Urological Research 7, 197-207 (1979)

Urological Research


# Medullary Sponge Kidney

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Accepted: August 31, 1978

Key words: Medullary sponge kidney, Nephrocalcinosis, Hypercalciuria

Medullary sponge kidney (MSK) is the term now commonly used to denote a congenital anomaly of the renal medullary pyramids characterised by dilatation and cystic malformation of the collecting tubules. It may be unilateral or bilateral and diffuse or confined to a few pyramids. The affected pyramids are often enlarged and there may be generalised renal enlargement. Very often the ectatic medullary structures contain small radiodense concretions and the disorder also predisposes to infection. It is probable that all the symptoms of MSK are caused by these two complications and the majority of patients present as cases of renal lithiasis or pyelonephritis.

The disorder was first reported in 1938 when, at an Italian Radiological Congress, Lenarduzzi (12) showed a case in which punctate areas of calcification in the pyramids of both kidneys were accompanied by the passage of contrast medium into dilated collecting tubules during pyelography. During the next ten years a few similar cases were reported in the Italian literature notably by Cacchi and Ricci (2) who coined the term "rene a spugna" but it was not until 1959 when Ekström and his colleagues (5) published their extensive and well illustrated monograph based on the study of 44 cases that the radiological, clinical and morbid anatomical features of the condition became widely known.

During the past 20 years we have seen 26 males and 21 females with the radiological signs of medullary sponge kidney. All but one of these patients were under our clinical care and 26 have undergone repeated review over periods of 5-20 years. The purpose of this paper is to describe the clinical and other features of this series of patients and to compare our findings with those reported by other authors.

Nothing is known of the aetiology of the condition. Although it is congenital and although it was described in three successive generations (10) no evidence of a raised incidence in the families of affected individuals has been found either in this study or other large studies (1, 5, 6, 15).

## Clinical Features

The age at which patients first experienced symptoms varied from 7-59 years. Table 1 shows that the mean age of presentation for the whole series was 34.1 years with females presenting about 7 years earlier than males.

The presenting symptoms and their relationship to the sex of the patients and the presence of stones on the initial X-rays are shown in Table 2. It will be seen that all patients except the four whose MSK was an incidental urographic finding presented with symptoms which could be ascribed to calculi or infection. Other workers have reported painless haematuria and loin pain in cases of uncomplicated medullary sponge kindey (1, 5) but we have seen only one case in which there was no infection or lithiasis nor any other disorder of the urinary system. This was a woman of 46 who underwent intravenous urography when a routine medical examination revealed a suspiciously high blood urea which later proved to be normal. This patient had no symptoms whatsoever. Table 2 also shows that 43 of our 46 patients had calculi or "nephrocalcinosis" when they were first seen at the St. Peter's Hospitals. In the majority the concretions were confined to the medullary pyramids but six patients had pelvicalyceal or ureteric calculi and two had ureteric calculi with no renal concretions. It is well recognised that a high proportion of patients with MSK have concretions when

0300-5623/79/0007/0197/$02.20

Table 1. Some clinical features of medullary sponge kidney

| | | Mean age at presentation in years | | Mean plasma calcium corrected to total proteins 72 g/l | | |
|---|---|---|---|---|---|---|
| | | | N | | N | SEM |
| Total cases | 47 | 34.1 | 46 | 2.356 | 40 | .0169 |
| males | 26 | 37.4 | 24 (7-59) | 2.363 | 20 | .0198 |
| females | 21 | 30.6 | 20 (11-50) | 2.341 | 16 | .0336 |
| With infected urine | 18 | 32.4 | 18 | | | |
| males | 4 | 40.8 | 4 | | | |
| females | 14 | 30.0 | 14 | | | |
| Without infected urine | 21 | 34.9 | 20 | | | |
| males | 17 | 35.5 | 16 | | | |
| females | 4 | 32.5 | 4 | | | |
| With hypercalciuria | 18 | 34.6 | 18 | 2.408 | 16 | .0253 |
| males | 12 | 35.4 | 12 | | | |
| females | 6 | 32.8 | 6 | | $\underline{P}$ = .001 | |
| Without hypercalciuria | 25 | 32.6 | 23 | 2.306 | 21 | .0200 |
| males | 11 | | | | | |
| females | 14 | | | | | |
| With hemi-hypertrophy | 13 | 27.0 | 11 | 2.401 | 12 | .0352 |
| males | 5 | 26.8 | 4 | | | |
| females | 8 | 27.1 | 7 | | $\underline{P}$ = < 0.1 | |
| Without hemi-hypertrophy | 17 | 33.5 | 17 | 2.346 | 13 | .0268 |
| males | 11 | 37.2 | 11 | | | |
| females | 6 | 26.7 | 6 | | | |
| Good urinary acidification | 15 | | | | | |
| Poor urinary acidification | 2 | | | | | |
| Sponge localised to one side or segment | 7 | 38.7 | With hypercalciuria (3) | | | |
| males | 5 | | | | | |
| females | 2 | | | | | |

Only four had hypercalciuria and infection; ten had normocalciuria and no infection. Mean age 36.8

they first present (1, 5) but the incidence of this complication is unusually high in our series. This may be partly explained by the fact that many patients were referred from other hospitals to our metabolic stone clinic for further investigations of a recurrent lithiasis or "nephrocalcinosis".

