LEUKOCYTOCLASTIC VASCULITIS: PREVALENCE OF HEPATITIS C VIRUS, CRYOGLOBULINAEMIA AND EVIDENCE OF IMMUNOLOGIC ACTIVATION

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ABSTRACT

Infection with hepatitis C virus has elicited considerable interest for its role in a spectrum of extrahepatic manifestation. Substantial evidence has implicated a causative role for hepatitis C virus (HCV) in many of skin diseases.

This study was conducted to estimate the prevalence of HCV infection and cryoglobulinaemia in patients with leukocytoclastic vasculitis (LcV) and to assess the immunologic changes associated with this disease.

The present study included 39 adult patients (14 males and 25 females, with mean age of 44.1±12.1 years) had LcV and 40 adult healthy controls. All patients were subjected to thorough history taking, clinical examination abdominal ultrasound and full laboratory investigations including urine and stool analysis, complete blood picture, liver function tests, kidney function tests and prothrombine time. HCV antibodies were determined by third-generation ELISA then polymerase chain reaction (PCR) was performed on seropositive cases in test group and controls. Assay of tumor necrosis factor-alpha (TNF–alpha), interleukin-8 (IL-8) and soluble IL-2 receptor (sIL-2R) and soluble intercellular adhesion molecule-1 (sICAM-1) were performed.

The prevalence of HCV antibodies was 46.2% in LcV patients versus 17.5% of the controls. However with PCR reaction 38.5% of LcV patients

were positive for HCV versus 12.5% of the controls (P=0.008). Cryoglobulinaemia was detected in 20.8% of LcV patients and none of the controls. Among 15 patients with LcV and HCV PCR+ve 46.7% had shrunken liver, 40% had enlarged liver and 53.3% had splenomegally while 80% of them had high ALT and AST, 53.3% had high serum bilirubin and 53.3% had +ve cryoglobulinemia, and all items were significantly higher when compared to LcV with PCR –ve patients. The serum levels of TNF-alpha, IL-8, sICAM-1, and sIL-2R were significantly higher in LcV patients than in controls. Furthermore, these immunologic changes were significantly higher in HCV infected than non-infected LcV patients.

From this study we conclude that hepatitis C testing is ext mely useful in evaluating a case of LcV even with normal liver enzymes. While suggesting that LcV could be considered as a dermatologic sign of active and advanced liver disease in HCV infection asking for further researching in the vast majority of HCV infections that lack this phenomenon and recommend good clinical examination for the state of the liver and spleen in those patients. The high serum levels of TNF-alpha and IL-8 suggest that they are actively involved in the pathogenesis of LcV. Furthermore the high serum levels of sICAM-1 and sIL-2R indicated endothelial cell damage together with lymphocyte activation in LcV, with more pronouncing of these immunological changes in LcV with HCV PCR +ve that could help to understand the immunotropic and lymphotropic effect of this virus.

INTRODUCTION

Leukocytoclastic vasculitis (LcV) is a small-vessel inflammatory disease mediated mostly by deposition of immune complexes [1]. Palpable purpura is the hallmark of this disease process[2]. LcV may occur in association with an underlying chronic disease, may be precipitated by infections, medications & chemicals [1] or develop for unknown reason [3]. It has become increasingly recognized that hepatitis C virus infection is a relatively frequent associated process in patients with vasculitis [4].

Hepatitis C virus (HCV) is an RNA virus which is a major cause of acute and chronic hepatitis[5]. Cutaneous manifestations may be the first sign of infection[6]. Mixed cryoglobulinaemia with LcV are the most frequent der-

matologic manifestation[5].

Mixed cryoglobulinaemia is one of the most frequent immunologic abnormalities with HCV infection [7]. Mixed essential cryoglobulinemia is a disorder characterized by presence of serum immunoglobulins that circulate as immune complexes, precipitate with cold temperature and resolubilize when rewarmed [8-11]. Clinical characteristics comprise palpable purpura on lower extremities, arthralgia and weakness[10]. It is now well established that more than 90% of mixed cryoglobulinemia is secondary to HCV infection [12].

Many authors [6,10,13,14] recommend searching for HCV in all patients with LcV. Also all cases of HCV should be searched for signs and symptoms of LcV [10].

AIM OF THE WORK

The aim of this study is to estimate the prevalence of HCV infection and cryoglobulinaemia in patients with LcV and to assess the possible role of proinflammatory cytokines (TNF–alpha, IL-8) and sICAM-1 in the pathogenesis of LcV. and the effect of HCV on that role Furthermore, we investigate for evidence of lymphocyte activation in patients with LcV and its relation to HCV infection.

