Renal and ureteral involvement in Erdheim-Chester disease: analysis of a single centre cohort

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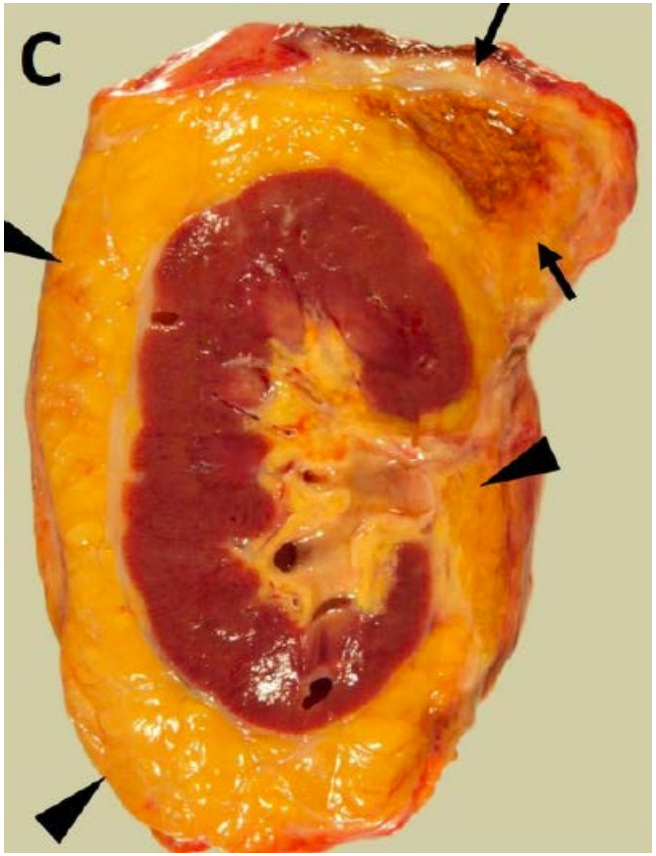
Background

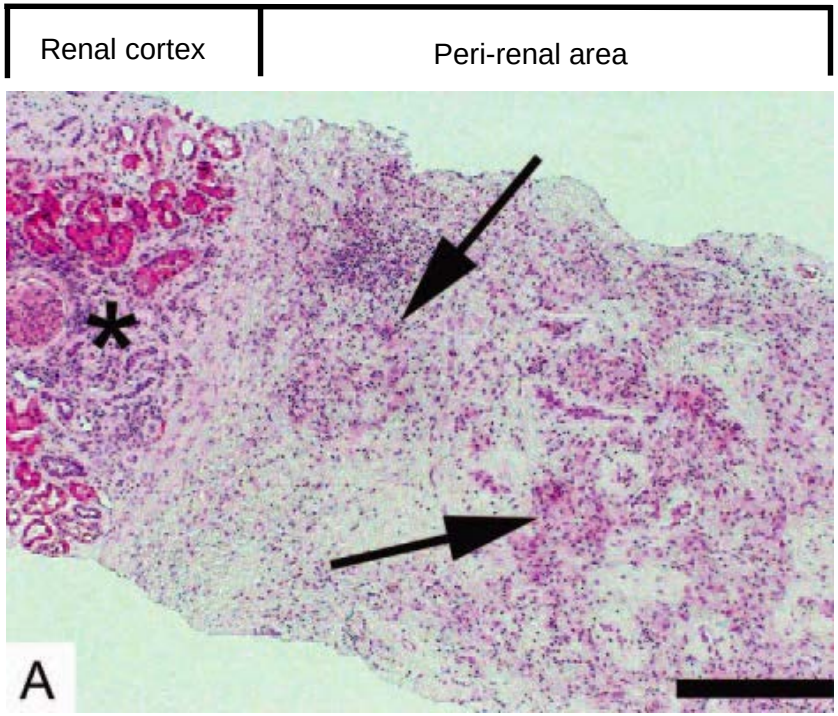
- Renal and ureteral involvement is common (approx 60%) in ECD patients
- It usually presents as “retroperitoneal fibrosis” involving the peri-renal (hairy kidneys), peri-ureteral and periaortic space
- It can be asymptomatic or cause varying degrees of acute or chronic renal failure
- Other renal complications (eg, renal artery or vein stenosis) are uncommon

