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Serum and Urinary Enzyme Activity After Renal Infarction

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ABSTRACT

Recently it has been observed that the activity of certain enzymes in serum and urine may be increased after renal infarction. Although aortography or selective renal angiography should be the diagnostic corner-stone on which one would proceed to embolectomy, it is possible that enzyme assays may serve as laboratory aids to suggest or confirm the diagnosis. This paper reviews the few existing clinical and experimental studies and reports on two patients who had a total of three episodes of renal infarction. Serial determinations after one episode showed increased activity of serum oxaloacetic glutamic transaminase (SGOT) and of lactic acid dehydrogenase (LDH) and alkaline phosphatase in the serum and urine; some elevated serum LDH and SGOT values were recorded after the other two infarctions. The time of onset and duration of these increases are discussed, and the possible difficulty in differentiating renal from myocardial infarction is illustrated.

SOMMAIRE

On a observé dernièrement que l'activité de certaines enzymes du sérum et de l'urine peut augmenter après infarctus rénal. Sans doute l'aortographie ou l'angiographie rénale sélective constituent-elles les pierres angulaires du diagnostic sur lesquelles on basera la décision de procéder à l'embolectomie, mais il est possible que les dosages biologiques des enzymes puissent représenter des auxiliaires utiles qui facilitent le diagnostic ou viennent le confirmer. L'article passe en revue les quelques travaux expérimentaux et cliniques sur la question et signale le cas de deux malades qui présentèrent un total de trois épisodes d'infarctus rénal. Des analyses en série faites après un épisode ont mis en évidence une augmentation de la transaminase sérique glutamo-oxalacétique (TSGO) de la déhydrogénase lactique (DHL), et de la phosphatase alcaline du sérum et de l'urine; certaines valeurs anormalement élevées de la DHL sérique et de la TSGO ont été notées après les deux autres infarctus. L'article expose les données sur le moment du début et la durée de ces montées et illustre les difficultés éventuelles à différencier l'infarctus rénal de l'infarctus du myocarde.

THE difficulty in diagnosing renal infarction by means of clinical criteria is exemplified by the study reported by Hoxie and Coggin,[1] who found on an autopsy review in 1940 that only two of 205 cases had been diagnosed during life. Accurate diagnosis of renal artery occlusion with renal infarction is more important now that advances in vascular surgery have made it possible sometimes to restore renal function even though up to four days may have elapsed since occlusion occurred.[2] Although at present aortography or selective renal angiography should be the diagnostic corner-stone on which one would proceed to an embolectomy, increased activity of certain enzymes in serum and/or urine has been reported after renal infarction. Enzyme assays might serve therefore as laboratory aids to suggest or to confirm the diagnosis, particularly in patients for whom one would not consider surgical treatment.

Elevation of the serum oxaloacetic glutamic transaminase (SGOT) values after renal infarction has been reported in man[3, 4] and in dogs,[3] and of serum and urine lactic acid dehydrogenase (LDH) after both renal infarction and ischemia in dogs.[5] An increase in serum SGOT and LDH, due possibly to renal infarction, has been reported in one patient.[6] Alkaline phosphatase activity was reported to have increased in the serum after ligation of the renal artery in dogs[7, 8] and in two patients in whom Duggan[4] found normal values some time before but elevated values after renal infarction.

In the following communication two cases are presented which add to our knowledge of changes in serum and urinary enzyme activity after renal infarction and illustrate the possible difficulty of distinguishing myocardial infarction from renal infarction, especially when SGOT and serum LDH activities are increased.

