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Original article

Chronic urticaria: frequency of anti-HCV antibodies

Ijaz Ahmed, Zarnaz Wahid,* Zaffar Ahmed

Baqai Institute of Skin Diseases, Baqai Medical University, Karachi.
*Dow Medical College/Civil Hospital, Karachi.

Abstract

Background Urticaria is defined as a skin disorder, clinically characterized by the presence of transient erythematous itchy weals presenting as an acute or a chronic disease, which may be caused by a wide variety of factors. Among infectious causes, hepatitis B virus is a known cause of urticaria; it would not be surprising if hepatitis C virus turns out to be an important one as well. The current study was aimed to determine the frequency of anti-BCV antibodies and HCV RNA in patients with chronic urticaria and to study HCV as a cause of urticaria.

Patients and methods Of all the clinically diagnosed cases of chronic urticaria presenting in the outpatient department of Baqai Institute of Skin Diseases, patients fulfilling the inclusion criteria were enrolled in the study from 1st January, 2002 till 30th June, 2003 over a period of eighteen months. Patients belonging to either sex were aged 11 to 55 years. A written consent was taken from all the enrolled patients to carry out various blood tests. Sera of all the enrolled patients were tested for anti-HCV antibodies. Patients with positive enzyme-linked immunosorbent assay were also tested for viral RNA in their blood (polymerase chain reaction). Other relevant investigations were also carried out in seropositive patients i.e. liver function tests and ultrasound abdomen.

Results Of the 114 patients enrolled in the study, 51 (44.8%) were males and 63 (55.2%) females, the gender ratio being 0.8. The maximum age of presentation was 55 years while minimum was 11 years. Maximum number of patients was 21-30 years of age (42.1%). Fifteen patients (13.2%) were positive for anti-HCV antibodies, comprising 9 females (7.8%) and 6 (5.6%) males ($p<0.003$). Maximum number of these patients (7.1%) was aged 21-30 years. Five (4.4%) of these seropositive subjects were also positive for HCV RNA including three males (2.6%) and two (1.8%) females. Deranged liver function tests were a feature in only 2 of these patients.

Conclusion There may be a significant association of chronic urticaria with anti-HCV antibodies. Further studies are necessary to establish or refute an aetiopathogenetic role of HCV in this condition.

Key words
Hepatitis C virus, hepatitis B virus, urticaria, anti-HCV antibodies, seropositive

Introduction

Urticaria is defined as a skin disorder, clinically characterized by the presence of transient erythematous itchy weals presenting as an acute or a chronic disease, which may be caused by a wide variety of factors. Among infectious causes, hepatitis B virus (HBV) is a known cause of chronic urticaria; it would not be surprising if hepatitis C virus (HCV) turns out to

Address for Correspondence
Dr. Ijaz Ahmad,
36/2, Khayaban-e-Shujaat, D-H-A, Phase 5,
Karachi.
Ph # 021-584842, 021-5848454

be an important one as well.[1] However, the association of chronic urticaria and hepatitis C remains tenuous. An association of chronic urticaria with hepatitis "C" was initially based on case reports.[2] Numerous extrahepatic disorders have been recognized in association with HCV infection among which dermatological diseases occupy a central place. Cutaneous necrotizing vasculitis, mixed cryoglobulinemia, porphyria cutanea tarda and lichen planus are the major skin diseases frequently associated with HCV infection, but other skin disorders, such as Behcet syndrome, erythema multiforme and nodosum, malakoplakia, urticaria and pruritus may also be linked to hepatitis C.[3] Recent investigations suggest that two cutaneous diseases, lichen planus and porphyria cutanea tarda, may signal the presence of HCV infection.[4,5] European trials noted much lower rates of infection in patients with chronic urticaria.[6-8] Regarding dermatoses e.g., in lichen planus, the frequency of anti-HCV antibodies is 23.5% in our country;[9] however, the frequency of anti-HCV antibodies in chronic urticaria has not been studied previously. The current study was aimed to determine the frequency of anti-HCV antibodies and "HCV RNA" in patients with chronic urticaria and to study HCV as a cause of urticaria.

Patients and methods

Of all the clinically diagnosed cases of chronic urticaria presenting in the outpatient department of Baqai Institute of Skin Diseases (BISD), patients fulfilling the inclusion criteria were enrolled in the study from 1st January, 2002 till 30th June, 2003 over a period of eighteen months. Detailed history and clinical examination comprising skin, general and systemic examination was carried out and the findings were recorded on a preformed pro forma. A history of jaundice, blood transfusion, medical, surgical and dental procedures was also taken. Patients belonging to both sexes were aged 11 to 55 years. Patients suffering from chronic urticaria not responding to conventional therapy for a period of 6 weeks were enrolled. Patients with a history of jaundice, hepatitis, impaired liver function tests or a history of hepatotoxic drug intake were ruled out from the study. Patients with a history of urticarial drug eruption or any other evident cause of urticaria were also excluded. A written consent was taken from all these patients to carry out various investigations. Sera of all the enrolled patients were tested for anti-HCV antibodies. The enrolled patients with positive enzyme-linked immunosorbent assay (ELSA) were also tested for viral RNA in their blood (polymerase chain reaction). Other relevant investigations were also carried out in seropositive patients i.e. liver function tests and ultrasound abdomen. Liver biopsy was not performed in any of the subjects.

