Protean presentation and multiple challenges of nephrocalcinosis in pregnancy (six pregnancies in four patients)

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Abstract

Background. Nephrocalcinosis is an umbrella term covering increased content of calcium salts in the renal parenchyma, interstitial damage and potential evolution towards renal failure. Pregnancy is often the first occasion for biochemical or imaging tests in young women and may allow early diagnosis. Conversely, even mild kidney disease may represent a challenge in pregnancy.

Aim. The aim of this study was to report on four patients in whom nephrocalcinosis was first diagnosed during pregnancy, exemplifying the protean presentation and multiple challenges of nephrocalcinosis in pregnancy.

Methods. This is a case series study including data on all pregnancies prospectively gathered in the Nephrological–Obstetric Unit dedicated to pregnancy and kidney diseases (2000–11).

Results. Six pregnancies were observed in four patients (31–35 years; one twin pregnancy, one ongoing, one patient with three pregnancies). Symptoms were oedema in two (later developed in a further patient), renal functional impairment and electrolyte imbalance in two each. Two patients developed hypertension late in pregnancy. Electrolyte imbalance was life-threatening in one patient (severe acidosis, severe hyperkalaemia: 7.5 mEq/L). Delivery was...
by Caesarean section in three patients, preterm in one. Multiple or long hospitalizations for metabolic reasons were needed in three patients, the fourth was hospitalized for obstetric reasons. In all patients, diagnosis of nephrocalcinosis was made at ultrasounds during basic nephrological evaluation, confirmed at computerized tomography scan in three. The pathogenesis was linked to diuretic abuse in one case and to collagen disease, inborn errors and prematurity, possibly associated with diuretic misuse, in the others.

**Conclusion.** Nephrocalcinosis may have protean presentations in pregnancy. The risk of severe electrolyte derangements, oedema and hypertension warrants strict clinical surveillance.

**Keywords:** acidosis; chronic kidney disease; diuretic abuse; nephrocalcinosis; pregnancy

**Introduction**

Nephrocalcinosis generically describes kidney diseases characterized by the deposition of calcium salts in the kidney parenchyma (often associated with acid–base and electrolyte derangements) and by a potential evolution towards end-stage kidney disease [1–3]. The first descriptions of nephrocalcinosis were in the context of primary hyperparathyroidism [3]. However, the diagnostic category was progressively widened to include different kidney diseases characterized by the diffuse calcium deposition, initially detectable at kidney biopsy and, in later stages, severe enough to be demonstrable at imaging. By definition, therefore, the diagnosis relies on imaging techniques, while renal biopsy plays a minor role, limited to the early phases [1, 2].

Diffuse renal calcifications may be detected by plain abdominal x-rays. However, the main diagnostic tool is spiral computerized tomography (CT) scan, due to its ability to disclose small parenchymal calcifications, allowing identification of the spatial relationships with the excretory system and thus discrimination between medullary and cortical calcifications. The role of nuclear resonance is minor because of its lower sensitivity to calcium deposits and to the non-specific appearance of the renal pyramids [3–6]. The role of kidney ultrasounds is more controversial: ultrasounds are commonly considered less sensitive than CT scans, but the diagnostic accuracy is high in experienced hands. Due to the widespread availability of ultrasounds and to the limitation of other imaging techniques in childhood or pregnancy, ultrasounds are presently a major diagnostic tool [3, 7, 8].

The clinical presentation of nephrocalcinosis is protean, reflecting the heterogeneity of the pathogenesis. Particularly in the first stages, it can be asymptomatic, even if subtle deficits in urine concentration or mild electrolyte derangements are often present. Distal tubular acidosis and nephrocalcinosis are often concomitant, with an entangled cause–effect relationship [1–3, 9, 10].

Since the disease is frequently asymptomatic, it is difficult to quantify its prevalence.