METHODS

Serum oxaloacetic glutamic transaminase (SGOT) was determined by the method of Reitman and Frankel;[9] serum lactic-acid dehydrogenase (LDH) by the method of Berger and Broida[10] or Cabaud and Wroblewski;[11] serum alkaline phosphatase by the Kind and King modification of the King-Armstrong method as adapted for the Auto-

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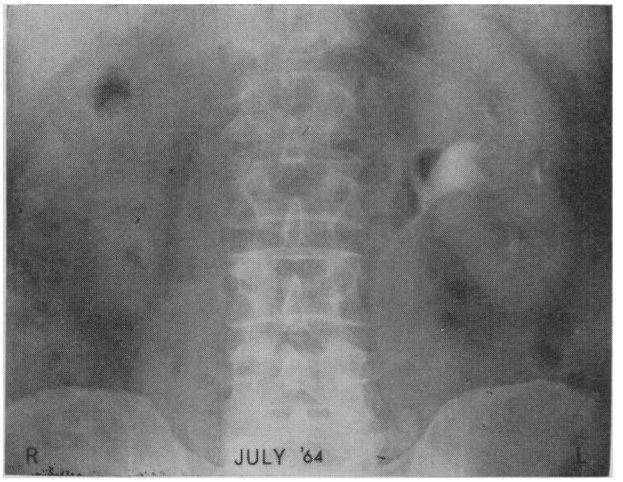

Fig. 1.—Case 1.—Intravenous pyelogram, July 1964. The right kidney fails to excrete dye but is of the same size as in March 1964. The left kidney shows a scalloped area at the junction of the middle and lower thirds.

Analyzer;[12] and serum ceruloplasmin by the method of Ravin.[13] The analytical methods used for determination of urinary LDH and alkaline phosphatase were the same as those for serum, except that the urine for both tests was dialyzed for two hours against cold running tap-water[14] in cellulose dialysis casing and urinary LDH was assayed using 1 ml. of undiluted dialyzed urine. The normal range for urinary LDH (0-15 units/g. creatinine) and for alkaline phosphatase (0-13 units/g. creatinine) has been determined in 26 and 35 normal subjects respectively, as part of a study of these enzymes in tumours and other disorders of the urinary tract.[15] Other determinations were carried out by standard methods.

CASE 1.—A 65-year-old man began to suffer from precordial pain in September 1962. In December of that year he was admitted to hospital for treatment of acute anterior myocardial infarction, the diagnosis of which was confirmed by electrocardiography. Atrial fibrillation occurred for a short time. Anticoagulant therapy was instituted, and the patient recovered without complications. On March 15, 1964, two months after discontinuance of anticoagulants, he was readmitted, complaining of left upper abdominal pain associated with nausea and vomiting. An intravenous pyelogram was considered normal, although the lateral one-third of the left kidney was obscured by intestinal gas. As values for SGOT and serum LDH were elevated (Table I), it was considered, we believe incorrectly, that despite the unchanged electrocardiographic findings, the patient had had another myocardial infarction. He made an uneventful recovery and was discharged without anticoagulants. One month later he began to suffer from left calf pain on moderate exertion.

TABLE I.—SERUM LDH AND SGOT VALUES AFTER RENAL INFARCTION

	Days after onset of pain: 0	1	2	3	4	5	
Case 1—March.....	—	58	61	64	42	—	
Case 1—July.....	32	147	104	58	46	42	SGOT
Case 2.....	30	134	108	—	—	—	(units per ml.)
Case 1—March.....	—	900	—	—	930	—	
Case 1—July.....	700	2140	>2000	>2000	>2000	2010	LDH
Case 2.....	—	—	1900	1980	—	—	(units per ml.)

On July 30, 1964, he was readmitted complaining of excruciating right flank pain of 12 hours' duration; this pain radiated to the right costovertebral angle and was associated with nausea and vomiting. His blood pressure was 160/80 mm. Hg, pulse 80/min. and regular, and temperature 97° F. Apart from marked diffuse right abdominal and loin tenderness, and absent left popliteal and pedal pulses, the physical examination was normal. The urine showed a specific gravity