Feature	(n = 47)
Median age, y (IQR)	57 (49, 68)
Median follow-up, y (IQR)	3.0 (1.8, 7.3)
Sex, n (%)	
Male	31 (66%)
Female	16 (34%)
Presenting symptom, n (%)	
Urologic	4 (9%)
Nonurologic	43 (9%)
Pathologic diagnosis by biopsy, n (%)	38 (81%)
Cross-sectional imaging (CT/MRI), n (%)	35 (74%)
Urologic involvement, n (%)	37 (79%)
Retroperitoneal involvement, n (%)	
Any	28 (60%)
Perinephric soft tissue inflammation	24 (51%)
Hydronephrosis, unilateral or bilateral	10 (21%)
Renal atrophy, unilateral or bilateral	15 (32%)
Other	6 (13%)
CKD, n (%)	18 (38%)
Hypertension, n (%)	18 (38%)
LUTS, n (%)	
Any	21 (45%)
Storage symptoms	11 (53%)
Voiding symptoms	8 (38%)
Stent irritation	4 (19%)
Urologic surgery, n (%)	
Any	13 (28%)
Ureteral stent placement	5 (11%)
Open retroperitoneal, renal biopsy	3 (6%)
Other	5 (11%)

Yelfimov DA, et al. *Urology.* 2014

Background





Naval Baudin P, et al. *European Congress of Radiology* 2017 (abstract C-3136)
Vaglio A, et al. *Circulation.* 2008

Background and aims of the study

- Obstructive uropathy is thought to be the major cause of renal failure in ECD patients, but its optimal management is unclear
- The true prevalence of CKD or ESRD in ECD is unknown
- Data on long-term renal outcome are lacking

STUDY AIMS

1. To assess the frequency and severity of renal and ureteral involvement in ECD
2. To investigate the impact of ureteral decompressive procedures on renal outcome
3. To provide long-term outcome data on renal function in ECD

Methods

- 31 consecutive patients seen at our unit between 2004 and 2017

- Median follow-up: 39 months

- Abdominal CT or MRI scans available for review
- Clinical data collected at baseline, 1,2,5 yrs and last follow-up

- Renal function evaluated using sCreat and the CKD-EPI formula for eGFR

- Medical treatment and urologic procedures according to our practice (no established therapeutic algorithm)

Results- study population

	N=31
Men, n (%)	25 (80.6)
Age, median (range)	45 (21-75)
CV risk factors (before diagnosis)	
diabetes, n (%)	7 (22.6)
smoking, n (%)	13 (41.9)
hypertension, n (%)	13 (41.9)
obesity (BMI >30), n (%)	9 (29.0)
hypertension, n (%)	15 (48.4)
Biopsy-proven ECD, n (%)	29 (93.5)
BRAF V600E mutation, n (%)	14/20 (70.0)

Results- study population

Patients with organ involvement, **n (%)**	**N=31**
CNS	9 (29.0)
Heart	13 (41.9)
Large vessels	12 (38.7)
Bone	27 (87.1)
Lung	9 (29.0)
Endocrine	16 (51.6)
Skin/sucutaneous tissues	12 (38.7)
Others	13 (41.9)

