

HEPATITIS PRESENTING AS TRANSIENT URTICARIA

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Abstract. Attention is drawn to 7 cases of hepatitis which were preceded by an acute urticaria. In all but one there was a free interval of $1\frac{1}{2}$ - $2\frac{1}{2}$ weeks between rash and icterus. Different types of hepatitis were represented in the material.

In many cases of acute urticaria an allergic pathogenesis may be demonstrated. Usually, the rash disappears in a matter of days with or without treatment and patient stays well if he is able to avoid contact with the allergen.

Sometimes, however, the acute urticaria is part of an infectious process. This has been observed, for example, in connection with infectious mononucleosis (1, 4, 10, 11), infection with Coxsackie A 9 virus (3), and with viral hepatitis (2, 5, 6, 7, 8, 9, 12, 14, 15). Urticaria developing during the icteric phase of a viral hepatitis is a well-known phenomenon (15). Although it has been reported, hepatitis starting with urticaria is much less frequent. Thus, we thought it warranted to describe 7 such cases.

CASE REPORTS

Case 1. Female, worker, 18, with a history of penicillin hypersensitivity and urticaria. In May 1968 acute urticaria treated with antihistamines orally. Two weeks later, when the eruption had cleared, abdominal pain, nausea and arthralgia. Slight rise of rectal temperature at hospitalization. Icteric sclerae and skin. The liver enlarged and somewhat painful, disturbed hepatic laboratory tests. After a short remission, disease course aggravated 3 weeks later with renewed icterus and raised SGOT and SGPT. Symptom-free when leaving hospital in July. The patient was a narcotic addict, had 3 months previously given herself an injection. Diagnosis: Serum hepatitis.

Case 2. Female, hospital aid, 18. Contraceptive pills since May because of dysmenorrhoea. One week after returning from holidays in Italy in August 1969 (gamma-globulin prophylaxis before the trip), acute urticaria of head, abdomen and thighs, later also with edema of hands

and fingers. Treated 1 week after falling ill with ACTH (Reactin®,—Ico, Hälsingborg, Sweden) and cyproheptadine (Periactin®,—MSD, New York, USA). Rash and acral edema disappeared and were replaced by arthralgia of fingers and knees, and epigastric pain. Slight but prolonged elevation of temperature. Some days later purpura of insteps and lower legs, and icterus. Liver laboratory tests pathological, transient thrombocytopenia, and changes of serum proteins of the hepatitis type in the serum electrophoresis. Left hospital after 2 weeks with decreased SGOT and SGPT. Rehospitalized 2 weeks later because of relapsing hepatitis. The patient had worked throughout the spring at the coagulation laboratory. Diagnosis: Probably serum hepatitis, but a hepatitis caused by contraceptive pills cannot be excluded.

Case 3. Male, hair-dresser, 19. In June 1969 two attacks of acute urticaria separated by a few days. When hospitalized, wheals on the face, trunk and extremities. Temperature 39.2°C but no icterus. Hives disappeared after a few days with prednisolone and cyproheptadine (Periactin®). Liver function tests pathological 10 days after the first rash; the liver enlarged and painful. Clinical recovery with normalization of hepatic laboratory tests. Again symptoms of hepatitis in January 1970, this time without preceding cutaneous disease. The patient denied abuse of narcotics but was known among addicts. Diagnosis: Probably serum hepatitis.

Case 4. Nurse, 22. Acute urticaria and arthralgia June 15, 1969, treated with injections of calcium salts and antazolin (Antasten®,—CIBA, Basel, Switzerland). Ten days later still extensive urticaria with slight lip edema. Treated with cyproheptadine (Periactin®), rash and arthralgia disappeared. On June 29 nausea, right abdominal pain and slight temperature rise. Icterus followed soon, with pathological liver lab. tests, and a serum electrophoresis consistent with hepatocellular damage. Uncomplicated course with normal lab. tests 6 weeks from start. (Another nurse from same department fell ill in hepatitis a few days later.) Diagnosis: Serum hepatitis?

Case 5. Female, shop assistant, 23. Contraceptive pills for 2 years. In December 1969 herpes genitalis and gonorrhoea. Gonococci with decreased sensitivity to penicillin, repeated penicillin injections for 6 weeks. Four days after the last treatment acute urticaria with spontaneous remission within a week. At that time interpreted as a possible penicillin hypersensitivity. The culture for gonococci still positive, no fever or arthralgia, no abdominal

Table I. Clinical symptoms and maximal laboratory values in 7 patients with hepatitis preceded by urticaria

SH = serum hepatitis, IH = infectious hepatitis

Case no.	1	2	3	4	5	6	7
Age	18	18	19	22	23	34	41
Sex	F	F	M	F	F	M	M
Time from onset of urticaria to onset of jaundice	3 w.	2 w.	2 w.	2 w.	1½ w.	3 w.	1 w.
Symptom-free interval	1 w.	1 w.	1 w.	—	½ w.	2½ w.	2 d.
Joint pains	+	+	—	+	—	+	(+)
Gastro-intestinal symptoms	+	+	—	+	—	+	+
Fever (at onset of jaundice)	+	+	+	+	—	+	+
Serum bilirubin, mg%	5.6	6.5	4.8	8.7	2.8	3.1	5.0
Alkaline phosphatase, U	17	11	18	15	6	16	13
Thymol, ext.	0.36	0.63	0.52	0.43	0.55	0.46	0.39
SGOT, U	1 470	2 250	850	1 330	360	825	1 265
SGPT, U	1 434	2 350	1 475	1 030	1 700	2 000	2 150
SGT, U	393	110	280	—	100	1 470	420
Type of hepatitis	SH	SH?	SH?	SH?	IH?	IH?	SH

complaints. Liver tests pathological 10 days after eruption with urticaria. Hepatitis pattern in serum electrophoresis; Au-antigen not present. Two weeks after leaving hospital increasing SGOT and SGPT, normalized 2½ months later. Diagnosis: Hepatitis, possibly infectious.

