

inferior surface of the liver; technetium-99m scanning, unexpectedly, did not identify this mass clearly within the liver area, although it showed a suspicious area at the lower edge of the liver.

We decided to use the human antibody as a possible targeting agent to delineate the extent of secondary growth. Thyroid uptake was blocked by 60 mg potassium iodide twice daily for two days before the procedure and thereafter for four days. A test dose of 50 µg unlabelled antibody (sterilised by a 0.22 µm filter) was administered intradermally and confirmed the absence of hypersensitivity. The patient's informed consent and the approval of the hospital ethical committee were obtained.

A total dose of 700 µg antibody labelled with 1.5 mCi ¹³¹I was injected intravenously. Immunoscintigraphy showed that within 45 minutes the radioactivity had concentrated in the liver area. At four hours this area was judged to be clear of iodine but some iodine was present in the right kidney and the bladder. After 20 hours the radioactivity coincided with the area corresponding to the subhepatic mass seen on ultrasonography (figure); the ¹³¹I in this area persisted for 24 hours.

Comment

There have been several attempts at immunoscintigraphy with rodent monoclonal antibodies labelled with various radioactive ligands.⁴ Epstein-Barr virus transformation of committed lymphocytes offers great potential in the production of antitumour antibodies of human origin. The degree of specificity in this case was remarkable and the dose given far below that normally used with mouse antibodies. A major problem with this type of viral transformation, however, is the low amounts of antibody secreted. Back fusion of these antibody secreting lymphoblastoid lines with other cell lines can increase this secretion and stabilise the hybrid lines produced.⁵

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- Steinitz M, Klein G, Koskimies S, Makela O. EB virus induced lymphocyte cell lines producing specific antibody. *Nature* 1977;269:420-2.
- Stimson WH, Al-Azzawi F, McAdam A. Monoclonal antibodies to human pregnancy serum-derived immune complexes react with ovarian cancer antigens. *Biochem Soc Trans* 1985;13:369-70.
- Stimson WH, McAdam A, Lang G, Dodd J. Pregnancy-associated β₁-macroglobulin: detection on the surface of ovarian cancer cell lines. *Int J Cancer* 1985;35:185-7.
- Epenetos AA, Britton KE, Mather S, et al. Targeting of iodine-123-labelled tumour-associated monoclonal antibodies to ovarian, breast and gastro-intestinal tumours. *Lancet* 1982;ii:999-1004.
- Kozbor D, Lagarde AE, Roder JC. Human hybridomas constructed antigen-specific Epstein-Barr virus-transformed cell lines. *Proc Natl Acad Sci USA* 1982;79:6651-5.

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Rapid progression of a growth hormone producing tumour during dopamine agonist treatment

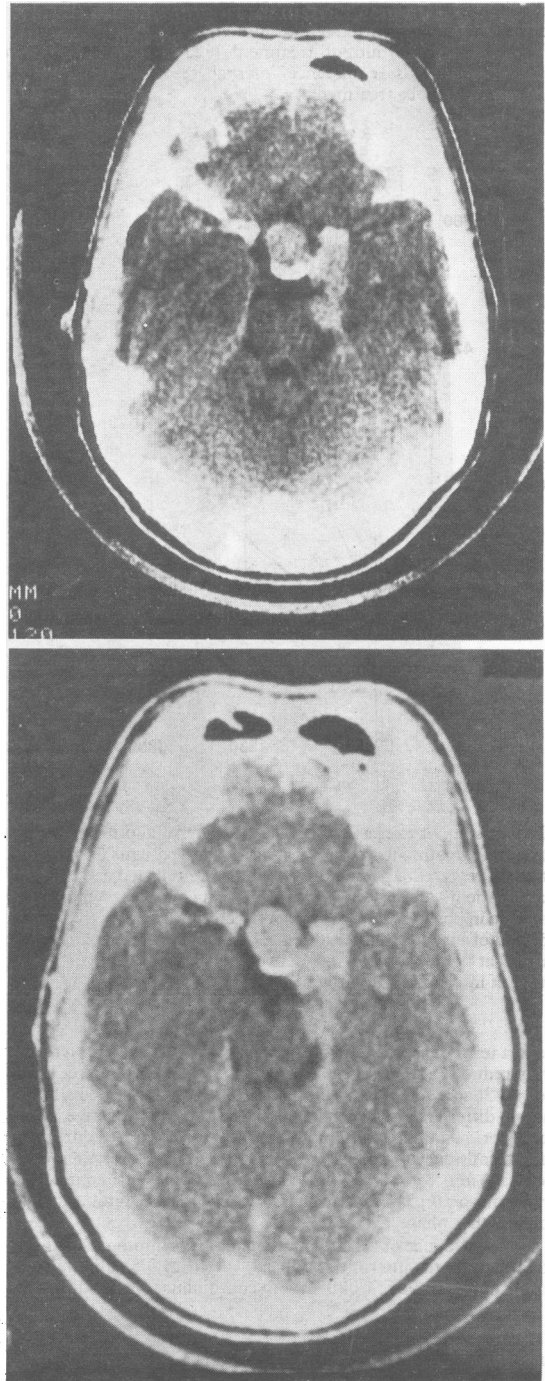
Treatment with dopamine agonists has been tried in patients with growth hormone producing tumours and acromegaly. Most reports show that the concentrations of growth hormone decrease in most patients with acromegaly,¹ but some claim that concentrations decrease only in patients who have shown a modest increase in growth hormone concentrations.² According to other authors, dopamine agonists are effective only in patients with acromegaly and hyperprolactinaemia.³

