SHORT REPORTS

Interpretation of amylase clearance in patients with abnormal creatinine clearance

Patients with acute pancreatitis may excrete increased amounts of amylase in their urine for several days after their plasma amylase concentration has become normal. The ratio of renal clearance of amylase (Cam) to clearance of creatinine (Ccr)^{1,2} is increasingly being used to distinguish this rise in Cam from changes due to variations in the glomerular filtration rate. The simple ratio of Cam to Ccr does not make a satisfactory allowance for large changes in Ccr, however, because it is usually higher in severe renal failure.^{3,4}

Implicit in calculating a ratio is the assumption that the variables are related in linear fashion and intercept at zero. Published graphs of Cam plotted against Ccr in patients without pancreatitis^{5,6} suggest that the relation is curved but might become linear if the data were plotted on log-log axes. Professor J D Blainey and Dr B E Northam kindly allowed me to re-examine their primary data on nine normal people and 101 patients with renal disease of varying severity⁵ to test this hypothesis.

Patients, methods, and results

The patients and methods have been described.⁵ Four patients were excluded from analysis because of internal inconsistencies in the laboratory data.

The correlation between Cam and Ccr was significant ($r=0.85$, $P<0.001$), and the linear regression equation of Cam on Ccr was $100 \text{ Cam} = 2.623 \text{ Ccr} + 5.653$. There was also a significant correlation between $\log_{10}$ Cam and $\log_{10}$ Ccr, and the correlation coefficient between these two indices ($r=0.91$, $P<0.001$) was significantly greater than that between Cam and Ccr ($P<0.001$). The linear regression equation of $\log_{10}$ Cam on $\log_{10}$ Ccr was $\log_{10} (100 \text{ Cam}) = 0.8467 \log_{10} \text{ Ccr} + 0.6888$. The upper 95% limit of the reference range was defined by $\log_{10} (100 \text{ Cam}) - (0.8467 \log_{10} \text{ Ccr}) = 1.0084$ or, rearranged as a ratio, $(\text{Cam}/\text{Ccr})^{0.847} \times 100 = 10.2\%$.

Because the timed urine volume was included in the calculation of both Cam and Ccr, the relation between the urine:plasma concentration ratios for amylase (Uam:Pam) and creatinine (Ucr:Pcr) was also examined (see figure). There were significant correlations between Uam:Pam and Ucr:Pcr ($r=0.83$, $P<0.001$) and between $\log_{10}$ (Uam:Pam) and $\log_{10}$ (Ucr:Pcr) ($r=0.88$, $P<0.001$). The correlation coefficient for the logarithmic indices was the greater ($P<0.01$). The upper 95% limit of the reference range was defined by $\log_{10} (100 \times \text{Uam:Pam}) - 0.7988 \log_{10} (\text{Ucr:Pcr}) = 1.0891$, or $(\text{Uam:Pam})/(\text{Ucr:Pcr})^{0.799} \times 100 = 12.3\%$.

Log-log relation between urine:plasma concentration ratios for amylase (Uam:Pam) and creatinine (Ucr:Pcr) in nine normal people and 101 patients with renal disease ($r=0.88$).

Comment

In patients with renal disease of widely varying severity the correlation between $\log_{10}$ Cam and $\log_{10}$ Ccr was significantly greater than that between Cam and Ccr ($P<0.001$). Thus the relation between Cam and Ccr is better described by a curve than by a straight line, with Cam:Ccr increasing as Ccr falls and vice versa. That the simple ratio Cam:Ccr fails to make full allowance for the effect on Cam of changes in Ccr may at least partly account for the controversy about its specificity and sensitivity as a test for the diagnosis of acute pancreatitis.

Thus, whatever the state of renal function, a single reference range based on the ratio of the logarithm of Uam:Pam to that of Ucr:Pcr should allow the detection with an untimed urine specimen of an amylase clearance that is disproportionately high for the patient's creatinine clearance.

¹ Levitt, M D, Rapoport, M, and Cooperband, S R, *Annals of Internal Medicine*, 1969, **71**, 919.

² Mulhausen, R, Brown, D C, and Onstad, G, *Metabolism*, 1969, **18**, 669.

³ Pedersen, E B, Brock, A, and Kornerup, H J, *Scandinavian Journal of Clinical and Laboratory Investigation*, 1976, **36**, 137.

⁴ Morton, W J, et al, *Gastroenterology*, 1976, **71**, 594.

⁵ Blainey, J D, and Northam, B E, *Clinical Science*, 1967, **32**, 377.