PATIENTS AND METHODS

The present study included 39 adult patients (14 males and 25 females) having cutaneous LcV, selected from outpatient and inpatient clinics of dermatologic and internal medicine departments of Mansoura University hospital between June 2002-December 2002. They were selected on the bases of clinical and histopathologic examination of recently evolved skin lesions (including necrosis of dermal vessel walls, with deposition of fibrinoid material and inflammatory infiltrate predominantly constituted of neutrophils, nuclear fragmentation and extravasation of erythrocytes). All patients were subjected to thorough history taking, with particular stress on history of chronic liver disease e.g. with or without decompansation, symptoms related to other system affection and drug intake.

Thorough dermatological examination to assess the severity of skin lesions and to exclude any associated disease. Thorough medical and abdominal examination and abdominal ultrasound to detect the state of the

liver, spleen and ascitis were done. Exclusion criteria were, patients with autoimmune connective tissue disease, lymphoproliferative disease, known infectious disease and/or recent history of drug intake that is suggested to cause vasculitis.

Forty adult healthy subjects who are age and sex matched served as control. They had minimal skin problems (e.g. syringoma, milia and wart) and they are all clinically free.

All patients and controls were subjected to the following laboratory tests:

(1) Routine laboratory investigations stool & urine analysis, complete blood picture and kidney function tests: serum creatinine, ESR

(2) Serum alanine aminotransferase (ALT) , aspartate aminotransferase (AST) determination (bioMerieux), serum bilirubine and prothrombine time.

(3) Cryoglobulin is measured by centrifugation of the sample at 37^{O}C, then serum was separated, stored at 4^{O}C and observed for one week. Presence of cryoglobulin is indicated by formation of white precipitate or gel after 24–72 hours, the reversibility of cryoprecipitate tested by rewarming an aliquot of precipitated serum.

(4) Serum anti-HCV antibodies were determined by third-generation ELISA (Murex anti-HCV-version 4.0), which utilizes antigens from the core, NS3, NS4 and NS5 regions of HCV.

(5) Polymerase chain reaction (PCR) was performed on the seropositive in test group cases and controls.

* Extraction of HCV –RNA from serum was performed by (QIAGEN).
* Reverse transcripition (RT) of extracted HCV RNA into complementary DNA (cDNA).
* Amplification of the synthesized cDNA by nested PCR (QIAGEN).
* Detection of amplified product by electrophoresis in 2% agarose gel stained with ethidium bromide. Specific band of HCV appears at 150 base pair.

(6) Assay of TNF-alpha by solid phase ELISA using commercial kits according to the manufacturer's instruction (Diaclone, France).

(7) Serum IL-8 was assayed using the

quantitative sandwich enzyme immunoassay technique (QuantikineTM R &D system).

(8) sICAM-1 levels were determined by immunoenzymatic assay (Medgenix).

(9) sIL2R was assayed by enzyme immunometric assay (Milenia).

Data was analyzed using SPSS (Statistical Package for Social Sciences) version 10. Qualitative data was presented as number and percent. Chi square or Fisher's exact tests of significance were used for comparison between groups, as appropriate. Quantitative data was presented as mean ± standard deviation. Student's t test was used for comparison between groups. $P \leq 0.05$ was considered to be statistically significant.

RESULTS

Table (1) illustrates the sociodemographic and clinical features of studied patients. Fourteen patients were males and twenty-five were females, their ages ranged from 22 to 80 years (mean 44.7 ± 12.7). As regard the skin lesions, all patients presented with palpaple purpura. Other skin lesions in descending order of frequency were purpuric macules, haemorrhagic vesicles, plaques, pustules and ulcers. Clinical examination of test group revealed shrunken liver in 7(17.8%) , Enlarged in 8(20.5%) and normal in (61.5% while splenomegally was present in 8 (20.5%), oedema L.L. was detected in 4(10.3%) ascitis present in 3(7.7%) and Jaundic was present in 7 (17.9%) of the studied LcV patients. Nineteen patients (48.7%) had arthralgia and 13 patients (33.3%) had associated weakness.

