Original Article

Anticardiolipine syndrome with immune hepatitis

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ABSTRACT

Anticardiolipine syndrome characterized by thrombotic events with positive antiphospholipid antibodies can occur with other diseases

Aim:

to detect the incidence of anticardiolipine syndrome among the Iraqi patients with immune hepatitis

Methods:

during one year period from April 2003-april 2004 every patient with suspected immune hepatitis were asked for occurrence of thrombotic events or fetal loss and measuring for antiphospholipid antibodies .

Results: From sixty patents had been diagnosed as immune hepatitis only six patients had history of thrombosis or recrrunt abortion or intrauterine death plus positive antibodies ,in addition to tow patients had only positive markers for antiphosphlipid antibodie s without history of thrombosis.

Conclusion:

patients with immune hepatitis should be evaluated for anticardiolipine syndrome especially if there is history of thrombosis or recurrent abortion.

Introduction :

The anti phospholipid, APL syndrome characterized by arterial or venous thrombosis , fetal loss,thrombocytopenia and anti phospholipid antibodies. APL may be primary when there is no other condition and secondary when there are other conditions such as systemic lupus erythematosus[1].

The mechanism of thrombosis in APL syndrome remain largely unknown ,antibodies to phospholipid inhibit the production of prostacyclin in the endothelium , inhibit the release of plasiminogen activators and may cause platelets activation by binding to platelet phospholipid[2].

The APL antibodies can be found in many conditions such as autoimmune diseases, infections, malignant diseases and uses of Drugs . they can be found in 2-6.5% of healthy persons with out risk of thrombosis(3) and in many liver disease such as chronic hepatitis C where they can cause thrombosis & thrombocytopenia (4) infection with HCV is present at 16.7% of the patient with thrombatic disorders and anticardiolipin $Ab_{(4)}$

Immune hepatitis is self-perpetuating hepatcellular inflammation of unknown cause. It is characterized by the presence of periportal hepatitis ,piecemeal necrosis or interface hepatitis on (10%) had Histologic examination, hypergammaglobulinemia ,and liver associated auto antibodies in serum[5]

The aim

: to detect the incidence of APL syndrome in Iraqi patients with immune hepatitis.

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Methods:

During one year period from April 2003 April2004 every patient who suspected to have immune hepatitis were involved in this study including those who are known to have immune hepatitis.Full history and physical examination with complete evaluation of liver functions include liver enzymes, prothrobin time(pt) &partial thrombplastin time(ptt) ,virological screen ,serum protein electrophoreses ,complete blood count (CBC) ,platelet count
, erythrocyte sedimentation rate(ESR) Serum complement C3,C4,immunoglobulin electrophoreses & immune markers which include the following: antinuclear antibodies (ANA) antimitochonderial Ab (AMA) ,anti smooth muscle Ab (ASA),if , these markers are negative we look for liver kidney micro some antibodies(LKM-1) Ab soluble liver antigen(SLA/LP) in additions to the anticardiolipin anti bodies IgG&IgM using enzyme linked immunosorbent assay for B2 glycoprotein dependent anticardiolipin antibodies and repeated the assay after 6 weeks.
Ultrasound. examinations of the liver & Doppler studies were done for all patients and liver biopsies if there is no contraindications.
Twenty age matched healthy persons as control were evaluated for present of anticardiolipin Ab.

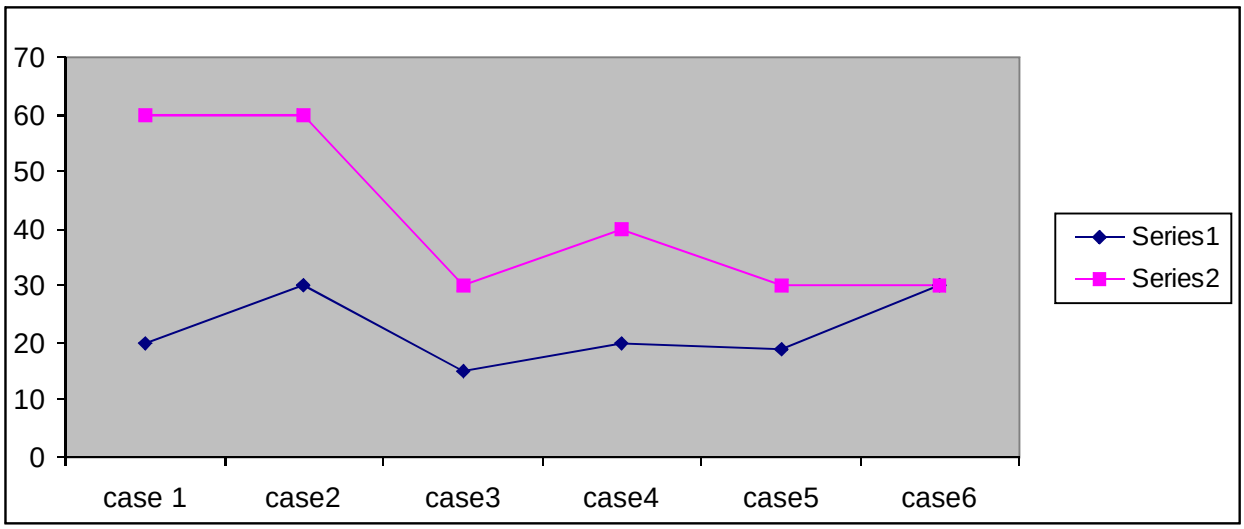
Results:

