

Laboratory and Epidemiology Communications

Acute Hepatitis Outbreak in Tokyo Caused by Hepatitis A Virus of Common Origin Transmitted through Oral and Sexual Routes

Masashi Baba, Hiroyuki Oka, Masako Asayama, Syuya Yoshinaga, Hiroko Yamashita, Natsuo Tachikawa¹, Jun-ichi Akiyama, Akira Yasuoka¹, Shin-ichi Oka¹, Shigeru Yamato, Ryosuke Shoda, Toru Muraoka, Naohiko Masaki, Kei Matsueda, Emi Shimojo and Shigeki Hayashi*

Department of Gastroenterology and ¹AIDS Therapy and Research Center, International Medical Center of Japan, Toyama 1-21-1, Shinjuku-ku, Tokyo 162-8655

Communicated by Hiroshi Yoshikura

(Accepted June 22, 2000)

Hepatitis A virus (HAV) is transmitted by fecal-oral routes. Outbreaks can occur in families (1) and among homosexuals (2). Infection acquired by ingestion of infected clams or oysters is frequent (3). Japan experienced large outbreaks in 1990 and 1991. One hundred and eighty-seven cases were reported at

national hospitals in 1990 and 115 cases were reported in 1991. The number of HAV cases gradually declined after 1991 and in 1995-1998, only 20-50 cases were reported annually.

In 1999, an unusually large number of HAV-infected patients visited our clinic: three patients were seen in January-March, four patients in May-June, five patients in July-September, and two patients in October-December. Patients' clinical

*Corresponding author: E-mail: shayashi@imcj.hosp.go.jp

Table 1. Patients' characteristics

Patient	Age	Date of Onset ¹⁾ (duration)	Severity ²⁾	Suspected route ³⁾	Other markers
1	26	2/07 (26)	-	sexual	HBsAg(+), HBeAg(+) HIV(+)/asymptomatic
2	40	3/07 (54)	-	shellfish	(-)
3	43	3/26 (78)	+	oyster	(-)
4	37	4/03 (40)	-	oyster	(-)
5	42	4/25 (28)	-	unclear	(-)
6	20	6/15 (34)	-	unclear	(-)
7	27	6/29 (27)	-	sexual	HBeAb(+), HBeAg(-)
8	35	7/06 (103)	-	shellfish	(-)
9	30	7/07 (22)	-	unclear	(-)
10	37	7/23 (82)	-	unclear	HBeAb(+), HBeAg(-)
11	41	8/28 (22)	-	shellfish	(-)
12	47	9/18 (23)	-	unclear	(-)
13	34	10/06 (35)	-	sexual	HBeAb(+), HBeAg(-) HIV(+)/asymptomatic
14	55	12/21 (30)	+	oyster	(-) Acute renal failure

¹⁾Month/Day (Days from onset of illness to return of alanine aminotransferase levels below 100).

²⁾Criteria of severity was a prothrombin time below 40% and/or presence of other serious complications. +: severe cases. -: not severe cases.

³⁾Route of infection was deduced from circumstantial evidence, for example, homosexuality, ingestion of clams or oysters, travel abroad, etc.

Table 2. Laboratory findings

Patient	T.Bil. (mg/dl)	D. Bil. (mg/dl)	AST (IU/l)	ALT (IU/l)	LDH (IU/l)	ALP (IU/l)	γ-GTP (IU/l)	PT (%)	HA IgM (C.O.I.)
1	2.2	1.1	467	1194	298	492	184	95.0	4.4
2	1.7	1.0	885	1842	498	1198	1281	73.5	3.9
3	8.1	6.1	4042	5264	1440	589	324	36.6	5.2
4	8.5	6.0	1078	5090	547	449	313	40.3	5.3
5	5.6	3.5	2370	4540	1210	1068	522	78.0	5.3
6	11.4	7.5	174	708	223	625	61	92.0	5.8
7	4.5	3.5	1798	1790	400	457	270	79.0	5.4
8	5.8	4.0	1154	2666	304	728	316	82.0	5.5
9	9.3	8.3	517	1479	759	676	179	99.1	4.9
10	15.0	11.8	505	1058	714	1401	412	81.7	
11	1.0	0.5	121	770	234	1003	179	95.0	5.6
12	7.9	5.2	774	2137	398	587	327	93.7	5.2
13	8.1	5.6	1476	2961	469	577	335	71.4	5.8
14	8.1	6.9	12257	9857	8192	852	266	48.7	4.7

T. Bil.: Total bilirubin
ALT: Alanine aminotransferase
γ-GTP: γ-glutamyl transpeptidase
C.O.I.: Cut-off index

D. Bil.: Direct bilirubin
LDH: Lactate dehydrogenase
PT: Prothrombin time

AST: Aspartate aminotransferase
ALP: Alkaline phosphatase
HA IgM: Anti-HA IgM Antibody

profiles and laboratory findings are shown in Tables 1 and 2.