Of the 39 studied LcV patients, 13 (33.3%) had high liver enzymes (ALT and AST) in comparison to 10% of the controls (P=0.011) while serum bilirubin was elevated in 8 (20.5%) in LcV patients compared to non of control. The prevalence of HCV positive antibodies was 46.2% in LcV patients versus 17.5% of the controls. The difference was statistically significant (P=0.006). On the other hand, with PCR only 38.5% of LcV patients were infected with HCV versus 12.5% of the controls (P=0.008). Mixed cryoglobulinaemia was detected in 8 (20.5%) LcV patients versus none of the controls (table 2).

Clinical examination of 15 (38.5%) patients with LcV and PCR+ve revealed significant changes of liver

size (shrunken liver 7(46.7%) Enlarged liver 6 (40%)), splenomegally 8 (53.3%), oedema L.L. 4(26.7), Ascitis 3(20%) and Jaundice 7 (46.7%) in those patients compared to patients with LcV and PCR –ve (table 3). Of the 15 patients with positive PCR for HCV, 12 (80%) had high ALT and AST, 8 (53.3%) had high serum bilirubin and 8 patients (53.3%) had +ve cryoglobulinaemia. Liver enzymes, serum bilirubin and cryoglobulinaemia were significantly higher in LcV patients with positive PCR than LcV patients with negative PCR (table 4).

Regarding the immunological changes among studied patients, we found that, serum TNF- alpha, IL-8, sICAM-1 and sIL-2R were significantly higher in LcV patients than controls (table 5). Furthermore, the proinflammatory cytokines TNF-alpha and IL-8 as well as sICAM-1 and sIL-2R were significantly higher in LcV patients with positive PCR for HCV than PCR negative patients (table 6).

Table (1): Sociodemographic and clinical features of studied patients

	Number	%
Sex: Male	14	35.9
Female	25	64.1
Age: Min – Max	22-80	
Mean ± SD	44.7±12.7	
Skin lesions #:		
Plapaple purpura	39	100
Purpuric macules and patches	27	69.2
Haemorrhagic vesicles	9	23.1
Haemorrhagic plaques	8	20.5
Pustules	4	10.2
Ulcers	4	10.2
Distribution of Lesions #:		
Legs	32	82.1
Feet	20	51.3
Thighs	16	41.02
Buttocks	11	28.2
Generalized	7	17.9
Forearms	6	15.4
Abdomen	4	10.3
Attack of vasculitic skin lesions:		
First attack	13	33.3
Recurrent	26	66.7
Liver (clinically):		
Normal	24	61.5
Enlarged	8	20.5
Shrunken	7	17.9
Splenomegally	8	20.5
Jaundice	7	17.9
Oedema L.L.	4	10.3
Ascitis	3	7.7
Arthralgia: -ve	20	51.3
+ve	19	48.7
Weakness: -ve	26	66.7
+ve	13	33.3
History of bilhariziasis: -ve	31	79.5
+ve	8	20.5

Figures are not additives

Table (2): Results of laboratory tests among patients & control

	LcV (39)		Control (40)		Sign. Test
	N	%	N	%	
ALT(SGPT): Normal	26	66.7	36	90	χ^2 =6.37,P=0.011
High	13	33.3	4	10	
AST(SGOT): Normal	26	66.7	36	90	χ^2 =6.37,P=0.011
High	13	33.3	4	10	
S. bilirubin: Normal	31	79.5	40	100	FET, P=0.0024
High	8	20.5	0	0	
HCV Ab +ve	18	46.2	7	17.5	χ^2 =7.5,P=0.006
-ve	21	53.8	33	82.5	
HCV PCR +ve	15	38.5	5	12.5	χ^2 =7.04,P=0.008
-ve	24	61.5	35	87.5	
Cryoglobulinaemia:+ve	8	20.5	0	0	FET,P=0.0024
-ve	31	79.5	40	100	

FET= Fisher exact test

Table (3) Comparison of Clinical Data among LcV patients with PCR positive Vs PCR negative.

	PCR+ve (15)		PCR-ve (24)		Sign. Test
	N	%	N	%	
Liver					
Normal	2	13.3	22	91.7	Normal Vs abnormal
Abnormal					χ^2 =23.9, P=0.000
Enlarged	6	40	2	8.3	
Shrunken	7	46.7	0	0	
Splenomegally					
+ve	8	53.3	0	0	FET, P=0.0001
-ve	7	46.7			
			24	100	
Jaundice					
+ve	7	46.7	0	0	FET, P=0.0001
-ve	8	53.3	24	100	
Oedema L.L.					
+ve	4	26.7	0	0	FET, P=0.017
-ve	11	73.3	24	100	
Ascitis					
+ve	3	20	0	0	FET, P=0.05
-ve	12	80	24	100	

FET= Fisher exact test

Table (4): Comparison between laboratory tests among LcV patients with PCR positive Vs PCR negative.