The list of potential causes is long [1–3, 9–12]. Nephrocalcinosis is increasingly described in newborns and children and bears a close relationship with both prematurity and very low birth weight [13, 14]. In adults, it may be caused by inborn and acquired tubular acidosis, in addition to primary hyperparathyroidism; distal acidosis associated with Sjogren’s syndrome is becoming an emerging diagnosis. Iatrogenic causes are frequent, including diuretic abuse, phosphate bowel preparations and laxatives [8, 15, 16].

Pregnancy is often the first occasion to perform basic clinical and laboratory evaluations in apparently healthy young women and thus constitutes a fundamental step in the diagnosis of non-symptomatic kidney diseases. The importance of a timely diagnosis must be underlined, since even mild kidney diseases may display severe manifestations during pregnancy, with increased risks of pregnancy complications [17, 18].

In spite of the growing interest in both nephrocalcinosis and pregnancy in chronic kidney disease (CKD), there are very few data on the management of nephrocalcinosis in pregnancy. Our search strategy, run on Medline in February 2011 and combining the free terms ‘pregnancy’ and ‘nephrocalcinosis’, yielded 46 titles and abstracts. Only two reports published in the last two decades were relevant, both regarding primary hyperparathyroidism [19, 20].

The protean presentation and the different challenges of nephrocalcinosis in pregnancy are exemplified in our case series of six pregnancies in four patients. To our knowledge, this is the only case series on patients diagnosed with nephrocalcinosis during pregnancy.

**Materials and methods**

**Setting of the study**

The study was performed in the Maternal–Foetal Unit of the University Hospital Sant’Anna, Turin, Italy, where all pregnant patients with kidney diseases have been followed by the same obstetric and nephrological team since 2000. Data on all pregnancies followed in the unit have been prospectively gathered since the start of the activity.

In our outpatient unit dedicated to kidney diseases in pregnancy, 230 pregnancies were observed in 211 women from January 2000 to January 2011. In 25 cases, the patients were referred for acute kidney diseases, mainly upper urinary tract infections; in 73 cases, diagnosis of CKD was made during pregnancy (in 41, a previous diagnosis of kidney disease had been overlooked, while in 32, the presenting symptoms were reported for the first time in pregnancy).

In the case of the analysis of specific diseases, such as nephrocalcinosis, recorded data are integrated with additional information, from the laboratory files, from the hospitalization charts and from post-pregnancy follow-up, when available.

**Approach to kidney disease in pregnancy and related definitions**

Patients are referred to the outpatient unit dedicated to pregnancy in kidney disease in the case of any renal function derangement, both known before pregnancy and suspected in pregnancy. The cases here described underwent routine workup for new diagnosis of kidney disease.

The diagnostic workup for patients with signs or symptoms of kidney disease (not previously diagnosed) includes renal function assessment (creatinine clearance and proteinuria on 24-h urine collection), coagulation and immunological screening (anti-nuclear factors, anti-extractable nuclear antigens screening, complement levels and immunoglobulin dosage) and abdominal ultrasounds.

**Biochemical data** were obtained by standard laboratory methods; in particular, of relevance for the present study, urinary pH was assessed by Multistix 10 SG (Bayer Corporation).

In the case of hypertension, 24-h blood pressure monitoring and echocardiography are performed; other analyses are prescribed on demand. Hypertension is defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg or anti-hypertensive therapy. CKD is classified according to K-DOQI guidelines.
Ultrasounds were performed in the same setting by a small group of skilled operators. All cases with suspect nephrocalcinosis were reviewed by the same expert (AD). Nephrocalcinosis was detected at ultrasound and confirmed, whenever possible, by CT scan after delivery. At both CT scan and ultrasounds, nephrocalcinosis was classified as medullary, cortical or diffuse according to the anatomical area involved. At ultrasounds, medullary nephrocalcinosis was further subdivided into three grades according to the degree of echogenicity: Grade I (mild increase of echogenicity around the pyramidal border); Grade II (mild increase of echogenicity at whole pyramid); Grade III (more severe hyperechogenicity of the entire pyramid), following literature indications [20, 21].