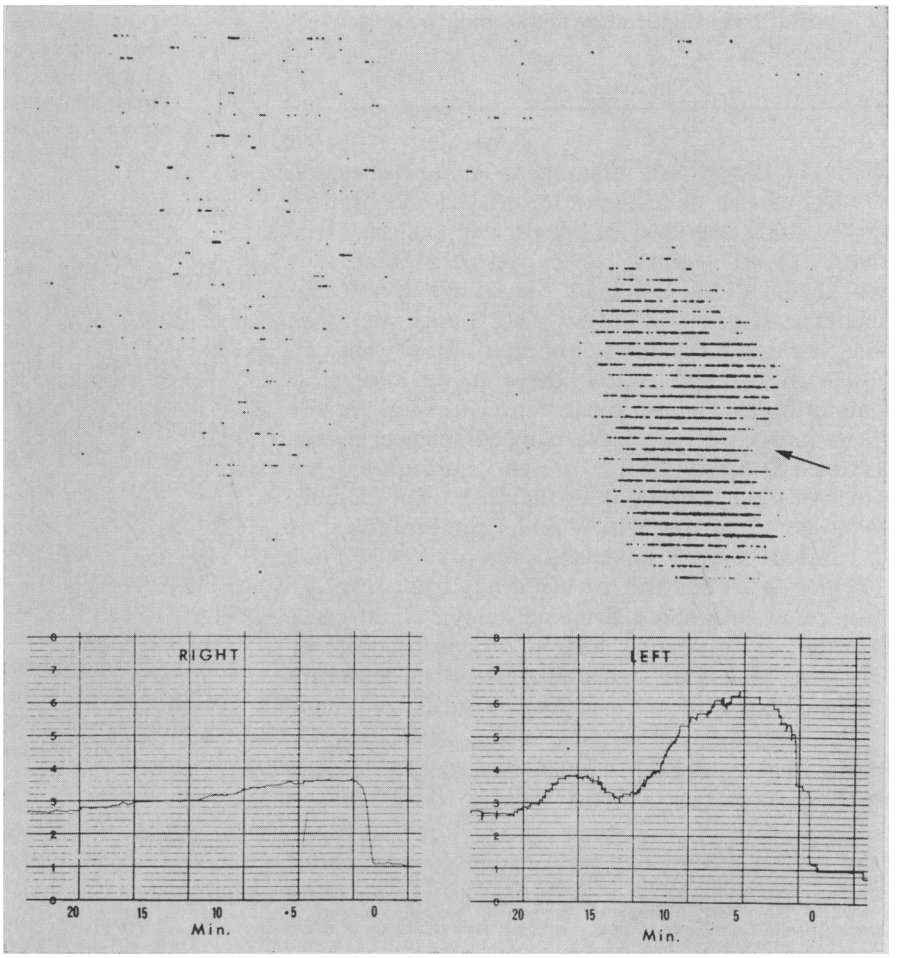

Fig. 2—Case 1.—July 1964. Hg^{203}-chlormerodrin (Neohydrin) renal scan *(above)* shows lack of significant uptake by the right kidney and a scalloped non-functioning area at the junction of the middle and lower thirds on the lateral border of the left kidney. I^{131}-iodohippurate (Hippuran) renogram is shown below.

of 1.030, no protein, and a normal sediment. His leukocyte count was 15,000 per c.mm., with a polymorphonuclear leukocytosis. The electrocardiogram was unchanged. An intravenous pyelogram (IVP) revealed that the right kidney failed to excrete dye, and there was a scalloped area on the lateral margin of the left kidney at the junction of the middle and lower thirds (Fig. 1). Hg^{203}-chlormerodrin (Neohydrin) renal scan and I^{131}-iodohippurate (Hippuran) renogram also indicated lack of significant function of the right kidney (Fig. 2), and the scan revealed an area without uptake corresponding to the scalloped zone on the left kidney seen on the IVP. Aortography, 20 hours after admission, demonstrated complete occlusion of the right renal artery about 4 cm. from its origin. One day after admission the urine contained 40 to 50 erythrocytes and four to six leukocytes per high-power field and 78 mg. protein /100 ml. The patient was treated conservatively with bed rest and anticoagulants.

