normal weight. As expected, the "negative" patients had known risk factors for IIH such as the use of tetracyclines, hGH, and polycystic ovaries.<sup>10 11 12 13</sup> The lack of obesity in the "positive" patients aids us in the assumption that they represent a unique subgroup of IIH. Indeed, obesity plays an essential part in the pathophysiology of IIH and may be found in up to 94% of patients.<sup>14</sup>

As our "positive" patients shared with the "negative" patients a benign clinical course and an excellent outcome, it may be highly speculative to assume that aCL-Ab play an important part in the pathogenesis of IIH in patients who lack other "prothrombotic" factors.

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