The presence of scattered intra-parenchymal calcifications at CT scan further supported the diagnosis. In our cases, the diagnosis was made by imaging techniques that revealed macroscopic calcifications. Hence, renal biopsy, able to reveal microscopic calcifications, was not performed [16]. The CT scans usually allow tridimensional discrimination between the parenchymal and papillary calcifications; furthermore, the two diseases may co-exist, and their relationship may be complex and entangled. However, the typical hyperechogenicity of the renal pyramids is not found in patients with ‘simple’ caliceal stones; in this context, CT scan was performed mainly as a tool to stage the calcifications, and the diagnosis mainly relied on the typical ultrasound picture [16, 22, 23].

Obstetric policy and main definitions

General policies. The frequency of nephrological and obstetric controls is individualized, from weekly to monthly. At each clinical consultation, blood pressure and weight are recorded; foetal well-being and foetal growth are controlled. In addition to the routine controls of pregnancy, all patients undergo (at least) a monthly determination of renal function and proteinuria (24-h urine collection), uric acid, urinalysis and urinary culture, serum electrolytes, coagulation and blood cell counts; other tests are required on demand. Ultrasound biometry and Doppler velocimetry of uterine and umbilical arteries are individualized (every 2–4 weeks if risk of foetal growth restriction).

Hospitalization is required in the presence of uncontrolled or new-onset hypertension, worsening of renal function, new onset or worsening of proteinuria or any inter-current problem of mother and/or foetus (abnormal foetal growth and/or severely abnormal umbilical Doppler) [17].

Preterm delivery is defined as delivery before 37 completed weeks of gestation. Indications for early delivery are severe worsening of maternal and/or foetal conditions until 32 weeks or moderate worsening after 32 weeks of gestational age. In these cases, beta-methasone is administered at standard doses (12 mg/day, repeated at 12–24 h) for the induction of lung maturation. Caesarean section is performed for foetal indications or in cases of unfavourable conditions for, or lack of response to, induction. Apgar scores are recorded at 1 and 5 min by the neonatologists. A newborn is defined as small for gestational age when the birth weight is below the 10th centile according to Italian birth weight references; intra-uterine growth restriction is defined as a flattening of the growth curve [17, 21].

All patients are routinely followed for at least 3 months after delivery, and information on the children is also gathered on this occasion. Metabolic testing was postponed to at least 1 month after discontinuation of breastfeeding.

Results

Overall data

In the study period (January 2000–January 2011), 230 pregnancies in 211 women were referred to the Outpatient Unit for Kidney Diseases in Pregnancy. Four of the women were diagnosed with nephrocalcinosis. The overall prevalence is ~2% but rises to 5.5% if only the new diagnoses are considered. The diagnosis was performed by ultrasounds in all patients and confirmed by CT scan in three (recent delivery in the fourth case) (Figures 1–4).

None of the patients had a history of stone disease or developed kidney stones or urinary tract dilatation during pregnancy or during the subsequent follow-up. None of the children presented echographic signs of nephrocalcinosis. In the presence of pre-existing kidney disease, the differential diagnosis with pre-eclampsia (PE) may be difficult; however, in our cases, the presence of PE was ruled out by normotension during pregnancy and, in the cases who developed hypertension after delivery (Case 2, first pregnancy, Case 4), by the lack of increase in the low-level baseline proteinuria.

Detailed descriptions of the patients are reported below.

Fig. 1. Case 1: Ultrasounds showing evident hyperechogenicity of the renal pyramids: Medullary Nephrocalcinosis Grades II-III.
Case reports

Case 1

Clinical data.—A 31-year-old primiparous woman was referred at the 12th gestational week for sudden onset of oedema (weight gain of 5 kg during the previous week). She was a preterm child, born at 34 weeks of gestational age, with low birth weight (1800 g). The clinical history was otherwise unremarkable, except for ‘cyclic oedema’ in adolescence.