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Primary symptomatic cytomegalovirus infection in a healthy woman: a possible case of intrafamilial transmission

Studies by the Klemola group^{1,2} in Finland and by others³ have shown that cytomegalovirus (CMV) infection may be associated with an infectious mononucleosis-like syndrome in healthy people and in patients who have undergone heart operations. The CMV infection in the latter group is thought to be transmitted by fresh blood transfusions² or to be a reactivation of a latent CMV infection.⁴

We describe here a woman with a primary CMV infection that might have been transmitted from her husband, who had recently undergone heart surgery.

Case report

On 8 November 1976 a 56-year-old woman was admitted to our department with fever ($\geq 39^\circ\text{C}$) and a three-week history of shivering. Her general condition was good, and physical examination showed no abnormalities. A chest radiograph was normal. Erythrocyte sedimentation rate was 21 mm in first h, haemoglobin 14.1 g/dl, and leucocyte count $10 \times 10^9/\text{l}$ ($10\,000/\text{mm}^3$). Her peripheral blood contained 36% lymphocytes, 10% monocytes, and 8% Downey cells. Liver-function tests showed normal serum bilirubin concentration, slightly raised aspartate aminotransferase (126 IU/l ($2.1 \mu\text{kat/l}$)) and alanine aminotransferase (168 IU/l ($2.8 \mu\text{kat/l}$)) concentrations, and a high alkaline phosphatase concentration (1257 IU/l ($21 \mu\text{kat/l}$)). Repeated blood and urine cultures for bacteria were negative. CMV was isolated from her urine. The first serum sample (11 November) showed a complement fixation (CF) antibody titre of 40 against CMV; this did not change during the period of observation. But IgM antibodies, tested by indirect immunofluorescence (IF), showed a high rising titre, from 1/256 to 1/>1024, against CMV (strain AD, 169). She gave a negative reaction on the Paul-Bunnell test.

We learnt that the woman's husband had received several units of fresh blood during and after an aortic bypass operation in April 1976. In June he had fallen ill with a longlasting, low-grade fever, and from then until the middle of September he had had a constant lymphocytosis (50-60%) in his

peripheral blood, 4-6% of his lymphocytes being Downey cells. Five months after the start of his illness he had a CF antibody titre of 40 and an IF titre of IgM antibodies of 8 against CMV. Unfortunately bacterial contamination spoilt our attempt to isolate CMV from his urine.

Comment

CMV can be isolated from urine during and sometimes many months after a clinical illness associated with this virus. For technical reasons we could not establish whether our patient's husband was a CMV excretor, but CMV was isolated from his wife's urine during her illness and both had serum antibodies against CMV.

It seems clinically highly probable, though it was not virologically proved, that the man's illness was associated with a CMV infection. He fell ill within the incubation period for a post-transfusion CMV infection³ and his clinical picture resembled that which appears in association with CMV infection.¹⁻³

Our patient became ill 15 weeks after her husband had recovered clinically, but only four weeks after his "haematological recovery." The virological findings showed that she had a current CMV infection, evidently a primary one,⁵ during the period she was ill with a mononucleosis-like syndrome of septic type. The couple lived alone in their house. A spread of CMV infection from the husband to his wife seems very likely, though we cannot explain why the virus transmission from husband to wife did not occur earlier.

This case history shows that clinicians must be aware of the possibility of a spread of CMV from a patient who has undergone heart surgery or renal transplantation to other members of the family. Even if most of the primary CMV infections are asymptomatic, a few may cause a longstanding fever.

¹ Klemola, E, and Kääriäinen, L, *British Medical Journal*, 1965, **2**, 1099.

² Paloheimo, J, et al, *American Journal of Cardiology*, 1968, **22**, 624.

³ Sterner, G, et al, *Scandinavian Journal of Infectious Diseases*, 1970, **2**, 95.

⁴ Olding, L B, Jensen, F C, and Oldstone, M B A, *Journal of Experimental Medicine*, 1975, **141**, 561.

⁵ Langenhuisen, M M A C, et al, *Clinical and Experimental Immunology*, 1970, **6**, 387.

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Hepatitis B: absence of transmission by gastrointestinal endoscopy

Endoscopy of patients carrying hepatitis B antigen carries a risk of transmitting infection, since instruments are not normally cleaned between examinations in a way that reliably removes the virus. Although two reports^{1 2} suggest that such transmission is rare, we know of no studies in which patients examined with a contaminated instrument have been followed up with sensitive tests for both HBsAg and anti-HBs.

Patients, methods, and results

The index patient was an agammaglobulinaemic man without known liver disease. Fifteen days after endoscopy with biopsy HBsAg and HBeAg were identified in his serum and saliva. Subsequent testing of stored serum obtained before endoscopy and of later samples showed persisting antigenaemia. On the day of the index endoscopy seven other patients had been examined with the same ACMI-F8 instrument; six were biopsied. Thirty-one more patients were examined with the instrument before its possible contamination was realised, when it was withdrawn from use.