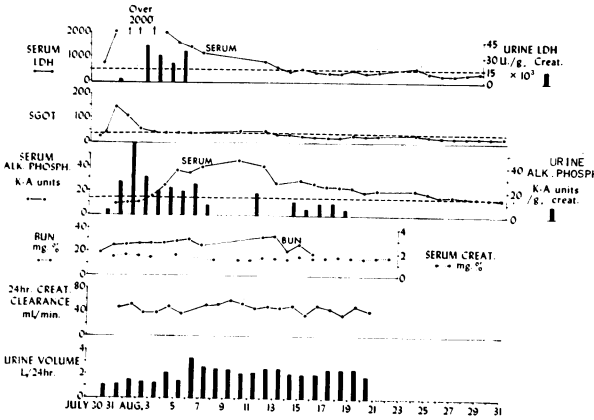

Fig. 3.—Case 1.—Alterations in serum and urine enzyme activity and in renal function after renal infarction. Urine enzymes are represented by bars. Upper limits of normal ranges for serum and urine LDH and alkaline phosphatase are indicated by dotted lines.

The changes in activity of serum and urine enzymes are depicted in Fig. 3. On admission the SGOT was 32 units and serum LDH 700 units. On the second hospital day, these values had increased to 147 and 2140 units respectively, and the serum alkaline phosphatase was 8.8 King-Armstrong units; the latter rose to a peak of 46 units on the 12th day. The serum ceruloplasmin, which was elevated at 55 mg./100 ml. one day after admission, reached a peak of 62 mg./100 ml. on the 20th hospital day and had declined to normal by the 26th day. Urinary alkaline phosphatase activity was normal on the second hospital day but was elevated one day later, and urinary LDH activity was normal on the third hospital day but was elevated two days later: values expressed as the more conventional units per eight-hour volume showed a degree of elevation comparable to values expressed as units/g. creatinine. The blood urea nitrogen (BUN) rose temporarily from 20 to 29 mg./100 ml. and the 24-hour creatinine clearance varied between 35 and 60 ml./min.: it had been 108 ml./min. in January 1963. There was no evidence of hepatic or biliary tract disorder and a patent hepatic artery was visualized on aortography. After six weeks in hospital the patient felt well and was discharged on anticoagulant therapy.

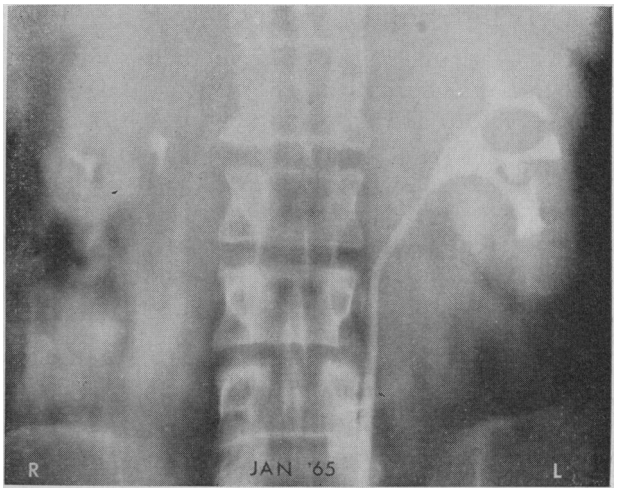

Fig. 4.—Case 1.—January 1965, six months after right renal infarction; combined tomography and IVP. The right kidney is much reduced in size compared with findings in March and July 1964. The left kidney shows loss of substance at the lower lateral border.

In January 1965, six months after the occurrence of right renal infarction, he was well and normotensive. Intravenous pyelography combined with tomography revealed that the right kidney measured 8 cm. x 3.5 cm. and excreted some dye (Fig. 4); in March and July 1964 it had measured 13 cm. x 6 cm.

CASE 2.—Serum LDH and SGOT activity after renal infarction were studied in a 47-year-old man who had mitral stenosis and atrial fibrillation. The diagnosis of renal infarction was based on the acute onset of severe left upper abdominal and loin pain, with nausea and vomiting, marked tenderness of the left loin, the presence in the urine of four to six red blood cells per high-power field (none had been seen previously), and the finding on intravenous pyelography of almost complete lack of dye excretion by the left kidney. Both SGOT and serum LDH values became elevated (Table I).