It will be noted that all the patients who have presented with upper or lower urinary tract infections were females. A similar finding has been reported recently by Feest (6) and it suggests that pyelonephritis in MSK is usually the result of ascending infection.

Hypertension was found on initial examination in eight patients and a further two developed this complication later, but only three patients had a diastolic blood pressure greater than 120 mm Hg. Nine of the ten were over 45 years old before they developed hypertension and seven had repeated or persistent upper urinary tract infections. Hypertension is not usually considered to be a direct consequence of MSK (5, 6) and in all our cases it was either associated with pyelonephritis or did not develop until late middle age.

Other anomalies of the urinary system were found in a few cases, namely: duplex pelvis and ureter (1 case), calyceal diverticulum (1 case), ureterocoele (1 case), and simple cyst (2 cases). The association of these relatively common disorders with MSK is probably fortuitous. However, congenital hemihypertrophy of the body was found in eight female and 5 male patients, that is in over 25% of the whole series. It is rather curious that

Table 2. Presenting symptoms

| | Males | | Females | | Total |
|---|---|---|---|---|---|
| | With stones | Without stones | With stones | Without stones | |
| Renal colic | 19 | 0 | 5 | 0 | 24 |
| Acute urinary tract infection | 0 | 0 | 6 | 1 | 7 |
| Painless haematuria | 3 | 0 | 2 | 0 | 5 |
| Loin pain | 1 | 0 | 5 | 0 | 6 |
| No relevant symptoms | 2 | 1 | 0 | 1 | 4 |

Fig. 1. Case of hemihypertrophy in a patient with bilateral MSK

although this association of MSK and hemihypertrophy was recognised as an occasional finding by some authors (13, 4) and as a frequent occurrence in a previous series from these hospitals (9) it has not featured in the large studies of others (1, 5, 6, 13). Congenital hemihypertrophy in the absence of MSK but associated with other congenital abnormalities has been described (18) but it seems rare to find the degree of hemihypertrophy found in patients with MSK in other conditions and we consider it unlikely that the association between these two disorders is fortuitous. Nevertheless only a brief description of these patients will be given here because detailed case histories of nine of them were published some years ago (9). In all cases the asymmetry of the body had become evident in early childhood and it was usually more pronounced in the limbs than in the trunk or face. In six the disproportion was so marked as to be almost grotesque (Fig. 1) and in the remaining seven it was clearly evident on clinical examination. Bilateral MSK was found in 11 patients, in one the disorder was confined to the very large kidney on the hypertrophied side of the body and in the remaining patient the contralateral kidney was affected. When considered as a group, the patients with hemihypertrophy presented at an early age (see Table 1) and had more severe and frequent symptoms than the remaining patients. This can be partly explained by the fact that a high proportion of them were females who either presented with a urinary infection or subsequently developed this complication.

## Radiological Findings

Except in the rare incidence where renal tissue is available for gross and microscopic examination, it is well established that the diagnosis of medullary sponge kidney has to be based entirely on the results of intravenous urography. Many excellent descriptions of the urographic appearances of MSK have been published (5, 11, 14) and here it is only necessary to state that they are due essentially to pooling of contrast medium in the cysts and dilated