We report on a patient with acromegaly and hyperprolactinaemia, in whom treatment with the dopamine agonist bromocriptine caused a rapid progression of the growth hormone producing tumour.

Case report

A 40 year old man had had symptoms of acromegaly for at least 10 years with headache, acral enlargement, thickening of the soft tissue of the face and lips, and hyperhidrosis. Radiography showed an intrasellar pituitary tumour with supra-sellar and parasellar extension. The plasma concentration of growth hormone was

180 pmol/l (normal <230 pmol/l), but the patient had detectable growth hormone concentrations throughout the day and night, as reported in other patients with acromegaly and "normal growth hormone concentrations."⁴ In addition, a rise in growth hormone concentration after intravenous injection of thyrotrophin releasing hormone was noticed, a common response in patients with acromegaly. The prolactin concentration was increased at 6.8 nmol/l (normal <1.15 nmol/l).



Computed tomograms showing mixed growth hormone and prolactin producing pituitary tumour of patient before (above) and after (below) 10 months of treatment with bromocriptine 10 mg/daily.

Treatment with bromocriptine was tried first because of the high prolactin concentrations together with the "normal" growth hormone concentrations in this patient. Two months after bromocriptine treatment 10 mg daily was started a rise in growth hormone concentration to 3400 pmol/l was noticed. Prolactin concentration decreased during this period to 1.4 nmol/l. Another five months later growth hormone concentration was 16 400 pmol/l and prolactin 0.9 nmol/l.

Radiography showed that the tumour had grown (figure). At this time the patient also developed visual field defects and because of this deterioration was submitted for surgery.

Comment

The normal secretion of growth hormone is inhibited by somatostatin and stimulated by growth hormone releasing factor. The same effects are also evident in most patients with acromegaly. Release of somatostatin may be stimulated and release of growth hormone releasing factor inhibited by reduced hypothalamic dopamine content, which in turn may be caused by chronic hyperprolactinaemia.⁵

The hyperprolactinaemia in our patient may thus have led to increased release of somatostatin and decreased release of growth hormone releasing factor, reflected by the "low" growth hormone concentrations despite this patient's longstanding, clinically active acromegaly. Treatment with a dopamine agonist inhibited prolactin secretion, which was followed by increased hypothalamic dopamine content. Release of somatostatin might then have been reduced and release of growth hormone releasing factor increased, leading to the rapid increase in growth hormone concentrations and the enlargement of the pituitary tumour.

- 1 Wass JAH, Thorner MO, Morris DV, et al. Long term treatment of acromegaly with bromocriptine. *Br Med J* 1977;i:875-8.
- 2 Pelkonen R, Ylikahri R, Karonen S-L. Bromocriptine treatment of patients with acromegaly resistant to conventional therapy. *Clin Endocrinol (Oxf)* 1980;12:219-24.
- 3 Lambert SWJ, Liuzzi A, Clodini PG, et al. The value of plasma prolactin levels in the prediction of the responsiveness of growth hormone secretion to bromocriptine and TRH in acromegaly. *Eur J Clin Invest* 1982;12:151-5.
- 4 Besser GM. Pathology of acromegaly. In: Molinatti GM, Martini L, eds. *International Congress Endocrinology, Italy '85, Torino, 5-8 June 1985*. Amsterdam: Elsevier Press, 1986.
- 5 Sarkar DK, Gottschall PE, Meitas J. Decline of tuberoinfundibular dopaminergic function resulting from chronic hyperprolactinemia in rats. *Endocrinology* 1984;115:1269-74.