Results- study population

***Patients with organ involvement,* n (%)**	**N=31**
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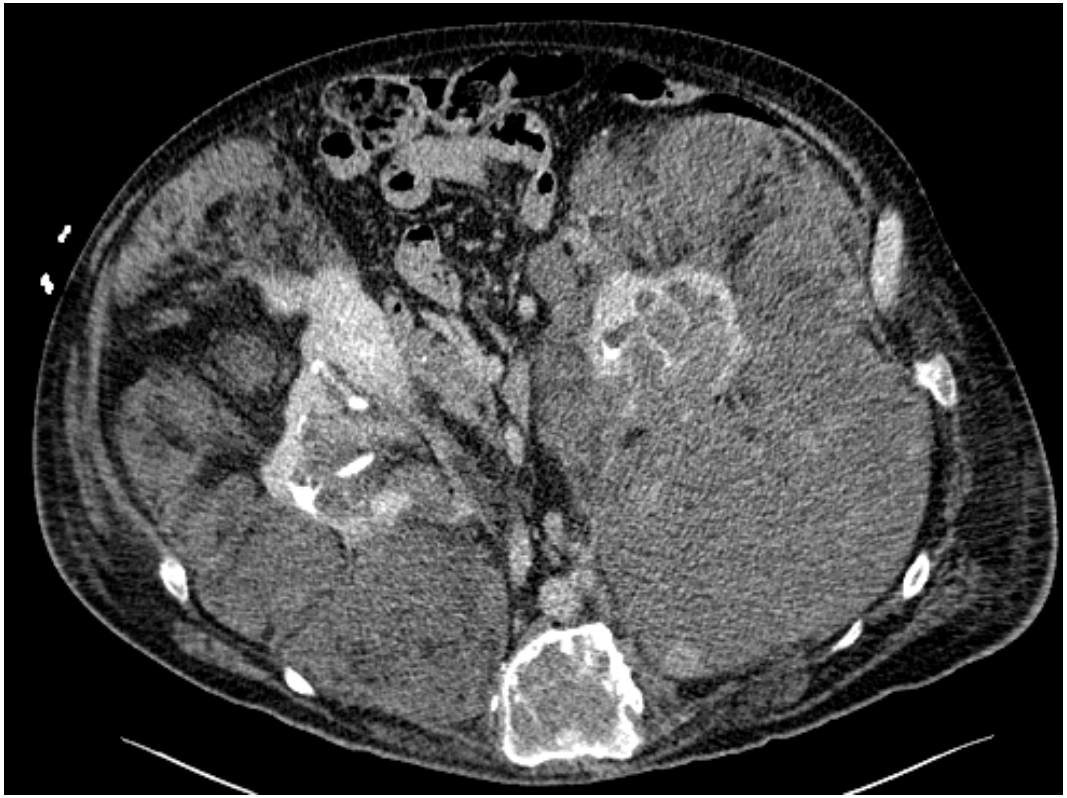
Endocrine	16 (51.6)
Skin/sucutaneous tissues	12 (38.7)
Others	13 (41.9)
Renal parameters at diagnosis	
sCreat >1.2 mg/dL, n (%)	7 (22.6)
eGFR < 90 mL/min, n (%)	17 (54.8)
eGFR < 60 mL/min, n (%)	7 (22.6)
Proteinuria > 300 mg/24h, n (%)	1 (3.2)

CT/MRI evaluation: peri-renal involvement

- Peri-renal infiltration was detected in 22 patients (71%)
- 11/15 tested (73%) BRAF *V600E*
- In almost all cases it extended to involve the renal pelvis
- It ranged from thin peri-renal tissue to huge masses
- On CT, peri-renal infiltration was muscle-isodense and had varying degrees of contrast-enhancement

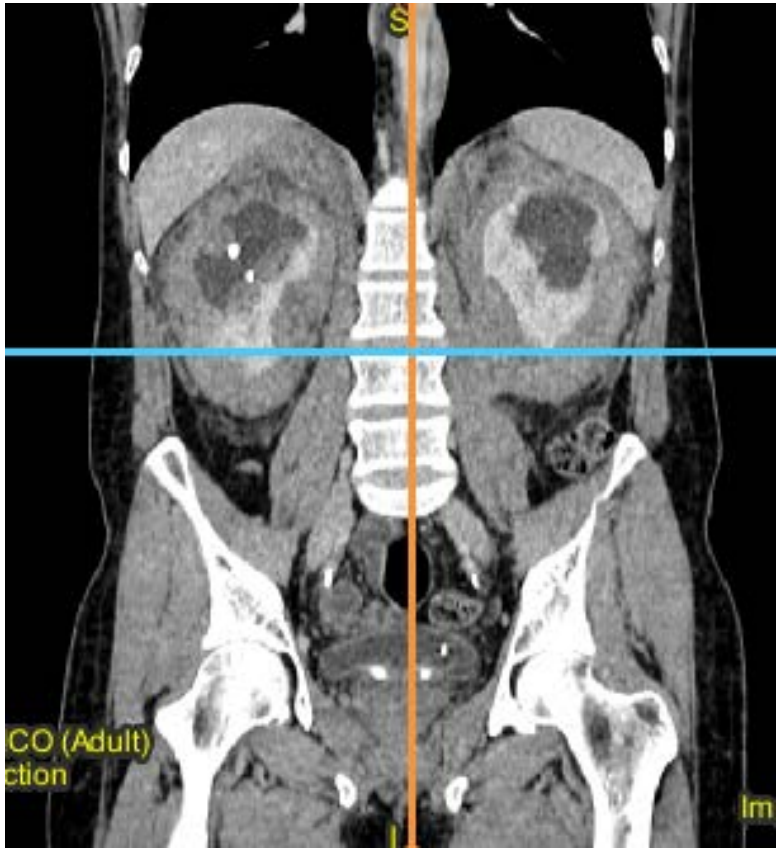
CT/MRI evaluation: peri-renal involvement