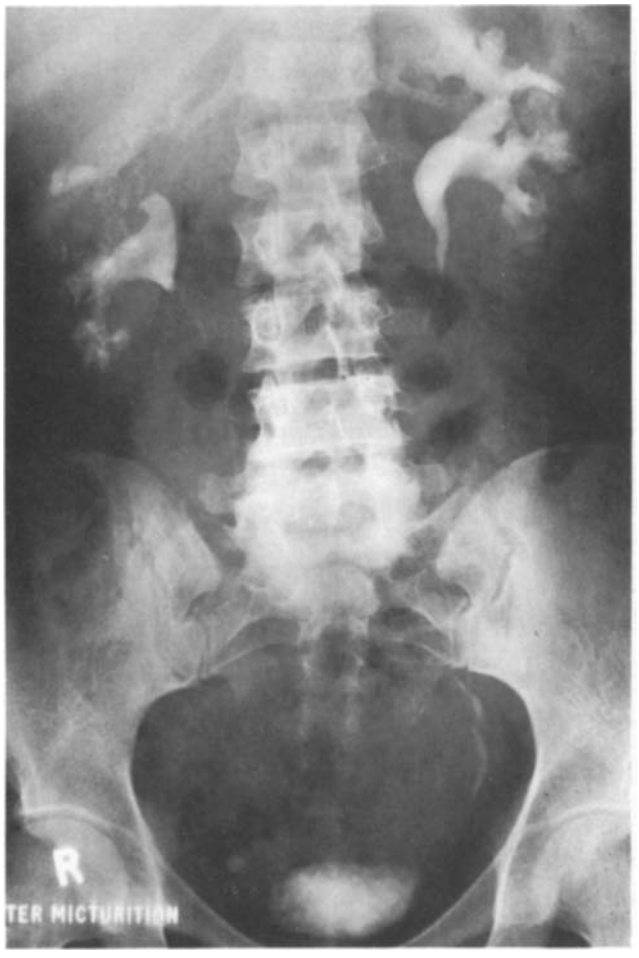
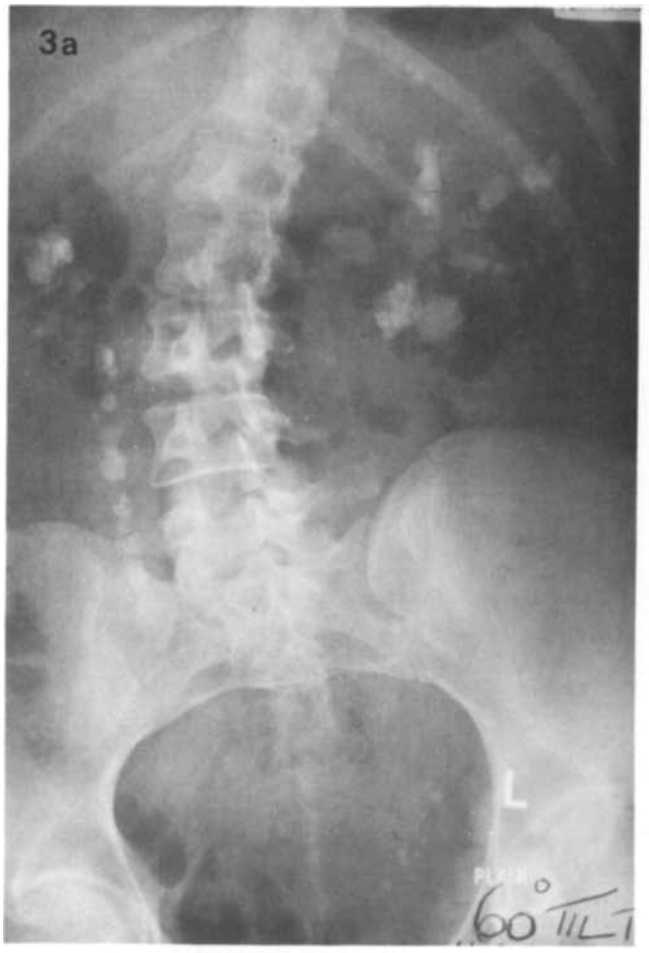



Fig. 2. Urogram of patient with MSK showing typical medullary cavities

tubules during the early phase of the procedure. In the majority of our cases the urographic signs were quite typical and diagnosis presented no difficulty. An example of such a case is shown in Fig. 2. In a few instances the X-ray appearances were however difficult to interpret. This can be illustrated by a brief case history. A married woman aged 29 presented with a history of numerous attacks of renal colic and several episodes of acute pyelonephritis during the preceding 10. years. On intravenous urography the control film showed multiple bilateral pelviureteric calculi and a string of medium sized calculi in the right ureter (Fig. 3a). Moderate hydronephrotic atrophy of both kidneys was seen on the excretion films but the concentration of contrast medium was poor and no medullary cavities were visualised. Her endogenous creatinine clearance was 42 ml/min. Some weeks later after she had undergone operation for removal of the ureteric calculi we obtained the films of the urogram taken two years earlier (Fig. 3B) and this showed fairly typical changes of medullary sponge kidney which were more marked on the left. Precisely the same difficulties were encountered in another very similar case and they illustrate the point that it may be difficult to diagnosis MSK in patients who present with numerous calculi in the upper urinary tract and renal damage as a result of obstruction and infection. Diagnostic problems also arose in some of our early patients who were referred as cases of nephrocalcinosis. These patients had diffuse involvement of both kidneys with countless small concretions occupying most of the medullary cavities and it was often difficult to be sure that these concretions were lying in preformed cavities.