Between examinations the endoscope was cleaned by swabbing the outside with water, with 5% Savlon (chlorhexidine and cetrimide), and again with

water. About 50 ml water was aspirated through the internal channels followed by 50 ml 5% Savlon. Biopsy forceps were rinsed with water and swabbed with alcohol. At the end of each endoscopy session forceps were soaked in a large volume of Savlon for at least 30 minutes.

Serum from all but one of the 38 patients was obtained two to 104 days after endoscopy and tested for HBsAg by reverse passive haemagglutination, anti-HBs by radioimmunoprecipitation³, and HBeAg and its antibody by gel diffusion. No antigenaemia was detected; two patients were anti-HBs positive. Thirty patients were retested 162-225 days after their endoscopy. Again, no antigenaemia was found, and no new appearance nor change in antibody titre. Two patients died before follow-up (neither from hepatitis) and six were untraceable. No staff acquired antigen or antibody.

To assess possible contamination of instruments during endoscopy and the effectiveness of cleaning procedures, an Olympus gastroscope and forceps were immersed for 15 minutes in gastric juice containing 1% serum and ¹²⁵I-HBsAg, with manipulations to simulate gastroscopy. The instruments were then cleaned as described. Residual contaminating HBsAg was sampled by soaking the forceps and channels of the endoscope in Savlon for 15-20 minutes, with further swabbing of the external surface, and then measuring the radioactivity of the swabs and washing and sampling fluids. The table shows that after routine cleaning ¹²⁵I-HBsAg could still be recovered. The coiled outer cover of the forceps was a particularly important trap for contaminated material. After the forceps had been coiled to open gaps in the spiral covering they were soaked for 15 minutes in the gastric juice. After thorough washing of the straightened forceps residual ¹²⁵I-HBsAg was rapidly released when the forceps were coiled and rinsed again.

Effectiveness of standard washing procedures in removing ¹²⁵I-HBsAg from the endoscope and biopsy forceps

Procedure	Type of sample	Volume of gastric juice removed by each procedure (μl)
Source: outside of instrument		
1st Wash (Water)	Swab	225
2nd Wash (Savlon)	Swab	116
3rd Wash (water)	Swab	17
Further sampling (Savlon)	Swab	126
Source: internal channel		
1st Wash (water)	Fluid	423
2nd Wash (Savlon)	Fluid	17
Further sampling (Savlon)	Fluid	41
Source: forceps*		
2nd Wash (70% alcohol)	Swab	16
Further sampling (Savlon)	Fluid	47
Source: coiled forceps soaked in contaminated gastric juice		
1st Wash: swabbing of straightened forceps with Savlon	Swab	130
2nd Wash: immersion of straightened forceps in Savlon for 6 hours	Fluid	300
3rd Wash: immersion of forceps in Savlon for further 15 minutes in coiled position	Fluid	250

*Volume of gastric juice removed from forceps by first wash not recorded. Instruments were exposed to 250 ml of human gastric juice containing 1% serum and ¹²⁵I labelled HBsAg. Radioactivity of washing fluid and swabs used in cleaning instruments is expressed as a volume of this gastric juice.

Comment

Two reports have suggested that hepatitis B transmission by endoscopy is rare^{1 2} and our findings, based on sensitive tests for the antigens and antibodies, support this opinion. Nevertheless, the ineffectiveness of routine instrument cleaning is disturbing and we have now modified the procedures as follows: (1) after examination of each patient, the outside of the endoscope is swabbed once with water, once with Savlon, and then scrubbed with Savlon. Each internal channel is cleaned by aspirating 100 ml water and 100 ml Savlon; (2) after each session the shaft and internal channels are soaked for at least 30 minutes in glutaraldehyde (Cidex) and the instrument is thoroughly washed with Savlon and with water; (3) separate biopsy forceps are used for each patient, and after use the coiled forceps are immersed in glutaraldehyde for 30 minutes and thoroughly rinsed with Savlon and water; and (4) a special instrument is reserved for patients known to be HBsAg-positive, which is exposed to glutaraldehyde for two hours after use.

Axon et al⁴ recommended cleaning instruments between examinations by 10 minutes' exposure to glutaraldehyde, but there is no evidence that this inactivates the virus, and prolonged washing is needed to remove the toxic glutaraldehyde. We believe that a non-toxic detergent and bactericidal agent is preferable and that no method currently available will inactivate hepatitis B virus rapidly enough to disinfect instruments between examinations.

Like our report⁵ of anti-HBs prevalence in high-risk patients this