- Thin peri-renal tissue could also cause hydronephrosis and renal dysfunction

CT/MRI evaluation: peri-ureteral involvement

- Peri-ureteral involvement + hydronephrosis was detected in 17 patients (54.8%) (all with peri-renal involvement) and was limited to the proximal third of the ureter



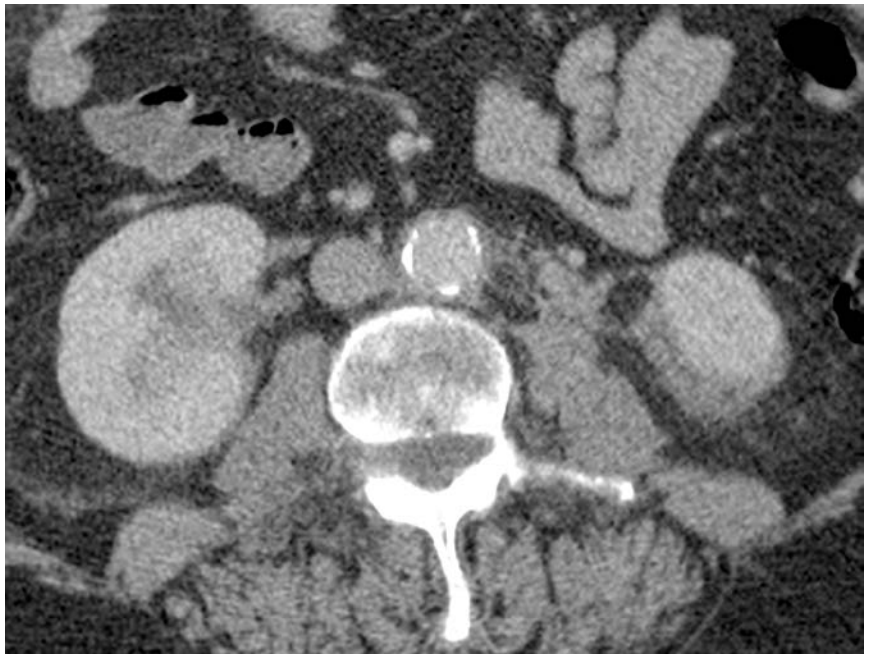
CT/MRI evaluation: peri-ureteral involvement

- Cases with isolated peri-ureteral involvement → consider other diagnoses

Non-Hodgkin Lymphoma

CT/MRI evaluation: renal atrophy

- Renal atrophy (maximal renal diameter <8 cm) was found in 5 cases (16.1%)