## Laboratory Investigations

Full biochemical investigations on plasma and urine samples were performed on most of the patients. In considering these results we have generally used the mean of the first two or three values before any treatment was given. Most of these proved to be normal except for those indicated below. Plasma urea or creatinine was recorded in all but one case and the initial values were normal (urea below 7. 5 mmol/1) in every case except two where they were 8. 9 and 10. 3 mmol/1 respectively. Plasma sodium, potassium, magnesium, bicarbonate and urate levels proved to be unremarkable. Hypercalciuria was defined as a 24 hour urinary calcium above 7. 5 mmols for women and 8. 75 mmols for men. The incidence of hypercalciuria in this series was 42% (Fig. 4 and Table 1) compared to about 50% found by Ekstrom et al (5), 50% of 10 cases studied by Lalli (11) and 19% by Feest (6) who however used 10 mmol/24 hour as the upper limit of normal of urinary calcium. It will be seen from Table 3 that urinary calcium measurements were made in approximately equal numbers of men and women and that hypercalciuria was found in 52% of the men and in 30% of the women. This is quite different from what is found in idiopathic hypercalciuria where males account for 95% of the cases (Table 3). This suggests that the cause of hypercalciuria could be different in the two conditions. Even in patients with idiopathic hypercalciuria, a condition that has been studied by numerous groups and in great detail, doubt remains as to whether the majority are primarily "over-absorbers" or have a primary renal tubular leak of calcium. We are unaware of any evidence in the literature relating to the cause of the hypercalciuria in MSK. It would be expected that the primary over-absorbers of calcium would show marginally raised plasma calcium values and that those with renal tubular leak of calcium would show marginally low plasma calcium values. In this series of patients with MSK, those with hypercalciuria had a higher mean plasma calcium level



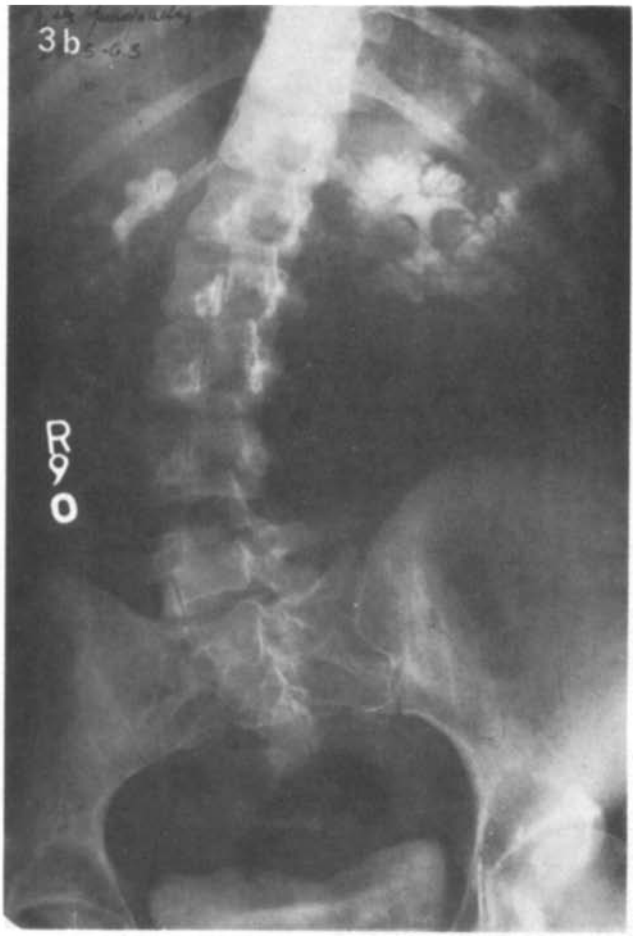




Fig. 3a. Plain radiograph showing multiple renal and ureteric calculi in 1965. The scoliosis is due to hemihypertrophy

Fig. 3b. Urogram of same patient in 1963 showing typical changes of MSK, especially on left

than those without the hypercalciuria (Table 1). Not only was this difference highly significant statistically but there was an overall correlation between plasma calcium and urinary calcium (Fig. 5). Admittedly the correlation coefficient of 0.516 was not very high but on removing the four cases of localised MSK the correlation coefficient rose to 0.580. It is seen in Fig. 5 that of 10 females with hypercalciuria, nine showed plasma calcium values above the mean while only one showed a value actually below our lower limit of normal. This suggests that apart from the one notable exception the mechanism of hypercalciuria was probably primary over absorption of calcium. This is perhaps a little surprising in a condition which appears to be mainly renal, but it must be recalled that there are non-renal manifestations of the condition as shown by hemihypertrophy, and the hypercalciuria could be another such non-renal manifestation.

The ability of the kidneys to secrete acid urine was tested in 17 patients (11 males and 6 females) by the short ammonium chloride test of Wrong and Davies (20). 15 of these patients gave a fairly normal fall in urinary pH to less than 5.3 but two (both males) only achieved pH values of 5.7 and 6.2 respectively. It therefore seems unlikely that renal tubular acidosis is usually the factor responsible for hypercalciuria in this series of patients, and somewhat similar results were obtained in a series of five cases by Morris et al. (15). Others however have found rather different results. Feest (6) found a defect in urinary acidification in 24% of 29 cases, but 6 out of these 7 had elevated serum creatinine levels which could have influenced the results whereas in the present series none of those tested showed raised plasma urea or creatinine levels. In two other series 3 out of 3 and most of 21 cases respectively (3, 7) were found to have impaired ability to secrete acid loads and the reasons for these conflicting results are not obvious.