DISCUSSION

In Case 1, an embolus from a mural thrombus following myocardial infarction is considered to be the most likely cause of the right renal artery occlusion with infarction in July 1964. The occlusion was confirmed by aortography and the infarction by the considerable reduction in kidney size (Figs. 1 and 4). Such an event is considered to account also for the episode of left upper abdominal pain in March 1964; in view of the elevated SGOT and serum LDH values, and despite the unchanged electrocardiographic findings, this had been diagnosed as due to myocardial infarction. In retrospect, the diagnosis of left renal infarction appears most likely when one considers the pain pattern, which was similar to that which occurred in July 1964 on the right side, and the presence of a scalloped non-functioning area seen subsequently on IVP, renal scan and aortography (Figs. 1, 2 and 4).

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SERUM ENZYMES

SGOT.—Frahm and Folse,[3] in their studies on dogs and on one patient, recorded a peak SGOT value of 62 to 155 units one day after the occurrence of unilateral renal infarction, with a return to normal by the fourth day. Duggan[4] reported two cases in which the SGOT was elevated after renal infarction, in the first case to 102 units at two days and in the second to 61 units at an unspecified interval after infarction. However, other disease processes complicated the picture in both cases. In the three episodes of renal infarction considered in the present paper (Table I and Fig. 3), SGOT activity on the day of onset of symptoms was normal in the two instances in which it was assayed; on the following day activity reached a peak in two episodes, and was close to the peak value found in the other instance. Four days after onset of symptoms activity was almost normal in the two recorded instances.

LDH.—The level of LDH may be a more useful parameter than the SGOT, though equally nonspecific. In Case 1, in July 1964 (Table I and Fig. 3) the LDH level was significantly elevated on admission, whereas the SGOT was not significantly elevated at that time. A similar early elevation of serum LDH after renal infarction was found by Bett *et al.*[5] in dogs. Also, in Case 1, serum LDH activity was significantly elevated for 14 days, compared with three for SGOT. The extent of elevation in each of the three episodes reported here was proportionally somewhat greater for LDH than for SGOT (Table I).

Alkaline phosphatase occurs in high concentration in the proximal convoluted tubular cells of the kidney.[14] Experimental studies in dogs have shown that, after renal artery ligation, serum alkaline phosphatase values rise within 12 hours but have begun to fall at 48 hours.[8] In Duggan's[4] two patients, although increases in activity were relatively slight and other disease processes complicated the picture, significant elevations appear to have occurred between five and 18 days after infarction in one patient and between three and 10 days in the other; and the duration of increased activity cannot be deduced from the data presented. After the right renal infarction in our Case 1 (Fig. 3), alkaline phosphatase activity first became elevated on the fifth hospital day, rose to a peak of 46 King-Armstrong units at 12 days, and remained significantly elevated until the 28th hospital day. Although activity was not increased in the early stages, because elevation is prolonged, assay might prove of value in the case presenting late or in helping to distinguish a renal from a myocardial infarction. Other disorders accompanied by destruction of renal parenchyma, such as acute cortical necrosis, might cause a diagnostically important increase in activity.

URINARY ENZYMES (Fig. 3)

Alkaline phosphatase activity in urine has been reported to be increased in patients with renal infarction;[16] also in persons with renal tumours[14] and renal parenchymal diseases,[20] and with acute disorders not primarily involving the kidney, such as pulmonary embolism.[14] In Case 1, alkaline phosphatase activity was normal in urine collected during the first day, was significantly increased on the second, reached a peak on the third day, and returned to normal at nine days. The reason for the earlier rise and fall in urinary alkaline phosphatase as compared with serum values is not apparent. Although activity has been found increased in the urine when serum values have been markedly elevated, for example in Paget's disease or obstructive jaundice,[15] it is clear that in Case 1 the rise in urinary enzyme activity preceded and was independent of the rise in the serum.

LDH activity in urine has been found to be increased in patients with renal infarction,[14] neoplasms of the kidney, bladder or prostate,[14, 17] and in various other renal and urological disorders.[18-20] The urinary LDH activity in our Case 1 was normal on the second day, was not assayed during the next 24-hour period, and was elevated during the next four days. In their experiments with dogs, Bett *et al.*[5] found that in most instances the urinary LDH activity began to increase 48 hours or more after renal infarction had occurred.