Results

Of the 114 patients enrolled in the study, 51(44.8%) were males and 63 (55.2%) females, the gender ratio being 0.8. The maximum age of presentation was 55 years while minimum was 11 years. The mean age of presentation was 34.8 years. The mean ages for males and females were 37.8 and 37.1 years, respectively. **Table 1** reveals that the maximum number of patients presented were 21-30 years of age (42.1%). **Table 2** shows that fifteen patients (13.2%) were positive for anti-HCV antibodies, comprising 9 females (7.8%) and 6 (5.6%) males ($p<0.003$). Maximum numbers of these patients (7.1%) were aged 21-30 years. Five (4.4%) of these seropositive subjects were also positive for "HCV RNA" including 3 (2.6%) males and 2 (1.8%) females. Deranged liver function tests were a feature in only 2 of these patients. Ultrasound examination of these patients didn't reveal any cirrhotic changes.

Table 1 Age and gender wise distribution of enrolled patients (n=114)

Age range (yrs)	*Male n (%)*	*Female n (%)*	*Total n (%)*
11-20	5 (4.4%)	9 (7.8%)	14 (12.2%)
21-30	23 (20%)	25 (22%)	48 (42.1%)
31-40	8 (7.2%)	11 (9.6%)	19 (16.6%)
41-50	9 (7.8%)	12 (10.5%)	21 (18.4%)
51-60	6 (5.2%)	6 (5.2%)	12 (10.5%)
Total	51 (44.8%)	63 (55.2%)	114

Table 2 Age and sex distribution of seropositive patients with urticaria (n = 114)

Age range (yrs)	*Male n (%)*	*Female n (%)*	*Total n (%)*
11-20	1 (0.9%)	1 (0.9%)	2 (1.8%)
21-30	3 (2.6%)	5 (4.4%)	8 (7.1%)
31-40	1 (0.9%)	1 (0.9%)	2 (1.8%)
41-50	-	2 (1.8%)	2 (1.8%)
51-60	2 (1.8%)	2 (1.8%)	2 (1.8%)
Total	6 (5.2%)	9 (7.8%)	15 (13.4%)

Discussion

Hepatitis C virus, also called "AIDS of 3rd world", is a single stranded "RNA" virus belonging to the family of viruses called *Togaviridae*.[9] HCV is a common problem worldwide in patients receiving blood transfusion. Injections, household contacts, sexual transmission and occupational contacts are the other risk factors for transmission of the disease.[10-12] The spectrum of hepatic disease ranges from acute to chronic hepatitis, cirrhosis and hepatocellular carcinoma. Among HCV positive subjects, 15% recover spontaneously and 25% have an asymptomatic disease.[13] Chronic hepatitis develops in 50%,[14] 15-25% patients with chronic liver disease[15] and 13-51% patients with carcinoma liver are seropositive.[16] Seroprevalence of anti-HCV antibodies among our normal population is 4-7%.[9,17] Prevalence rate among other groups stands as; blood donors 21%,[18] various surgical ailments 16.5%,[19] nephritic syndrome 68%,[20] hemodialysis 62%,[21] chronic liver disease 25%.[22] Regarding dermatoses lichen planus has a frequency of 23.5%.[9] Frequency of anti-HCV antibodies in our series was 13.4%. These figures are different from the past studies.[23,24] The frequency (13.4%) in our study indicates a significant association between chronic urticaria and anti-HCV antibodies. Five (4.4%) of the subjects positive for anti-HCV antibodies were also positive for HCV RNA including 3 (2.6%) males and two (1.8%) females. European trials noted much lower rates of infection in patients with chronic urticaria.[6-8] Cribier *et al*.[23] reported that chronic urticaria is not significantly associated with hepatitis C, as antibodies to HCV were found in 1 patient with chronic urticaria and in 1 of the control group (0.9% of each group). Thus, the frequency of anti-HCV antibodies was similar to those of the general population. Dega *et al*.[24] reported that among 1060 patients with hepatitis C followed in a hepatology unit, 26 patients had pruritus of which 5 had urticaria; one of these had leukocytoclastic vasculitis in the setting of cryoglobulinemia. Karlsberg *et al*.[25] did a systematic dermatological evaluation of 408 patients with hepatitis C: vasculitis was found in 10, only one of which had urticaria. In a Japanese study 24% (19/79) of patients with urticaria were seropositive.[26] Thus, it can be elucidated from these studies that the association of urticaria and hepatitis C remains tenuous. Whether the prevalence of HCV in chronic urticaria in other geographic areas is similar remains to be seen.[1] In the current study, (13.4%) patients were positive for anti-HCV antibodies. Anti-HCV antibodies are unlikely to be the cause of urticaria in these seropositive patients, because of the absence of HCV RNA and changes in liver function tests. Only (4.4%) had HCV RNA in their blood while deranged liver function tests were a feature in only 2 (1.8%) of these patients. Ultrasound examination

of the abdomen in patients with HCV RNA positive did not reveal any cirrhotic changes. Cribier *et al.*[23] claimed that hepatitis C virus is unlikely to be the cause of urticaria in the absence of HCV RNA and changes in liver function tests. Therefore, in our study despite a significant frequency of anti-HCV antibodies in patients with chronic urticaria, HCV may not be the underlying cause.[23] As the number of patients infected with the hepatitis C virus (HCV) continues to increase, early diagnosis remains paramount. Recent investigations suggest that two cutaneous diseases, lichen planus[27-29] and porphyria cutanea tarda[9] may signal the presence of HCV infection. Chronic urticaria may also be significantly associated with hepatitis C virus infection.

Conclusion

There may be a significant association of urticaria with anti-HCV antibodies. Patients with acute or chronic urticaria of undetermined origin be tested for HCV if features of the presentation or epidemiology raise the level of suspicion.

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