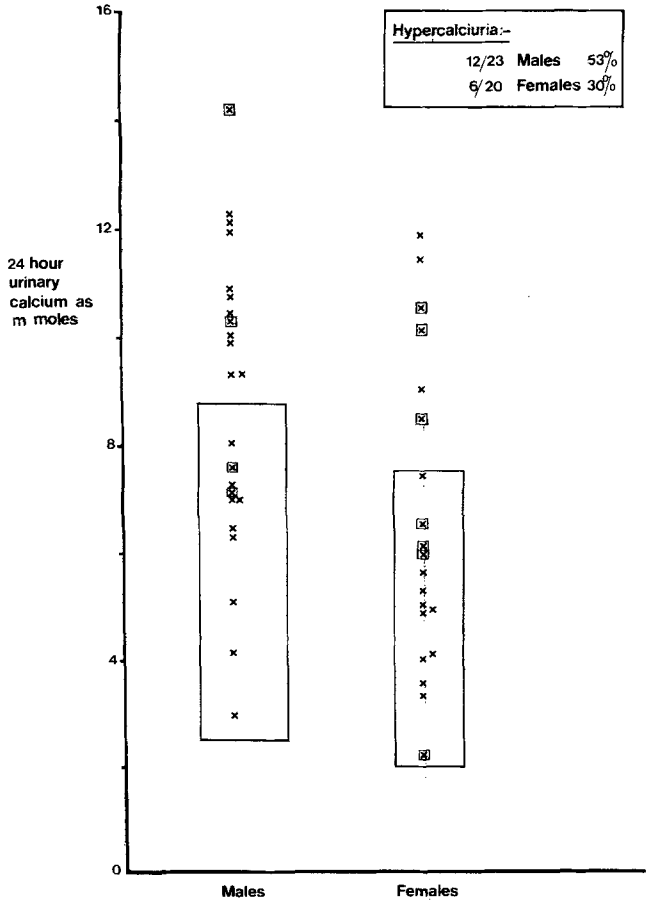



Fig. 4. 24 hour urinary calcium values from 43 patients with MSK. Each cross represents one patient but is the mean of one to three urinary collections prior to treatment. Crosses inside squares indicate patients with hemihypertrophy. The large rectangle indicates our limits of normality

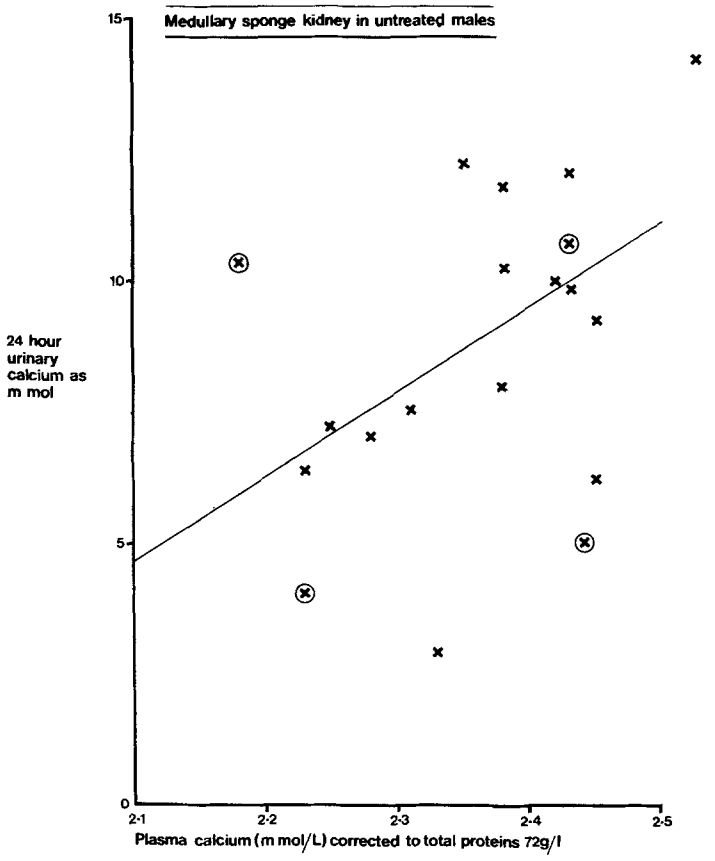



Fig. 5. Relationship between 24 hour urinary calcium and plasma calcium (corrected to plasma proteins 72 g/l) in 19 male patients with MSK. Each cross represents the mean of several plasma and urinary values (see text) not necessarily coincident in time. The encircled crosses are from patients with unilateral MSK. Correlation co-efficient for the whole series is 0.516 and for the bilateral cases only 0.580. Normal range for corrected plasma calcium 2.22 to 2.258 mmol/l