In the clinical conditions being considered, the probable greater specificity of urinary than of serum enzymes, with respect to renal pathological states, should constitute an advantage. Unfortunately, at least during the first day after infarction when diagnostic assistance is most required, changes in urinary as well as serum enzyme activity, if present, may not be great enough to be of diagnostic value. A prerequisite for elevation of urinary enzyme activity is the formation of urine by the infarcted kidney.

Further knowledge of the time when activities of these enzymes in serum and urine become elevated, reach a peak and decline to normal, and of information correlating lesion size with alteration in enzyme activity is necessary for their accurate interpretation in the differential diagnosis of abdominal and thoracic disorders which may have features in common with renal infarction.

SUMMARY

Case histories of two patients who suffered a total of three renal infarctions are presented. Increased activity of serum oxaloacetic glutamic transaminase (SGOT) and of serum and urine lactic acid dehydrogenase (LDH) and alkaline phosphatase were noted after one episode, and elevated serum LDH and SGOT values after two other episodes. The pertinent literature is reviewed and the possible difficulty in distinguishing renal from myocardial infarction is illustrated. Assay of serum and urinary enzymes may prove to play a limited role in suggesting or confirming the diagnosis of renal infarction, and awareness

that this lesion may result in increased activity of these enzymes in the serum is important.

ADDENDUM

Recently, a study[21] came to our attention in which values for alkaline phosphatase and LDH were found to be elevated in serum and urine following myocardial infarction. Also, we have followed a patient with pulmonary infarction without evidence of hepatic congestion, who developed an elevated serum alkaline phosphatase. It appears therefore that a rise in serum alkaline phosphatase activity may not necessarily favour the diagnosis of renal infarction over myocardial or pulmonary infarction.

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Evaluation of a Tuberculosis Mass Survey Conducted in the City of Chatham and in Kent County, Ontario, in 1963

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ABSTRACT

Computer analysis of the results of a mass tuberculosis survey of the population of Chatham city and Kent County, Ontario, was carried out to assess the efficacy of such surveys as a case-finding device. Six cases of active tuberculosis were found during the survey and approximately 50% of the 89,427 inhabitants of Chatham and Kent County were surveyed with radiographs and Heaf skin tests.

A follow-up study of the Heaf test conducted in the public school of Wallaceburg detected 70 Heaf-positive children out of a total of 1190. These Heaf-positive children were further tested with a Mantoux test (5 T.U.) and chest radiography. Only 11 children of the original 70 were Mantoux-positive.

These findings further support the hypothesis that the Heaf test, as now read, overreads for *M. tuberculosis* infections.

SOMMAIRE

Les résultats d'une enquête de masse sur la tuberculose au sein de la population de la ville de Chatham et du comté de Kent, en Ontario, ont été analysés par un ordinateur électronique, en vue d'évaluer l'efficacité de ces enquêtes comme moyen de découvrir de nouveaux cas. Six cas de tuberculose active ont été décelé pendant l'enquête, et à peu près la moitié des 89,427 habitants de Chatham et du comté de Kent subirent des radiographies pulmonaires et les cuti-réactions de Heaf.

L'analyse subséquente d'une série d'épreuves de Heaf effectuées dans les écoles publiques de Wallaceburg a décelé 70 cas positifs au test de Heaf sur un total de 1,190 enfants. Ces enfants qui présentaient un test de Heaf positif furent ensuite soumis au test de Mantoux (5 U.T.) et à une radiographie pulmonaire. Des 70 cas positifs au test de Heaf 11 seulement présentaient une réaction positive au test de Mantoux.

Ces constatations viennent confirmer l'hypothèse que le test de Heaf, comme on l'interprète actuellement, donne des résultats surfaits pour les infections tuberculeuses.

A GREAT deal has been written which suggests that tuberculosis is decreasing in North American communities. Present methods of finding active cases of tuberculosis, however, were developed in the period when tuberculosis was still a major cause of morbidity and death. Because of the changing pattern of the disease, it is now imperative to evaluate the efficacy of mass tuberculosis surveys and other case-finding methods. Data processing by machine is relatively common now in industry and these facilities can be used with advantage in the evaluation of such surveys.

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