At hospitalization, the renal function was reduced, in particular in relation to pregnancy standards (creatinine clearance: 60 mL/min); she was normotensive and remained so throughout pregnancy. Moderate hyperuricaemia and microalbuminuria were present (Table 1). With bed rest, control of fluid intake and moderate sodium restriction, the oedema gradually resolved and the patient started a strict outpatient follow-up. No sign of thyroid derangement, autoimmune disease or coagulation disorder was found in repeated testing during and after pregnancy. Mild hyperparathyroidism, secondary to vitamin D deficiency [parathyroid hormone (PTH): 75 pg/mL; 25-OH vitamin D: 9 pg/mL], was detected shortly after pregnancy but resolved after vitamin D supplementation (PTH: 35 pg/mL; 25-OH vitamin D: 38 pg/mL).

At 37 weeks, she was hospitalized on account of a decrease in kidney function, with a severe increase in uric acid and hyperkalaemia (peak serum potassium: 7.5 mEq/L). The presence of metabolic acidosis with high urinary pH indicated a renal loss of bicarbonates. Due to the severe electrolyte derangement, Caesarean section was performed at 37 weeks, 4 days; a healthy female child was delivered. Four years after delivery, the patient is on regular nephrological follow-up; renal tubular acidosis is corrected by supplementation with bicarbonate, potassium and magnesium salts. The daughter is developing normally.

Diagnostic details.—Renal ultrasounds showed a typical pattern of hyperechogenicity of the renal pyramids, suggestive of Grades II–III medullary nephrocalcinosis (Figure 1). CT scan performed after delivery confirmed the presence of scattered medullary calcifications (Figure 2).

The aetiological diagnosis of nephrocalcinosis remains partially obscure and may be multifactorial; after repeated questioning, she admitted occasional diuretic abuse since adolescence. In the absence of previous ultrasounds, it is impossible to define the relative role of prematurity in the development of nephrocalcinosis; one cannot either exclude hereditary Distal Renal Tubular Acidosis.
The metabolic testing performed 2 years after pregnancy, ~6 months after discontinuation of breastfeeding, revealed a low-normal fractional sodium excretion (0.85%) with high fractional potassium excretion (26.2%, in spite of low serum potassium: 3 mmol/L) and low calcium fractional excretion (1.45%); fractional excretion of phosphate was high 20.5% (normal: <15%), in keeping with a role of hyperphosphaturia in the pathogenesis of some forms of nephrocalcinosis, eventually linked with low citrate excretion (0.29 mmol/24 h) [1]. On the contrary, oxalate excretion was low (0.3 mmol/24 h).

Case 2

Clinical data.—This patient was referred at the time of her first pregnancy, was followed through a second pregnancy and is presently undergoing her third pregnancy.

She was 35 years old when first referred at the seventh week of gestation because of reduced renal function (Table 1). At the clinical history, she reported anorexia in adolescence but denied diuretic abuse. Three and half years previously, she had been hospitalized for acute pyelonephritis; on that occasion, the renal function was moderately reduced [serum creatinine 1.2 mg/dL, estimated glomerular filtration rate 60 mL/min (Cockroft)]. Three years previously, in summer, she developed acute rhabdomyolysis, after prolonged sunshine exposure. The patient remained normotensive and kidney function was stable throughout the whole pregnancy. Immunological and coagulation screenings were normal. She delivered a healthy male baby at 37 weeks (premature rupture of the membranes) (Table 1).

The post-partum phase was complicated by the development of arterial hypertension (140–145/100 mmHg) without proteinuria or oedema. The blood pressure slowly normalized after 3 months of anti-hypertensive therapy with angiotensin-converting enzyme inhibitors, which were then discontinued. A miscarriage (sixth week) occurred 1 year after delivery.

At 37 years of age, she started a second pregnancy. From the 12–14th week of pregnancy, she complained of muscle cramps. Hypokalaemia, hypophosphataemia and hypomagnesaemia were observed; dietary correction with potassium, magnesium supplements and phosphate-rich foods was performed. She remained normotensive throughout pregnancy and after delivery. Under regular nephrological follow-up, mild hypokalaemia and hypomagnesaemia persisted after delivery, while phosphate levels slowly corrected.

At the time of the present report, she is 39 years old, at the 20th week of her third pregnancy, normotensive and with normal serum electrolytes, on potassium and magnesium supplementation; phosphate levels are in the normal range.