	PCR +ve (15)		PCR -ve (24)		Sign. Test
	N	%	N	%	
ALT(SGPT): Normal	3	20	23	95.8	χ^2 =23.89,P=0.000
High	12	80	1	4.2	
AST(SGOT): Normal	3	20	23	95.8	χ^2 =23.89,P=0.000
High	12	80	1	4.2	
s. bilirubin: Normal	7	46.7	24	100	FET,P=0.0001
High	8	53.3	0	0	
Cryoglobulinaemia:+ve	8	53.3	0	0	FET,P=0.0001
-ve	7	46.7	24	100	

FET= Fisher exact test

Table (5): Cytokines, sICAM-1 and sIL-2R among studied patients and control

	LcV (39)	Control (40)	Sign. Test
	Mean ± SD	Mean ± SD	
TNF-α (pg/ml)	41.3±6.4	10.7±1.4	t=29.5,P=0.000
IL-8 (pg/ml)	40.6±7.1	12.5±2.4	t=23.7,P=0.000
sICAM-1 (pg/ml)	25.9±5.5	12.4±2.4	t=14.2,P=0.000
sIL-2R (pg/ml)	371.7±62.9	138.5±8.9	t=23.2,P=0.000

Table (6): Comparison of immunolgic changes between Lcv patients with and without positive PCR

	PCR +ve (15)	PCR -ve (24)	Sign. Test
	Mean ± SD	Mean ± SD	
TNF-α (pg/ml)	45.5±4.6	38.6±5.95	t=3.8,P=0.001
IL-8 (pg/ml)	44.9±8.4	37.8±4.4	t=3.5,P=0.001
sICAM-1 (pg/ml)	29.9±2.96	23.4±5.3	t=4.3,P=0.000
sIL-2R (pg/ml)	427.4±21.6	336.9±54.4	t=6.1,P=0.000

DISCUSSION

Hepatitis C is an important and common cause of chronic hepatitis and cirrhosis. Cutaneous manifestations may be the first sign of infection (6). It has become increasingly recognized that hepatitis C virus infection is a relatively frequent associated process in patients with vasculitis (4).

In the present study the prevalence of HCV antibodies was significantly higher in LcV patients than the controls (46.2% versus 17.5%, respectively). In another study in Egypt[15] including 19 LcV patients 36.8% were anti-HCV antibodies positive. In contrast, a study[16] in Turkey revealed a low prevalence of anti-HCV in LcV patients with no significant difference between patients and the control group. This difference may be attributed to very low prevalence of antibodies to HCV in general population in Turkey (0.3 – 1.8%) [17,18] in comparison to that of Egypt, one of the highly endemic areas of the world[5]. The prevalence rate ranges from 10% to 30% [19] in one study and 22.4% in another study [20] and in 17.5 % of our control. Considering this, it seems reasonable to investigate the presence of HCV in cases of LcV in Egypt.

In our study, 20% of LcV patients with positive PCR to HCV had normal serum liver enzymes (ALT and AST). This agrees with data reported by Bonkovsky and Mehta [5], who indicated that some patients with chronic HCV infection have persistently normal serum aminotransferases although they have evidence of persistent infection as shown by detectable HCV RNA. Also Duskeiko and Rizzeeto [21] reported that 25% to 50% of all patients with HCV have normal liver enzymes six months to one year after the onset of the disease. On the other hand in our study 80% of LcV patients with PCR +ve showed rise of ALT and AST with 53.3% of them showed rise of serum bilirubin and 53.3% had +ve cryoglobulinemia and also show significant liver changes (shrunken 46.7 and enlarged 40%), splenomegally 53.3% and ascitis 20% in LcV patients with PCR +ve compared to those with PCR-ve and so long as the usual presentation of chronic HCV infection in a majority of cases is mild [49] with minimal physical signs, slow course with mild to moderate elevation of transminases fluctuating over years and with Jaundice only in a minority of cases[50] and considering our results which show that half of our LcV with PCR

+ve patients show fairly advanced and active biochemical and clinical variety of HCV infection so we could agree with Cacoub and his colleagues[11] who suggested that LcV could be considered as a dermatologic sign of active and advanced liver disease in cases of HCV infection and with those Authors[3] who recommended thorough medical examination in patients with LcV with special stress on abdominal examination searching for the state of the liver and spleen and asking about the vast majority of our HCV infections that lack this LcV phenomenon?