: In this study 60 patients had been diagnosed as AIH by excluding other causes of liver diseases and positive immunological markers. Every one were screen for anticardiolipin Ab IgG&IgM types .
8\60 (13.3%) had elevated IgG ACL Ab in whom 6\60 past history of thrombosis or history of recurrent abortions or intrauterine death and two had only positive markers without evidence of thrombosis.So 6\60 has diagnosed as antiphospholipid syndrome in addition to the immune hepatitis with F: M ratio 5:1 and age range 14-35 years .five of them had history of other autoimmune diseases and 3 of them had family history of autoimmune diseases(Table 1). 1/3of them had recurrent abortion or still birth, two patients had deep venous thrombosis, one had portal vein thrombosis and the other had thromboses of hepatic veins Liver enzymes are elevated (range) 2-5folds.and the platelets count is decrease (90-130000).
All six patients have type(1) auto immune hepatitis with positive ASA Ab & ANA.
C3 is elevated in all 6patiens while C4 is normal.Gamma globulin is elevated in all of them the range in 2.2 4gm.
4\6 had liver biopsies the mild activities the range of fibrosis II-III.
Re evaluation of IgG&IgM type of ACL Ab reviled further increase in the markers of IgG antibodies especially in those with initial elevation in IgM antibodie

Table(1)age, gender ,history of patients with AIH&APL syndrome

Case	*Gender*	*age*	*other AI disease*	*Family history*	*history of thrombosis*
Case1	*M*	*22*	Ulcerative colitis	Ulcerative colitis	Deep v thrombosis
Case2	F	22	Diabetes mellitus	Arthritis	Portal v thrombosis
Case3	F	35	Arthritis	- ve	Recurrent abortion
Case 4	F	35	SLE	Arthritis	Intrauterine death
Case 5	F	72	-ve	-ve	DVT extended to IVC
Case 6	F	25	thyroditis	-ve	hepatic v thrombosis

Figure(1) the value of ACL antibodies of the study group at the time of examination and after 6 weeks



Figure(2) the results gammaglogulin in the study group

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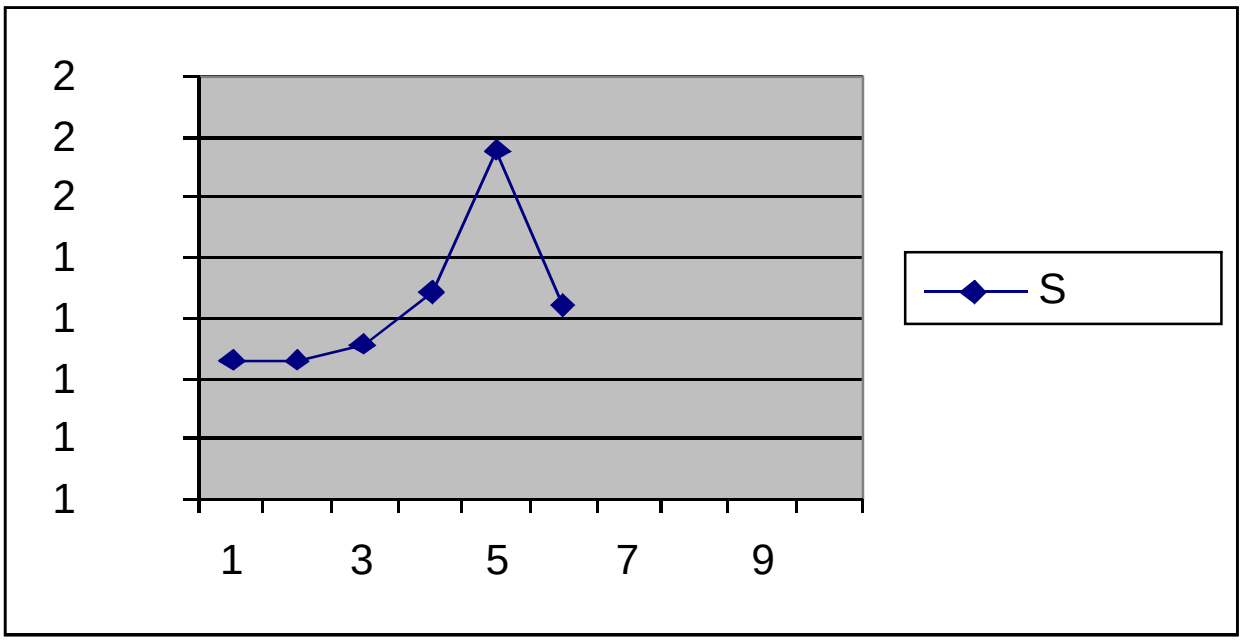