## Stone Type

Stones were analysed from 24 patients with MSK, 14 males and 10 females (see Table 4). In several respects the pattern of chemical composition resembles that reported from these hospitals for renal stones in general (19). Thus stones composed of calcium oxalate with or without phosphate accounted for the majority and this was especially the case in males. Stones made of triple phosphate with or without calcium phosphate or oxalate predominated in females, presumably because of the associated higher incidence of UTI. The results in Table 4 are remarkably similar to those previously reported from these hospitals for idiopathic hypercalciuria (16) and do not support the finding of Ekström et al. (5) who reported a higher incidence of calcium phosphate and lower incidence of calcium oxalate stones in MSK than expected.

## Histopathology

The whole of one kidney was removed from one female patient who had had recurrent UTI, and the lower pole of one kidney from a male patient who was making large numbers of calculi at this site. These specimens were examined histopathologically by Dr. R. C. B. Pugh who noted the following:

Macroscopically the renal papillae were broad-

Table 3. Comparison of sex incidences for idiopathic hypercalciuria (IH)[a] and medullary sponge kidney (MSK)

| | Idiopathic hypercalciuria | | Medullary sponge kidney | | | | |
|---|---|---|---|---|---|---|---|
| | | | All cases | | With hypercalciuria | Without hypercalciuria | % With |
| | No. | % | No. | % | No. | No. | % |
| Males | 133 | 95 | 26 | 55 | 12 | 11 | 52 |
| Females | 7 | 5 | 21 | 45 | 6 | 14 | 30 |
| Total | 140 | 100 | 47 | 100 | 18 | 25 | |

[a] Up-dated from (16)

Table 4. Chemical composition of stones from 24 patients (14M: 10F) with MSK

| | Males | Females | Total |
|---|---|---|---|
| Calcium oxalate "without" phosphate[a] | 5 | 1 | 6 |
| Mixed calcium oxalate and phosphate[b] | 8 | 4 | 12 |
| Calcium phosphate and magnesium ammonium phosphate | 1 | 2 | 3 |
| Mixed triple phosphate and oxalate | 0 | 3 | 3 |

[a] Not more than 0.8% P.

[b] Mean of 9.6% and 27.3% oxalate

ened and "mushroomed" with a spongy appearance, and contained a number of tiny cysts some of which contained calculi. Microscopically the outer medulla was not significantly abnormal and changes in the cortex, i.e. some scarring, destruction of nephrons and local lymphocytic infiltrations, seemed attributable to pyelonephritis. The most striking changes were in the inner medulla where the greater parts of each renal pyramid were abnormal. The regular outlines of the papillae were lost and there were many widely dilated collecting tubules which frequently contained calculi or pus and were lined by thick layers of transitional epithelium which had sometimes undergone well marked squamous change. In a few places the wall of the tubule had disappeared and the calculi had become interstitial. All the above was quite consistent with the changes described by Ekström et al. (5) but in addition both kidneys showed some tubular changes similar to those seen in dysplastic kidneys, with small tight bunches of tubules in one case and dilated collecting tubules surrounded by connective tissue in the other case.

