Hepatitis A Associated with Other Focal Infections

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Abstract

Background: Concomitant bacterial and viral infection is a well-known phenomenon, however only very rarely has a bacterial infection been reported during hepatitis A virus infection.

Objective: To evaluate retrospectively the clinical records of children hospitalized with HAV infection for a concomitant infection proved or presumed to be bacterial.

Method: A retrospective study was conducted on all the children hospitalized with hepatitis A infection from 1988–96 in our center. The records were evaluated for a concomitant infection.

Results: Of 40 children hospitalized with HAV infection, 13 were found to have a concomitant infection: these included 6 with pneumonia, 4 with pyelonephritis and 1 case each of purulent otitis media, osteomyelitis and staphylococcal bacteremia.

Conclusion: In areas where hepatitis A is endemic, a simultaneous infection with hepatitis A and other common bacterial infection during childhood may co-exist. A permissive role for HAV infection is suggested.

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The co-existence of viral and bacterial infections is a well-known phenomenon. However, only very rarely has bacterial infection been reported during hepatitis A virus infection [1,2]. The diagnosis of pneumonia during HAV infection in two children within 2 months led us to review our hospital's patient records of 7½ years to identify children with concomitant HAV and bacterial infection. We found another 11 children who had had a concomitant infection. We report the clinical and laboratory findings of these 13 children and discuss the permissive role of hepatitis A infection in the development of these infections.

Patients and Methods

Two hospitalized children with concomitant HAV infection and pneumonia were diagnosed in January and February 1996. This led to a retrospective study of all the children diagnosed with HAV infection from 1 July 1988 to 31 December 1995. Data were collected from computerized patient records and from the laboratory records.

Results

During this 7½ year period, 40 hospitalized children were diagnosed with acute HAV infection. Diagnosis was made in children with hepatitis in whom anti-hepatitis A virus IgM antibodies were found. In 11 children a concomitant infection proven or presumed to be bacterial was found (supported by X-ray findings, elevated erythrocyte sedimentation rate and C-reactive protein, and high white blood cell count with a shift to the left) [Table 1]. There were 12 girls and 1 boy, whose ages ranged from 1.5 to 10.5 years (mean age 4.5 years).. *Staphylococcus aureus* was isolated in one blood culture and *Escherichia coli* in four urine cultures [Table 1].

Discussion

Hepatitis A is a common illness in Israel and has a variable symptomatology. In addition to the classical features of acute hepatitis, other problems may manifest. These include nephritis and renal failure in non-fulminant hepatitis [3,4], myocarditis pericarditis and pleural effusion [5,6], as well as pancreatitis [7] and vasculitis [8].

Epidemiological and experimental data suggest the co-existence of viral and bacterial infection [9]. The altered immunity that develops during the prolonged incubation period of viral infection may expose the host to secondary bacterial invasive diseases. Several mechanisms may play a role. Among these are defective Kupffer cell function, and reduced chemotaxis and myeloperoxidase activity, which could be due to a direct effect of the virus or mediated by the cytokines released upon a viral infection [10–12]. Another effect, as reported by Rajkovic and Williams [13], is reduced levels of serum complement, particularly in early stages of acute viral hepatitis. Impaired opsonization of *S. aureus* by serum of patients with acute viral hepatitis was found by Saunders et al. [14].

The presence of the HAV in respiratory secretions may trigger an inflammatory process in the respiratory epithelium and may result in impairment of the local barrier and facilitation of concomitant bacterial infection [15]. A similar mechanism may explain the development of

HAV = hepatitis A virus

Table 1. Concomitant bacterial and HAV infection

Age/Gender	Diagnosis	HAV (IgM)	ALT (IU)	Bil. (μmol/L)	Fever (°C)	ESR (1 h)	WBC (mm^3)	Main complaint	Hepatitis phase
4 yr/F	LLL pneumonia	+	470	NR	40	NR	27,000	Fever, cough, chest pain	Non-icteric
3 yr/M	LLL pneumonia	+	387	95	39	100	26,000	Fever, vomiting	Icteric
*3.5 yr/F	RML+RLL pneumonia	+	N	N	40	50	19,000	Fever, apathy	Post-icteric
2.5 yr/F	LLL pneumonia	+	600	108	40	30	8,200	Fever, cough	Icteric
3.5 yr/F	RLL+RML pneumonia	+	330	90	39	NR	10,500	Fever, cough	Icteric
1.5 yr/F	LLL+RML pneumonia **	+	300	95	40	120	18,000	Fever, cough	Icteric
10 yr/F	*S. aureus* bacteremia	+	322	194	40	NR	7,200	Fever, vomiting	Icteric
1.5 yr/F	Osteomyelitis	+	442	N	40	40	16,000	Fever, reduced movement of Rt. hand	Non-icteric
9 yr/F	Purulent OM	+	2,000	50	38.8	75	8,000	Ear discharge	Icteric
1.5 yr/F	Pyelonephritis (*E.coli*) SPA	+	180	56	40	125	29,000	Fever, cough, vomiting	Icteric
6 yr/F	Pyelonephritis (*E.coli*)	+	145	313	39	115	10,300	Fever, vomiting	Icteric
5 yr/F	Pyelonephritis (E.coli)	+	2,200	N	40	35	12,600	Fever, cough, dysuria	Non-icteric
9 yr/F	Pyelonephritis (*E.coli*)	+	200	100	40	45	6,800	Fever, vomiting, abd. pain	Icteric

* On recovery from hepatitis
** With pneumatocele
RML = right middle lobe, NR = not reported, ALT = alanine aminotransferase, OM = otitis media, Abd = abdominal, Bil. = bilirubin, LLL = left lower lobe, SPA = supra-pubic aspiration

urinary tract infection since the HAV is isolated from urine [15].

Extensive search of the literature with Medline revealed only two reports of concomitant HAV and bacterial infection [1,2]. A single case report describes a child with HAV infection and parotitis, and one study demonstrated a rise in anti-staphylococcal antibodies during hepatitis A and B infection in adults [2]. Nevertheless, secondary bacterial infection during fulminant hepatitis is known to have a deleterious effect. O'Grady and Williams [10] reported the occurrence of localized infection and septicemia in patients with fulminant hepatitis of various causes, while Wyke et al. [16] found a bacteremia rate of 23%, mostly gram-positive, among 103 patients with fulminant liver failure due to hepatitis.

Our study lends some support to the aforementioned report describing an increase in anti-staphylococcal antibodies during hepatitis A infection in adults. One child in our study had *S. aureus* bacteremia and two had probable *S. aureus* infection – one with osteomyelitis and the other with pneumonia and a pneumatocele.

The characteristic presenting symptoms of HAV infection in another study included abdominal pain (in 65%), involvement of the upper respiratory system (up to 7%) and musculoskeletal pain (up to 69%) [17]. Vomiting, cough, abdominal or musculoskeletal pain may herald pneumonia, pyelonephritis and osteomyelitis. Thus, superimposed bacterial infection may mimic the clinical picture of HAV. If unrecognized, appropriate treatment will be delayed.

In our study, the concomitant bacterial infection occurred at different stages of HAV disease: in the unicteric stage (n=3), during florid hepatitis and jaundice (n=9), and in the immediate recovery phase (n=1). The female predominance in our group may be partially explained by the four girls with urinary tract infection, a disease known to have a female predominance.

Based on our experience we suggest that in areas where hepatitis A is endemic, a simultaneous infection with hepatitis A and other common bacterial infection during childhood may co-exist.

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