Discussion:

The role and the type of APL antibodies found in hepatic disease still unclear . Until recently few cases of immune hepatitis and antiphospholipid antibody syndrome were reported(five cases 1966-2001). So the etiology & the optimal treatment of them are not clear ,although the steroid therapy is the main stay of treatment for both[6]Eight patients have positive APL Ab this is high compare to the study done for detection of APL Ab in different types of liver diseases, it was found that APL Ab are not significantly increased (3%)in immune hepatitis when compared to the control group(0%)[7] . this is difficult to explain and in need to further evaluation or could be due to an increasing a problem noted elsewhere that consider ACL Ab detection as a marker for diagnosis of immune hepatitis [8] or due to hypergammagloinemia that may cause hyper viscosity syndrome because it was found ACL IgG and IgM anti-beta-2 GPI IgM titer are significantly higher in patients without APS but with hypergammaglobinemia ,in this case other additional risk factor must be considered for the etiological diagnosis of thrombosis[9].

According to preliminary criteria from international conference have been proposed for classification of APS in which APS may be consider present in patients with only one thrombatic events and positive ACL Ab assay that verified on at least two occasions 6 weeks apart[10]. Re estimation of ACL Ab revealed increase in the value(Figer1) ,so 6/60(10%) patents of autoimmune hepatitis have fulfill these criteria and considered to have APS, in spite of that still some consider that the diagnosis of APS in single thrombatic episodes can not be made in whom the present of APL Ab may be incidental finding rater than causal event[11].

All of those patients are type 1 autoimmune hepatitis which characterized by positive markers ASA and/or ANA. Gamma globulin is elevated in the range2.2-4g/dl (Figer2) and immunoglobulinis also elevated, cases of hyper viscosity syndrome secondary to the high IgG level are reported .

Five of those patients (83.3%) patients with history of thrombosis had history of other autoimmune diseases(Table1) ,this is higher than what was reported about the association between type 1 autoimmune fibrosis it is supposed that there was no relation between the activity of AIH& the one of antiphospholipid syndrome[6].IgG &/or IgM type of anticardiolipin antibodies were elevated in all six patients in the range 19-30GPL U/ml(Figer1) and re estimation revealed increase in the level of antibodies and IgM was converted to IgG this indicate that IgM is valuable indicator in the diagnosis of beginning of autoimmune disease where IgG will be found in the progressive stage of manifested autoimmune disorders[12]

Serum complement C3&C4 is decrease AIH which may reflect decrease hepatic synthesis [13] C3 level is elevated in all six patients while C4 is normal the significant of this raise is not explained but it may have role in thrombosis. It has been hypothesized that APL antibodies activate the complement in placenta generating split product that mediate placenta injury and complement activation by APL Ab in other vascular area cause inflammation and thrombphilia,therefore this pathway acts up stream of other important effecter mechanism[14]. In conclusion, we should evaluate the patient with autoimmune hepatitis and with either thrombosis or fetal loss for antiphospholipid syndrome and regular follow up may be necessary because there is risk of new episodes of thrombosis or to safe the fetus. it is unclear how the presence of these antibodies influences the prognosis of autoimmune hepatitis.

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