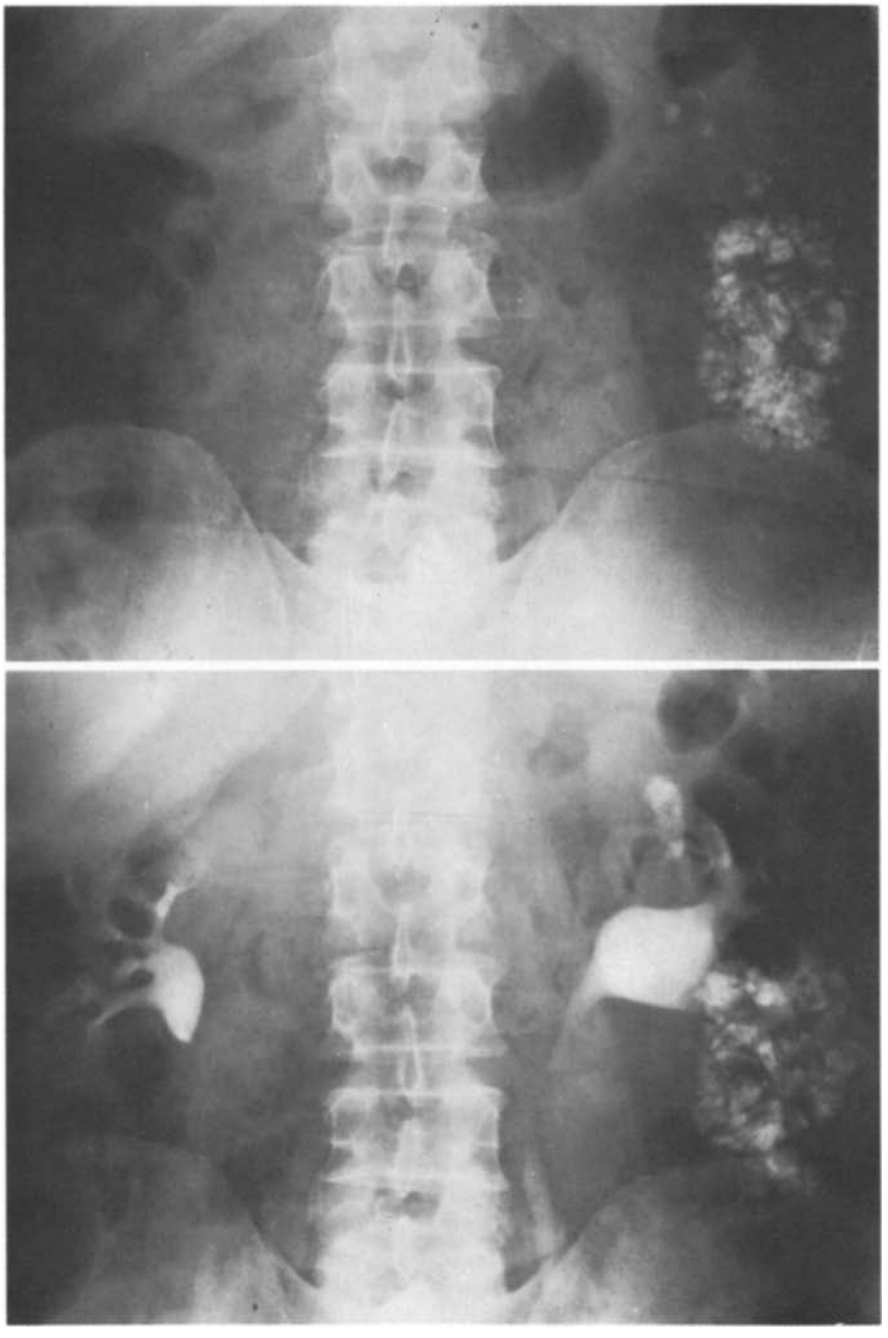


Fig. 6. Control and excretion radiography sith numerous medullary concretions mainly confined to enlarged left lower pole

Treatment

Essentially this consists of the prevention and treatment of the two complications, namely, stones and infection.

1. Metabolic Control of Urinary Calcium Concentration

As seen in Table 3 the majority of the stones that were analysed in the present series of cases of MSK were made of calcium oxalate sometimes accompanied by phosphate. Although figures are not shown here, urinary oxalate studies have been performed on many of the patients and values have always been normal, just as was found by Feest (6). On the other hand urinary calcium is frequently raised (see above) and it seems logical to treat these patients as though they had idiopathic hypercalciuria. However, many patients with MSK form urinary stones despite normal urinary cal-

cium levels and in the absence of UTI. The reason for this is presumably stasis in the ectatic collecting tubules. It therefore seems logical to us to attempt to lower the urinary calcium of all patients presenting with MSK and to aim at levels well below the limits of 7.5 mmols for females and 8.75 for males that we set for idiopathic hypercalciuria. It is not possible to quote precise target figures but only to say that the treatment should be pushed to the point where stone formation ceases. The treatment may be summarised thus:

(a) Urinary Output. Patients should drink sufficient fluids to yield a 24 hour urinary value of three litres or more. They should be educated to monitor this for themselves by occasionally measuring the 24 hour urinary volume and by observing the colour of the urine. The hardness of the water is not a valid objection to drinking but admittedly soft water is better than hard water and if the patient wishes to install a water softener for his personal supply of drinking water there is no objection. Hard water, however, is better than no water.

(b) Diet. This should be low in calcium and oxalate. The foods to be avoided are milk, cheese, yogourt, rhubarb, beetroot, strawberries, nuts and spinach. Many of these foods are easily avoided and such a diet can be sustained by most patients.

(c) Drugs. The result of treatment with water and diet should be reviewed before the use of drugs is considered. If the urinary calcium content and volume of 24 hour urine remain unsatisfactory, then there are three main types of drug which can be added. Firstly, thiazide diuretics, which are cheap, convenient to take and have lowered the urinary calcium in many of our patients with MSK. They should be avoided however if there is a family history of gout or diabetes mellitus. Secondly, sodium cellulose phosphate has also been effective in our patients in lowering urinary calcium but it can cause unacceptable gastrointestinal symptoms (16), and must be taken with each main meal, is expensive and requires strict attention to avoidance of oxalate-rich foods because being a substance that binds calcium in the gastrointestinal tract it results in increased absorption of dietary oxalate (8). Although Bendrofluazide and sodium cellulose phosphate individually have apparently been effective in preventing urinary stone recurrences in some of our cases of MSK, a small number have required a combination of both in order to reduce the urinary calcium to the point where stone formation has ceased. The third treatment recommended is inorganic phosphate in the form of sodium and potassium hydrogen salts. Although it is claimed, (17) that this treatment both lowers urinary calcium and prevents stone formation in patients with hypercalciuria, there are as yet no reports on its use in MSK and we have no experiences to report with this form of therapy.