HCV infection may be associated with numerous immune disorders[22] including development of autoantibodies, immune complex formation and deposition[23]. Mixed cryoglobulinaemia is one of the most frequent immunologic abnormalities[7]. In the present study, cryoglobulinaemia was detected in 20.5% of LcV patients, only in patients with positive PCR to HCV (53.3%). Nearly similar percentages of cryoglobulinaemia was previously detected in hepatitis C patients, 54% in one study [24] 36% and 40% in other studies [7,25].

In HCV the trigger of immunologic process leading to dermatologic manifestations are the activated T cells ($CD8^+$ cytotoxic T lymphocytes), cytokines, the expansion of certain B cells and also the generation of immuncomplexes and mixed cryoglobulinaemia manifested as various forms of cutaneous vasculitis [26-28].

General speaking the immunopathologic events that initiate the process of vascular inflammation and damage are unclear[29]. Upregulation of adhesion molecules and cytokine expression on endothelial cells and infiltrating inflammatory cells occur in most vasculitis syndromes [30]. They represent a key factor in the deposition of immune complexes [31]. Furthermore, the involvement of adhesion molecules and endothelial cell activation is documented in the pathogenesis of cutaneous LcV [32]. In our study, we investigated the possible role of cytokines such as TNF-alpha and chemokines (IL-8) in patients with LcV. Also sICAM-1 and sIL2R were chosen as markers of activated lymphocytes, monocytes and/or endothelial cells. Cryoglobulinaemia served as marker of B lymphocyte activation and formation of immuncomplex.

TNF-alpha upregulates the endo-

thelial expression of adhesion molecules[33]. This cytokine can enhance with different severity, immune complex induced lung and dermal vascular injury[34]. Furthermore, on exposure to TNF-alpha, endothelial cells, fibroblasts and other cells produce IL-8, which is one of the main chemoattractants for neutrophils[35]. The present study revealed increase circulating levels of TNF-alpha together with elevated levels of IL-8 in patients with LcV. These results highlight to the important pathogenic role of these cytokines in association with immune complex deposition with subsequent recruitment and activation of neutrophils in LcV. Moreover, we found that LcV patients with positive HCV infection had significantly higher TNF-alpha and IL-8 levels than non-infected LcV patients. This agrees with previous reports that indicated elevated levels of TNF-alpha[36] and IL-8 in HCV infected patients than normal healthy subjects [37].

Soluble ICAM-1 represents a fragment of surface expressed ICAM-1 from mononuclear cells and endothelial cells, which is shed after induction by cytokines, reflecting inflammation and endothelial damage [38,39]. The present study revealed that sICAM-1 levels were significantly higher in LcV patients than control. Furthermore, sICAM-1 levels were significantly higher in LcV patients with HCV infection than LcV patients without HCV infection. On concordance with previous reports, vasculitic patients that accompanied by cutaneous neutrophilic small vessel vasculitis, such as Henoch-Schonlin purpura, polyarteritis nodosa and Wegner's granulomatosis [40,41] had elevated levels of sICAM-1 in active phase of the disease [42-44].

It was found that ICAM-1 is induced on hepatocytes in the areas of inflammation in chronic hepatitis[39,45]. Furthermore, increased serum levels of sICAM-1 have been found in acute and chronic hepatitis[39] and in patients with HCV associated with cryoglobulinaemic vasculitis[46]. This can explain the higher levels of serum sICAM-1 in patients with positive HCV infection than LcV patients without infection in our study.

Activated lymphocytes and monocytes express IL2R. These receptors are shed on activation, and the soluble form of the receptor, sIL2R, indirectly reflects activation

of these cells[47]. In the present study, we found that sIL2R levels were significantly higher in LcV patients than the control. These results indicate that lymphocyte activation is likely to be operative during LcV, at least in activation and proliferation of B cell which is necessary for formation of immunoglobulin, subsequent immune complex formation and deposition which is essential in the pathogenesis of LcV. Similarly, the study of Papi et al [48] revealed significantly higher sIL2R in patients with cutaneous small vessel vasculitis than the control. Also high sIL2R during disease activity is reported in patients with cryoglobulinaemic vasculitis [46].

In our study, sIL2R levels were significantly higher in LcV patients with HCV infection than LcV patients without infection. This can be attributed to the presence of activated T and B lymphocytes that associates HCV infection[26]. Furthermore, increased serum levels of sIL2R have been found in acute and chronic hepatitis [47].