Case 6. Male, builder, 34, previously a heavy alcohol consumer. In February 1969 a generalized exanthema, probably a toxicoderma caused by acetylsalicylic acid/quinine chloride (Chinaspin®,—Bayer, Leverkusen, GFR). In August acute urticaria, mainly on pressure sites, and a Quincke-type edema of the right arm. One week later arthralgia in shoulders, wrists and fingers, treated with acetylsalicylic acid (Magnecyl®,—ACO, Stockholm, Sweden). Hospitalized 2 weeks later with fatigue, a rectal temperature of 38.2°C, and slight icterus, but no hives. Crude needle liver biopsy: hepatic changes. Liver function tests pathological and stationary for 1 month, motivating corticosteroid therapy. Normal lab. tests 2 weeks later, treatment discontinued. Two to three months previously, the patient had met a brother who had contracted enteritis in Biafra. Diagnosis: Infectious hepatitis?

Case 7. Male, typographer, 41. Acquired multiple fractures in an air crash in June 1969. Developed oliguria and uremia, was repeatedly hemodialysed and received whole blood transfusions. Acute urticaria on thighs and back in September, followed the next day by swelling of lips and eye-lids. Slightly raised rectal temperature, nausea and arthralgia. One week later dark urine, light-coloured stools and icteric sclerae. Pathological liver tests, somewhat normalizing 1 week later. Serum electrophoresis typical hepatitis pattern. Increasing SGOT and SGPT after leaving hospital, entirely normal 2 months from start. Diagnosis: Serum hepatitis.

Summing up, 3 of the patients were males and 4 were females, between the ages of 18 to 41 years (Table I). Five of the cases occurred during

a time period of four summer months. Only one patient had an allergic history (penicillin hypersensitivity). The urticaria started 1–3 weeks before the appearance of icterus and the duration was 1½–2 weeks. There was a free interval between urticaria and icterus in all cases but one. The skin changes included purpura in 1 case. Several of the patients had joint pains before the hepatitis became manifest. In 2 cases the urticaria receded during treatment with corticosteroids and antihistamines, in 2 cases with antihistamines only, and in 3 cases spontaneously. The clinical diagnosis was serum hepatitis in 5 patients, and infectious hepatitis in two.

DISCUSSION

One type or other of cutaneous eruption appears during the course of many cases of hepatitis, with some predominance of serum hepatitis (9, 12, 13, 14). Thus, Findlay et al. (7), in a thorough study of 432 cases of hepatitis following vaccination against yellow fever, observed 24 patients (5.5%) with some type of rash accompanying the disease. In 16 patients the rash was urticarial, and in 9 of these (2.1%) the urticaria was the presenting sign. In 6 of these 9 cases there was a free interval of 2–6 days between urticaria and icterus, not so in the other 3 cases. It is noteworthy that in the present material (Table I) the free interval was comparatively longer. Mirick & Shank (12),

in a controlled study of 750 serum inoculated subjects of whom 302 developed serum hepatitis, noted urticaria as the presenting symptom in 15%. Actually, urticaria occurred about equally in all inoculated patients, whether they contracted hepatitis or not. Ford (8) observed urticaria in the prodromal phase of hepatitis in 2 out of 300 patients.

Eeckhoutte (6) described 2 patients hospitalized together and receiving the same type of injection therapy. Six weeks later both of them developed hepatitis, in one preceded by urticaria during 3-4 days, in the other by severe arthralgia for a few days. Crismer (5) reported on a woman who during the course of 5 months fell ill, first with an infectious hepatitis, later with a post-transfusion serum hepatitis. Both times the liver disease was preceded by urticaria and arthralgia. This may be interpreted as if two different hepatitis viruses, infecting one and the same patient, are capable of inducing identical urticarial prodromes. On the other hand, a certain hepatitis virus may provoke urticaria in one patient, and arthralgia in another. The urticarial reaction pattern thus appears connected with the infected individual, and not with the viral strain. Sometimes, however, a hepatitis virus may induce urticaria only (12).

Apparently, the syndrome of urticaria followed by icterus, both expressions of hepatitis, occurs more frequently than earlier believed. It has been noted (12) that the frequency of urticaria in non-icteric cases of hepatitis is not less than in the icteric ones. As a consequence, a laboratory follow-up including a liver profile of all cases of acute urticaria should be seriously considered. Hereby it would be possible to diagnose some cases of hepatitis at an earlier stage, and perhaps even reveal abortive cases which otherwise had escaped notice.

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