Diagnostic details

The diagnosis of medullary nephrocalcinosis was made by ultrasounds and confirmed at CT scan after delivery (Figures 3 and 4). The clinical history suggests that nephrocalcinosis preceded the first pregnancy: the rhabdomyolysis points to a urinary concentration deficit, contributing to dehydration, and upper urinary tract infections are known to be associated with nephrocalcinosis. Furthermore, nephrocalcinosis is

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**Table 1.** Summary data at referral of the four patients (six pregnancies) with diagnosis of nephrocalcinosis

<table>
<thead>
<tr>
<th></th>
<th>Case 1</th>
<th>Case 2 (first pregnancy)</th>
<th>Case 2 (second pregnancy)</th>
<th>Case 2 (third pregnancy)</th>
<th>Case 3</th>
<th>Case 4</th>
</tr>
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<tbody>
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<tr>
<td>GFR (mL/min)</td>
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<td>61</td>
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<tr>
<td>Uric acid (mg/dL)</td>
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<td>3.3</td>
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<tr>
<td>Na (mmol/L)</td>
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<td>136</td>
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</tr>
<tr>
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<td>4.3</td>
<td>4.1</td>
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<tr>
<td>Calcium (mmol/L)</td>
<td>2.65</td>
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<td>2.55</td>
<td>2.45 (P 3.9)</td>
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<td>2.3</td>
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<tr>
<td>Albumin (g/dL)</td>
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<td>3.8</td>
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<td>pH 7.5</td>
<td>pH 7.5</td>
<td>pH 6</td>
<td>pH 6</td>
</tr>
<tr>
<td>Proteinuria (g/24 h)</td>
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<td>0.15</td>
<td>0.2</td>
<td>0.1</td>
<td>0.5</td>
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<td>Density</td>
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<td>1010</td>
<td>1010</td>
<td>1012</td>
<td>1020</td>
<td>1011</td>
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<tr>
<td>HCO3 (mmol/L)</td>
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<td>24</td>
<td>23.5</td>
<td>22.5</td>
<td>22</td>
<td>21</td>
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<td>BE</td>
<td>−3</td>
<td>−1</td>
<td>−1.2</td>
<td>−1.8</td>
<td>−3</td>
<td>−4</td>
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associated with diuretic abuse, while in anorexia nervosa, tubular dysfunction is usually associated with severe and prolonged hypokalaemia, which does not seem to have been present in this patient. Therefore, the most likely diagnosis is a congenital type of tubular acidosis, even if a contribution of self-prescribed drugs cannot be completely ruled out.

At the metabolic screening, performed between the first and the second pregnancy, fractional sodium excretion was 1.1%, with high fractional potassium excretion (43%, in spite of low-normal serum potassium: 3.8 mmol/L, under oral potassium supplementation) and low calcium fractional excretion (1.38%); in her case too, fractional excretion of phosphate was high 22%; citrate excretion was in the lower range (0.75 mmol/24 h).

Case 3
Clinical data.—A 33-year-old secondiparous woman was referred for severe refractory oedema, with an 8 kg weight gain (baseline: 45 kg) at the fifth gestational week.

At the baseline assessment, there was moderate reduction of renal function (Table 1). She was normotensive and the protein excretion rate was normal. She reported anorexia in adolescence and chronic use of diuretics since then. Diuretics had been discontinued at the start of pregnancy, but they needed to be resumed at low doses, under strict clinical control, for the refractory oedema. With a combination of moderate sodium restriction, bed rest, elastic compressive stockings and low-dose diuretics (furosemide 25 mg, tapered to 12.5 mg at the fifth month of gestation), renal function remained stable and oedema improved enough to allow daily chores. No electrolyte immunological or coagulation derangement was present. After pregnancy, she resumed moderate diuretic use and discontinued regular follow-up.

Diagnostic details.—Medullary Grade II nephrocalcinosis was diagnosed at ultrasounds during pregnancy and confirmed by CT scan 3 months after delivery. The diagnosis of diuretic-induced nephrocalcinosis seems quite clear in this case. The patient discontinued follow-up before the end of the breastfeeding period and did not comply to perform metabolic assessment based upon 24-h urine collection.