In conclusion, the high prevalence of HCV infection in studied patients highlights the importance to test for HCV infection in LcV patients especially in high endemic countries such as Egypt, even when there is no abnormalities of liver enzymes. While suggesting that LcV could be considered as a dermatologic sign of active and advanced liver disease in HCV infection and recommend good clinical examination for the state of the liver and spleen in those patients and asking for further researching to the vast majority of our HCV infections that lack this phenomenon? Also there is substantial evidence of the role of proinflammatory cytokines (TNF-alpha and IL-8) together with endothelial cell injury (high sICAM-1) in pathogenesis of this disease. Furthermore, lymphocyte activation (high sIL-2R) is likely to be operative during LcV and these immunological changes were more pronounced in LcV with HCV infection, which could help to understand the immunotropic and lymphotropic effect of this virus and asking about which could be a promise treatment for such patients immunotherapy or antiviral therapy?

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الإلتهاب الوعائى الجلدى : معدل إنتشار الفيروس الكبدى سى والكريوجلوبيولنيميا ودلائل النشاط المناعى

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كلية الطب - جامعة المنصورة

هناك دليل جوهرى أن الفيروس الكبدى سى متورط فى كثير من الأمراض الجلدية. ولهذا أجريت هذه الدراسة لتقييم معدل إنتشار العدوى بالفيروس الكبدى سى والكريوجلوبيولين لدى مرضى الالتهاب الوعائى الجلدى وكذلك لتقييم التغيرات المناعية المصاحبة لهذا المرض.

شملت الدراسة ٣٩ مريضاً بالغاً (١٤ ذكراً و ٢٥ أنثى وكان متوسط أعمارهم ٧ر٤٤ + ٧ر١٢ عاماً) يعانون من الالتهاب الوعائى الجلدى وكذلك ٤٠ شخصاً بالغاً من الأصحاء كمجموعة ضابطة. وقد تم تعيين مضادات الفيروس الكبدى سى فى مصل الدم باستخدام الجيل الثالث من اختبار الإليزا ثم تم عمل التفاعل البوليميريزى المتسلسل للمرضى وكذلك للمجموعة الضابطة الايجابيين لاختبار الإليزا. وتم قياس مستويات عامل النخر الورمى -ألفا والانترلوكين -٨ ومستقبلات الإنترلوكين -٢ الذائبة وايكام-١ الذائبة فى مصل الدم لدى المرضى وكذلك المجموعة الضابطة.

وقد أظهرت النتائج أن معدل إنتشار مضادات الفيروس الكبدى سى فى مرضى الالتهاب الوعائى الجلدى ٢ر٤٦٪ مقارنة ب ٥ر١٧٪ فى المجموعة الضابطة. وعند إستخدام التفاعل البوليميريزى المتسلسل وجد أن ٥ر٣٨٪ من مرضى الالتهاب الكبدى الوعائى لديهم العدوى بالفيروس الكبدى سى مقارنة ب ٥ر١٢٪ فى المجموعة الضابطة. وقد وجد الكريوجلوبيولين فى ٨ر٢٠٪ فى مرضى الالتهاب الكبدى الوعائى. وكذلك وجدت زيادات ذات دلالة إحصائية فى مستوى عامل النخر الورمى الفا والانترلوكين-٨ والايكام-١ الذائبة ومستقبلات الانترلوكين-٢ فى مصل مرضى الالتهاب الوعائى الجلدى مقارنة بالمجموعة الضابطة، وعلاوة على ذلك وجدت زيادة ذات دلالة راحصائية فى هذه التغيرات المناعية

فى مرضى الالتهاب الوعائى الجلدى المصابين بالالتهاب الكبدى سى مقارنة بالمرضى غير المصابين بالفيروس الكبدى سى.

وقد أظهرت هذه الدراسة أهمية الكشف عن الالتهاب الكبدى سى فى مرضى الالتهاب الوعائى الجلدى حتى اذا كانت أنزيمات الكبد طبيعية فى هؤلاء المرضى. كما تشير الزيادة فى مستويات عامل النخر الورمى -الفا والانترلوكين-٨ الى أهميتها ففى نشأة هذا المرض. كما أن زيادة الايكام-١ الذائبة فى مصل الدم تشير الى وجود تكسير فى الخلايا البطانية للأوعية الدموية. كما أن زيادة مستقبلات الانترلوكين-٢ الذائبة فى مصل الدم تشير الى وجود نشاط للخلايا الليمفاوية فى مرضى الالتهاب الوعائى الجلدى.