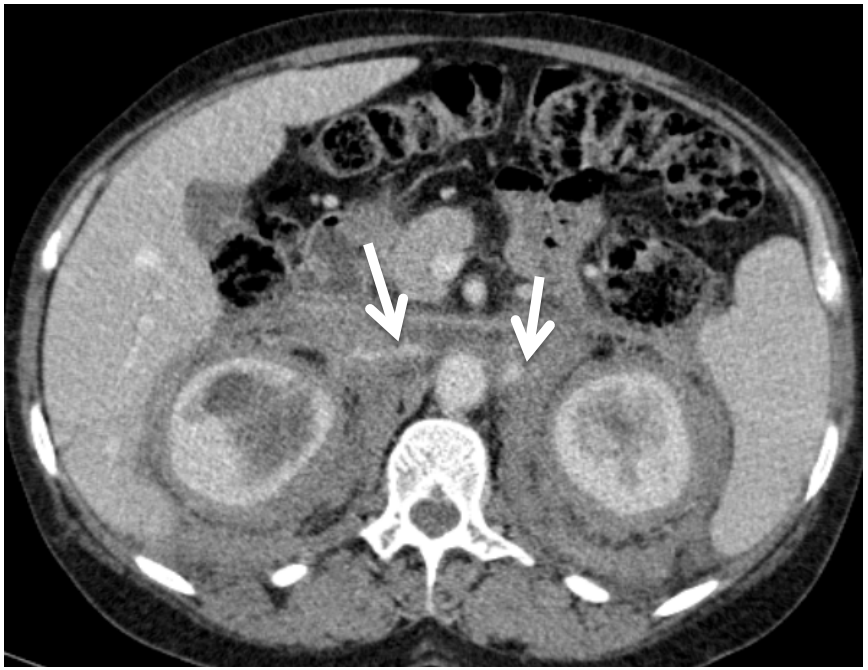


Unilateral (consider renal artery stenosis)

Bilateral

CT/MRI evaluation: renal vessel involvement

- Involvement of the renal vascular peduncle was detected in 15 patients (48.4%)
- Reno-vascular hypertension was diagnosed in only 1 patient
- Renal artery involvement probably contributed to chronic kidney ischemia and renal failure



Treatment and outcome

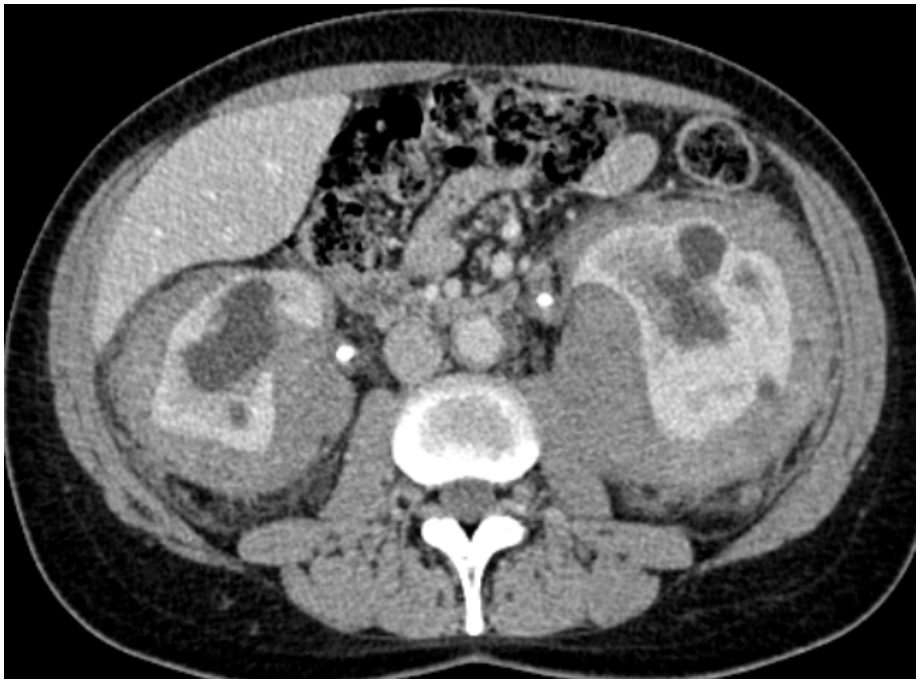
***First-line treatment*, n (%)**	(n=31)
Interferon-a	9 (29.0)
Sirolimus/everolimus (± prednisone)	9 (29.0)
Vemurafenib	4 (12.9)
Other treatments	7 (22.6)
No treatment	2 (6.4)
***Ureteral procedures*, n (%)**	
Double-J stents	9/17* (52.9)
Nephrostomy tubes	2/17* (11.7)
No procedure	6/17* (35.3)