Case 4
Clinical data.—A 33-year-old primiparous woman was referred at the 32nd week of a twin pregnancy because of urinary tract dilatation (right side) and incidental evidence of nephrocalcinosis at ultrasounds. She had undergone a fecundation in vitro and embryo transfer procedure and had suffered urinary tract infections throughout pregnancy. She was normotensive before and throughout pregnancy.

Her clinical history was characterized by autoimmune hypothyroidism diagnosed 5 years previously and coeliac disease diagnosed 4 years previously. Positive anti-nuclear antibodies (ANA) (1/80 granular pattern) were present on several occasions; no specific complaints were reported, except periods of profound asthenia and occasional joint pain. On this basis, a generic diagnosis of collagen disease had been made in the past. Positive low-titre ANA test were reported, 6 months before pregnancy, but were not confirmed in pregnancy.

The follow-up of pregnancy had been unremarkable, besides the presence of frequent urinary tract infections. However, at the 36th week of gestation, she suddenly developed severe oedema (weight gain of 5 kg in 2 days), presumably as a consequence of steroid therapy routinely performed to induce pulmonary maturation. On that occasion, she also developed moderate hypertension (145/100 mmHg), which persists 2 months after delivery. The maximum level of proteinuria was 0.4 g/day; no electrolyte derangement was evident.

Diagnostic details.—In this patient, the diagnosis of medullary Grade II nephrocalcinosis was incidentally performed by ultrasounds alone. The pathogenesis of nephrocalcinosis is rather difficult to identify in her case, as both hypothyroidism and malabsorption may be associated with stone disease and with nephrocalcinosis. The presence of immunological derangements, occasional joint pain and fatigue suggests an extensive workup for Sjogren’s syndrome, together with the evaluation of the metabolic picture, in the near future (the patient is presently breastfeeding).

Discussion

The present report combines two interesting topics in nephrology: pregnancy in CKD and nephrocalcinosis, a disease attracting increasing attention due to the growing number of reports in different conditions, including prematurity, use of phosphate-containing enemas or bowel preparations, and immunological diseases, in particular Sjogren’s syndrome [6, 12–16].

In spite of the increased attention to both subjects, the literature is scant in this regard. Indeed, our series is the largest thus far on nephrocalcinosis in pregnancy, analysing the reasons for referral and the main clinical problems occurring in this delicate phase of a woman’s life. Interestingly, the reported cases (four women with six pregnancies) account for ~2% of all cases referred in the last decade to our outpatient unit dedicated to ‘kidney and pregnancy’; the prevalence rises to 5.5% if only the patients with new diagnoses of CKDs are considered.

Within the limits of a small series, the relatively high prevalence suggests that nephrocalcinosis is more frequent than usually considered, at least in young women, and/or that pregnancy represents a specific challenge in this disorder, leading to overt clinical presentations, with oedema or electrolyte derangements (Tables 1–3)[1–4, 6, 8]. Our series includes a spectrum of diagnoses and diagnostic challenges: only one case (Case 3) was easily interpreted as due to prolonged diuretic abuse, while different and possibly multiple causes were postulated in the others, including genetic defects, prematurity, malabsorption, Sjogren’s syndrome or other collagen diseases (possibly combined with diuretic abuse in two patients).

In keeping with the protean pathogenesis, the referral symptoms were heterogeneous. They included, in different
combinations, oedema and electrolyte derangements (occasional varying over time in the same patient), hypertension and reduced kidney function (or lack of pregnancy-related increase) (Table 3).

The pathogenesis of oedema, in the absence of significant proteinuria, is not clear. Pregnancy is per se a situation of water and sodium retention, and the presence of a tubular disorder may enhance this baseline tendency, eventually in the presence of a further sodium-retaining challenge, such as steroid therapy. As, however, tubulo-interstitial disease is usually associated with salt wasting, an association with the cause(s) thereof, such as diuretic abuse, could also be suspected.