2. Surgical Treatment

Despite the tendency of the small medullary calculi to be expelled spontaneously once they had ulcerated through into the pelvi-calyceal system, surgical procedures for the removal of stones have been required in 22 patients. To date, these 22 patients have undergone a total of 46 operations including 13 pyelolithotomies, 14 uretero-lithotomies and 19 endoscopic procedures. Two radical surgical procedures were undertaken. Firstly, a lower pole partial nephrectomy was carried out in 1 patient who had multiple calculi mainly confined to the pyramids of the lower pole of the left kidney (Fig. 6). Secondly a nephrectomy was performed in another patient on account of recurrent UTI (see below).

3. Urinary Infections

These were treated initially with short courses of the appropriate antibiotic in full therapeutic dosage. Such treatment usually led to the disappearance of bacteriuria and the relief of symptoms, but frequent recurrence or persistence of infection was a problem in 8 patients, all females, and in 5 of these it led to the use of long term suppressive antibacterial therapy. One patient, a young women of 22, presented with a history of repeated attacks of acute right sided pyelonephritis. Intravenous urography showed a normal left kidney and typical changes of MSK complicated by multiple medullary calculi on the right. It proved impossible to control, let alone eradicate, her infection with antibacterial agents and after she had five further attacks of severe acute pyelonephritis she was submitted to a right nephrectomy.

Course and Prognosis

As already stated 26 patients have been followed for periods of 5-20 years (mean follow-up period 10.2 years). The clinical course in these patients has been so variable that it is difficult to summarise, but all but 1 of these 26 patients have had recurrent symptoms following their initial presentation. Rather surprisingly the sole exception is a women who was found to have extensive changes of MSK with multiple medullary calculi in her left kidney when she presented in 1969 with a urinary infection at the age of 35. Fifteen patients (11 males and 4 females) have had recurrent attacks of renal colic, the majority of which have been followed by the expulsion of small calculi. In general, these attacks have been frequent (1 patient has had 5-6 a year for the past 13 years) but the majority have

been transient and mild and in some instances they have amounted to little more than the almost painless expulsion of stones. Urinary infections have occured in 8 female patients but in only 4 of these have such infections dominated the clinical picture. Urinary infections have also occured in 3 male patients but in all instances the infection followed instrumentation. Only 3 patients have had macroscopic painless haematuria.

Repeated X-ray examinations have usually shown no change or else a gradual increase in size and number of medullary concretions and four patients (3 females, 1 male) developed pelvi-calyceal calculi some years after they had presented. Two of these four patients, both women with urinary infection have had recurrences of stone following pyelolithotomy. In most cases serial urograms have shown no change in the extent or appearances of the medullary cysts apart from the occasional enlargement or coalesence of cavities containing concretions. However in three cases, intravenous urograms taken some years after the initial examinations showed typical changes of MSK in pyramids which had originally appeared to be unaffected. In each instance careful comparison of the excretion films showed that the changes in the appearances were not due to true progression or extension of MSK but were the results of improvement in the quality of the later urograms. The difficulty of delineating the extent of the disease should be borne in mind whenever radical surgery is under consideration. One of the cases discussed above was that of a young man who was scheduled to undergo a left upper pole partial nephrectomy for "localised" sponge kidney but whose operation was cancelled when a pre-operative high dose urogram showed that the disease was much more diffuse than originally thought.

Although 3 patients had hydrocalycosis with a moderate degree of cortical atrophy when they first presented, no patient has subsequently developed any appreciable degree of obstructive atrophy, nor has any patient developed focal pyelonephritic scars. Two patients had slightly raised plasma urea levels when they were first seen (see above) but neither has subsequently developed any further deficiency in renal function and their latest plasma creatinine levels are .14 and .15 mmol/l. Normal plasma and creatinine levels were found in the other 24 patients when they first presented and all had plasma creatinine levels of less than .14 mmol/l when they were last examined. Similar findings were reported recently by Feest (6).

The follow-up studies in the present series of patients support the widely held belief that MSK has a high morbidity when it is complicated by concretions or infections. However none of the 26 patients has yet developed any serious renal damage, and in this respect our findings differ from those reported by Ekström (5). Doubtless this reflects the advances made in the surgery of urinary lithiasis and the treatment of urinary infections since the Swedish survey was published. Since most of the symptoms of MSK are due to the concretions, it is logical to try and reduce the concentrations of urinary calcium and oxalate. Such measures have been adopted in some but not all of our patients (see above) but it has been extremely difficult to determine whether they have been beneficial.

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