* Pts with ureteral involvement

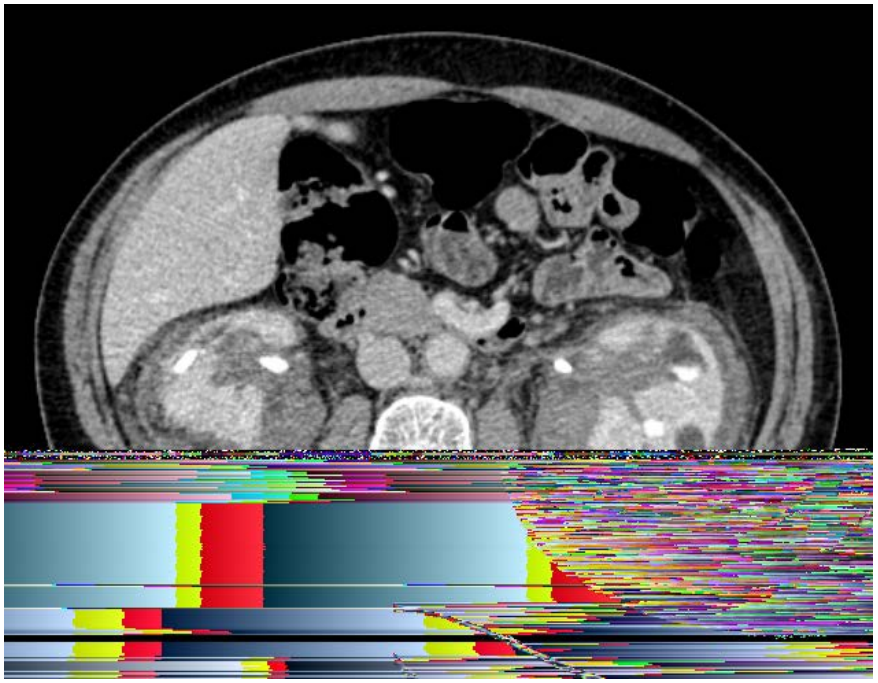
Treatment and outcome

- Ureteral stenting often did not resolve hydronephrosis
- Significant improvement in renal function parameters was achieved in only 3/11 patients treated with stents/nephrostomies
- Nephrostomy (performed because stenting was not technically feasible) prevented recurrent pyelonephritis in 1 case

Treatment and outcome



With stents, before therapy



With stents, month 6 of Everolimus therapy

Treatment and outcome

At last follow-up (median 39 months, range 7-127)

- 6/11 patients became ureteral stent/nephrostomy-free
- No additional patient required stenting
- 1 patient was started on dialysis → Renal Tx waiting list
- 4 pts died (all with normal renal function)

Renal parameters	**Baseline (n=31)**	**12 mo (n=31)**	**Last follow-up (n=31)**
sCreat >1.2 mg/dL, n (%)	7 (22.6)	7 (22.6)	6 (19.4)
eGFR < 90 mL/min, n (%)	17 (54.8)	14 (45.2)	16 (51.6)
eGFR < 60 mL/min, n (%)	7 (22.6)	6 (19.4)	6 (19.4)
ESRD	0	1 (3.2)	1 (3.2)
Proteinuria > 300 mg/24h, n (%)	1 (3.2)	1 (3.2)	1 (3.2)

Conclusions

- Peri-renal involvement is detectable by CT/MRI in 70% of ECD patients and is accompanied by peri-ureteral disease (+hydronephrosis) in most cases
- Renal vascular peduncle involvement is common although reno-vascular hypertension is rare
- Ureteral stenting is often ineffective in achieving remission of hydronephrosis → need to perform ureteral stenting in all cases with hydronephrosis?
- Long-term renal outcome of ECD patients is usually favourable (<5% ESRD, approx 20% CKD stages 2-3)

NEED FOR MORE CASES

- CLINICAL DATA AT BASELINE, 1, 2, 5 YRS AND LAST FOLLOW-UP
- BASELINE ABDOMINAL CT/MRI (CD NEEDED)

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