In one case (Case 1), the main problem was life-threatening: severe hyperkalaemia, reaching 7.5 mMol/L, at high risk for cardiac arrhythmias. The problem developed quite abruptly in a patient under weekly controls in our setting. The reason for such a sudden change in the metabolic asset is not clear. Indeed, pregnancy remains a poorly understood ‘accelerator’ of several diseases, and the rapidity at which renal problems may develop is well known in the case of PE. The differential diagnosis with the latter is a crucial clue. In fact, three of our patients presented features potentially overlapping with PE at different times of their pregnancy: proteinuria, hypertension and oedema. Of note, all patients were hyperuricaemic late in pregnancy, another potentially confounding element in the differential diagnosis between PE and CKDs.

Interestingly, three of four cases suffered from repeated urinary tract infection. This is a non-specific sign and symptom in pregnancy and thus of limited use for diagnosis, but it is important for further surveillance of pregnancy once a diagnosis of nephrocalcinosis is made.

The reason why our report is the first one documenting a relatively high incidence of this rare disease in pregnancy is not clear. What can be stressed, however, is that the diagnosis was made at ultrasounds by a team of skilled operators and could have escaped in a different setting. Yet, this is not an over-diagnosis, as witnessed by the concordance with the

<table>
<thead>
<tr>
<th>Table 2. Main data at the last control before delivery (five cases, one pregnancy is ongoing)</th>
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<tr>
<td>Creatinine (mg/dL)</td>
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<td>Uric acid (mg/dL)</td>
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<td>Na (mmol/L)</td>
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<td>Calcium (mmol/L)</td>
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<td>Urinalysis pH</td>
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<td>Proteinuria (g/24h)</td>
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<td>Density</td>
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<td>HCO3 (mmol/L)</td>
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*P, phosphate: 1.3 mg/dL (normal 2.50–4.80).

<table>
<thead>
<tr>
<th>Table 3. Main clinical data at delivery and main clinical problems in pregnancy</th>
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<tr>
<td>Age at start of pregnancy</td>
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<td>Oedema</td>
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<td>Hypertension</td>
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<td>Urinary tract infections</td>
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<td>Gestational age</td>
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<td>Type of delivery</td>
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<td>Indications for delivery/Caesarean section</td>
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<td>Apgar 5’</td>
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Clinical History

Nephrocalcinosis is a rare condition, with an estimated incidence of 1 per 10,000 live births. The most common presentation is neonatal nephrocalcinosis, which can be either primary or secondary. Primary nephrocalcinosis is characterized by calcium deposition in the kidneys without an identifiable cause, while secondary nephrocalcinosis is associated with underlying conditions such as primary hyperparathyroidism, hypophosphatemia, and renal tubular acidosis.

Pregnancy and Chronic Kidney Disease

Pregnancy is a significant risk factor for the development of nephrocalcinosis. During pregnancy, there is an increased risk of hypercalcemia, hyperphosphatemia, and hyperparathyroidism due to the increased production of parathyroid hormone. This can lead to the precipitation of calcium phosphate stones, which are common in patients with nephrocalcinosis.

This report highlights the importance of considering nephrocalcinosis in the differential diagnosis of kidney diseases in pregnancy, also with respect to PE, whose features may occasionally overlap with those of nephrocalcinosis, especially late in pregnancy. The relatively high prevalence, as compared with the literature, suggests that this condition may be under-diagnosed, with potentially relevant consequences. The rarity of the disease does not support a systematic use of kidney ultrasounds in pregnancy but may support a wider use of this non-invasive diagnostic tool in the differential diagnosis between PE and CKD.

Conclusions

This report underlines the importance of considering nephrocalcinosis in the differential diagnosis of kidney diseases in pregnancy and supports the need of a multidisciplinary workup of pregnant women with kidney diseases. The described cases also suggest that pregnant women with a previous diagnosis of nephrocalcinosis should be closely followed on account of the risks of severe electrolyte derangements, development of oedema and hypertension and urinary tract infections.

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Conflict of interest statement

None declared.

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