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Hepatitis B: risk to expatriates in South East Asia

We assessed the prevalence of markers of hepatitis B virus in all white expatriate staff and their families attending routine physical examinations during one year.

Subjects, methods, and results

We included 234 subjects in the trial: 117 were resident in Thailand, 98 in Indonesia, and 19 in the Philippines. Radioimmunoassay (Ausria 11, Corab, and Ausab-RIA; Abbott) or enzyme immunoassay (Auszyme, Corzyme, and Ausab-EIA; Abbott) was used to test for the presence of hepatitis B surface antigen, antibody to hepatitis B core antigen, and antibody to hepatitis B surface antigen. Testing for hepatitis B virus had not been done before the staff went to South East Asia, but the prevalence of markers of hepatitis B virus in similar low risk groups is only 3-5%.¹ Activities of alanine aminotransferase, aspartate aminotransferase, and γ -glutamyltransferase were measured at each examination.

The table shows that a significantly greater proportion of married men were positive for hepatitis B virus compared with married women and dependants. The men were divided into groups according to their length of stay in South East

Asia. The proportion of married men who were seropositive was: among those who were in the first year of their stay 0% (0/11), second year 9% (2/22), third 18% (6/34), fourth 16% (3/19), fifth 47% (9/19), and sixth or more 43% (12/28) ($p=0.0001$). A higher proportion of single men were seropositive after a fairly short time in the area, but there was no consistent trend with length of stay.

Among married men in their 30s, 40s, and 50s the proportion positive for hepatitis B virus was 18% (9/50), 39% (17/44), and 21% (5/24), respectively. Eleven out of 21 (52%) who were in their 40s and had been in the area for five or more years were seropositive. Among married office employees 10% (8/82) were positive for hepatitis B virus, compared with 47% (24/51) of married field employees ($p=0.001$). Among single male office employees 29% (5/17) were positive for hepatitis B virus, compared with 40% (4/10) of single field employees.

We took a result 25% above the laboratory upper limit of normal as an arbitrary definition of raised enzyme activity: 13% (6/46) of those who were positive for hepatitis B virus and 6% (12/188) of those who were negative had raised activities of one or more of the enzymes tested ($p=0.132$) and 9% (4/46) of those positive compared with 2% (4/188) of those negative had raised activities of two or more of the enzymes ($p=0.050$). Though we cannot conclude that these differences were caused by hepatitis B virus infection, the low prevalence of raised enzyme activities among those who were positive for hepatitis B virus is consistent with mild infection. Only eight (17%) of those with markers of hepatitis B virus gave a history of jaundice.

Comment

Among the four groups shown in the table the two at greatest risk of acquiring hepatitis B virus infection are single and married men. Blood transfusions, dental treatment, and acupuncture would be expected to cause equal distribution of markers of infection among the four groups. No employees had looked after patients, there was no evidence of drug abuse, and tattooing was rare. Mosquitoes have never been shown to be a realistic means of transmission.² Homosexual transmission is unlikely to occur to such a high extent among married men. With an estimated 10-20% of the general population of South East Asia being healthy carriers of hepatitis B surface antigen³ it is reasonable to conclude that the high risk employees had been exposed to hepatitis B virus by sexual contact with the local population.

The company now complies with recommendations of the Centers for Disease Control by giving hepatitis B immunisation to all non-immune expatriate adults planning to live in South East Asia for more than six months.¹

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- 1 Anonymous. Recommendations for protection against viral hepatitis. *MMWR* 1985;34:313-35.
- 2 Byron NA, Davidson CC, Draper CC, Zuckerman AJ. Role of mosquitoes in transmission of hepatitis B antigen. *J Infect Dis* 1973;128:259-60.
- 3 Tong MJ, Sun SC, Schaefer BT, Chang NK, Lo KJ, Peters RL. Hepatitis-associated antigen and hepatocellular carcinoma in Taiwan. *Ann Intern Med* 1971;75:687-91.

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Prevalence of markers of hepatitis B virus among 234 subjects studied

Hepatitis B surface antigen	Presence or absence of marker			Married men (n=133)	Married women (n=50)	Single men (n=27)	Dependants less than 18 years (n=24)
	Antibody to hepatitis B core antigen	Antibody to hepatitis B surface antigen					
+	-	-					
+	+	-	2				
-	+	-	3	1	2		
-	+	+	24	3	6		
-	-	+	3	1	1		
Total No (%) positive			32 (24)	5 (10)	9 (33)	0	0.005
p^*				0.039	0.338		

*Fisher's exact test for independence for 2x2 table. Each category is compared with married men. Outcome variable is either negative for hepatitis B virus (if all three tests give negative results) or positive.