Observations on 10 years' HBs antigenaemia after renal transplantation

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SUMMARY A renal transplant patient became a carrier of HBs Ag within four weeks of a successful transplant. The level of antigenaemia was extremely high, and approximately 3% of the particles were 42 nm Dane particles, although anti-HBe was present from at least 20 months after transplant.

After four years the antigenaemia declined to a low level, and five years later HBs Ag became undetectable for the first time. During the past 18 months no antigen has been detected although immunosuppression continues and the original kidney is still functional.

It has been possible to record in detail a renal transplant patient with HBs antigenaemia from before the onset until the cessation of carriage while he remained on immunosuppression and retained the transplanted kidney for 12 years.

Case report

A man aged 35 received a cadaver kidney on 6 August 1968 which was rejected and removed on 9 September 1968. After bilateral nephrectomy on 14 October 1968 he was given a second cadaver kidney on 9 November 1968. He became a carrier by 5 December 1968 and his level of antigenaemia was subsequently found to be very high. His renal function recovered well and he was discharged on 24 December 1968, since when he has remained well with good renal output. His early history was recorded in 1970.¹

Methods

The extent of HBs antigenaemia was initially measured by the complement fixation test (CFT) which was replaced by the introduction of the reverse passive haemagglutination test (RPHA) in 1974.² The RPHA test (Hepatest, Wellcome Reagents Ltd) titres are about two- to fourfold higher than those of the CFT with this patient, which compares well with observations on other *ad* subtype carriers.³

The radioimmunoassay test (RIA) used was Ausria II (Abbot Laboratories Ltd).

The proportion of 42 nm HBs antigen (Dane) particles was derived from counts made on electron micrographs of centrifuged antigen in serum samples, as previously described,¹ and from 1973 onwards antiserum had to be added to concentrate the antigen.⁴

The anti-HBc test used was counter-immuno-electrophoresis.⁵ RIA tests for anti-HBc were undertaken by Dr DS Dane, Middlesex Hospital, who was also able to demonstrate anti-HBs in the 1979 sample by means of RIA.

Results and discussion

The patient already had anti-HBc by 5 July 1968, before his first transplant on 6 August 1968, so it is likely that his liver was already infected and that his antigenaemia was the result of immunosuppression after the second transplant on 9 November 1968, that is, he had reactivation or recrudescence of existing infection and not a primary infection.⁶

Antigenaemia was found within 26 days of the second transplant on 9 November 1968 and reached a very high blood level (approx. 10^{11} particles/ml), which was maintained for 4 years. During this time the patient was symptomless although his liver function tests were abnormally high (Table).

Approximately 3% of the antigen particles were 42 nm (Dane) particles so that his serum was potentially highly infectious, and it is probably very fortunate that dialysis was not required during this time.

We have been unable to establish his HBe, anti-HBe status for the first 21 months because the sera

Summary of HBs antigen titres, anti-HBc, and anti-HBe in relation to immunosuppressive drug dosage and liver function

Year	HBs Ag—maximum titre during year			42 nm (Dane) particles %	Anti -HBc	Anti -HBe	Immunosuppression dosage		Liver function: ALT (U/l)
	CFT	RPHA	RIA				Prednisolone (mg/day)	Azathioprine (mg/day)	
1968	<8	ND	ND	1	+	NA	200-75	150	110
1969	8000	ND	ND	3	+	NA	45-19	„	204
1970	4000	16 000	ND	„	ND	+§	18	„	138
1971	4000	ND	ND	„	ND	ND	16-13	„	ND
1972	1000	ND	ND	„	ND	ND	13	„	104
1973	16	64	ND	<1	ND	ND	13	125	18
1974	64	64	ND	„	ND	ND	12-10	„	15
1975	8	32	ND	„	ND	ND	10-9	„	20
1976	<8	32	ND	„	ND	ND	9-8	„	23
1977	„	16	+	ND	+	+	8	„	30
1978	„	<8	+	ND	+	ND	8	„	82
1979*†	„	„	-	ND	+	+	8-6	„	ND
1980†	„	„	-	ND	+	ND	6	„	26

*Three specimens
†Two specimens

ND = test not done
NA = not available

§Serum taken 20 August 1970
‡anti-HBs 0.1 IU/ml, 15 November 1979

were no longer available, but by 20 August 1970 he was anti-HBe positive and has remained so. The presence of anti-HBe is associated with a reduction in infectivity, but in some series up to one-third of anti-HBe positive carriers have been found to have significant numbers of 42 nm virus particles.⁷

The level of antigenaemia fell sharply during 1973 for no obvious reason, and at the same time the alanine transferase liver function test results moved within the normal range.

In 1979, for the first time, antigen ceased to be detectable by the most sensitive available RIA tests, and a trace of anti-HBs appeared (0.1 IU/ml—DS Dane, personal communication). No HBs Ag has now been detected in five sera taken in the first 18 months of 1970-80, and the patient may be considered no longer antigenaemic for practical purposes.

It is unlikely that his liver is free from infection, and evidence from the work of Katchaki *et al.*,⁸ who found 'occult' HBs Ag in two RIA-negative individuals, and of Kojima *et al.*,⁹ who found that high anti-HBc titres were associated with infected hepatocytes, suggests that an increase in immunosuppressive therapy might still cause reversion to antigenaemia.

Nevertheless it is felt that this case history has provided a unique illustration of the course of antigenaemia during long-term immunosuppression for the maintenance of a renal allograft.

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