VP1-2A region of HAV was PCR-amplified from ten serum/plasma preparations. Among them, eight sequences (patients 1, 2, 4, 8, 9, 10, 11 and 13) were identical. HAV from patient 7 was different from that of the others, but by only one transitional base change. Thus, these nine patients were considered to have been infected by a strain of HAV of the same origin. The sequence had a homology to the HAV IB group, GBM strain, which caused a large outbreak in Germany in 1997. HAV from patient 3 had a quite different sequence; the sequence was close to that of the IA group, which caused outbreaks in Japan in 1990-1991.

In the previous outbreaks in 1990 and 1991, the infection was clustered in January-April. In 1999, however, infection was distributed evenly throughout the year. In 1990-1991, infected oysters or clams were the most likely major sources of infection, whereas in 1999, infections contracted via sexual and other routes were observed. A similar situation has been reported (4).

REFERENCES

1. Frosner, G. G., Overby, L. R., Flehmig, B., Gerth, H. J., Haas, H., Decker, R. H., Ling, C. M., Zuckerman, A. J.

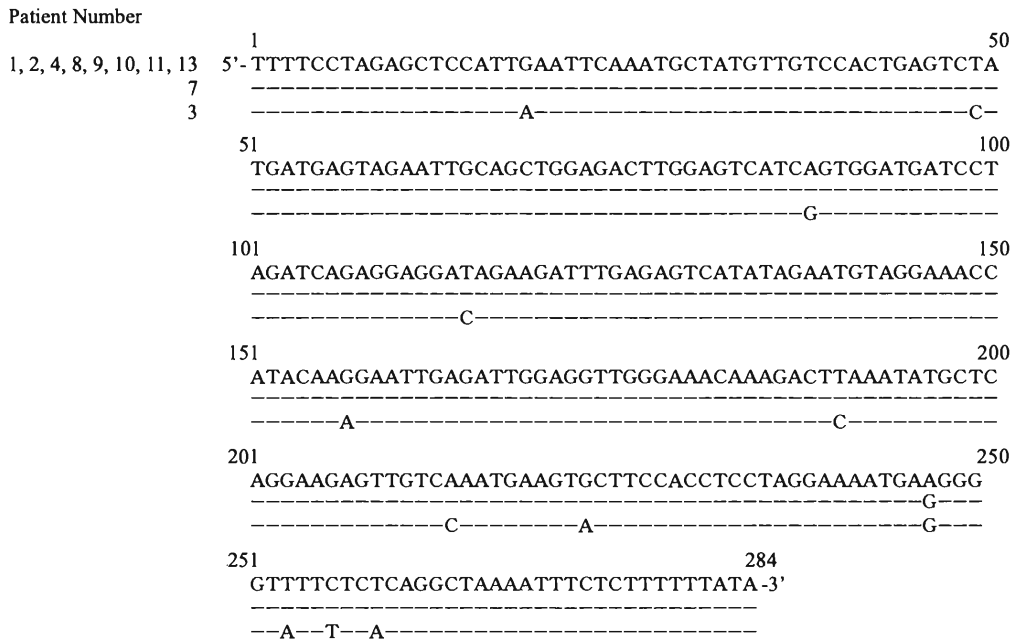


Figure. Sequence of the HAV VP1-2A region amplified by PCR.

RNA was extracted from 80 μ l of serum or plasma preparations by using Sumai-test (Sumitomo, Tokyo). VP1-2A region was RT-PCR-amplified with external PCR primers, 5'-GGTTTCTATTCAGATTGCAAATTA-3' and 5'-AGTAAGAACTCCAGCATCCATCTC-3' and internal primers, 5'-TTTAGTTGTTATTTGTCTGTC-3' and 5'-CATTATTCATGCTCCTCAG-3'. PCR products were purified by Wizard[®]PCR prep (Promega, Madison, Wis., USA) and sequenced by Bigdyeterminatorcycle sequencing ready reaction kit (ABI Ltd.). The sequences were analyzed by Neighbour-Joining method by using CLASTAR W software.

and Frosner, H. R. (1977): Seroepidemiological investigation of patients and family contacts in an epidemic of hepatitis A. *J. Med. Virol.*, 1, 163-173.

2. Corey, L. and Holes, K. K. (1980): Sexual transmission of hepatitis A in homosexual men. *N. Engl. J. Med.*, 302, 435-438.

3. Mitchell, J. R., Presnell, M. W., Atkin, E. W., Cummins,

J. M. and Liu, O. C. (1966): Accumulation and elimination of poliovirus by the Eastern oyster. *Am. J. Epidemiol.*, 84, 40-50.

4. Gust, I. D. and Feinstone, S. M. (1988): Epidemiology. p.163-192. *In* Boca Raton, F. F. (ed.), *Hepatitis A*. CRC Press, Inc., Boca Raton, Fla., USA.