NEPHROTOXICITY OF IFOSFAMIDE IN ADULT PATIENTS

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INTRODUCTION

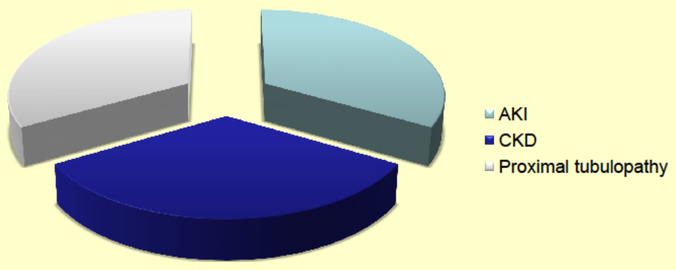
Ifosfamide (IFO) is an alkylating agent used as an antineoplasic drug in several types of cancers, especially sarcoma [1]. IFO renal side-effects have previously been described in pediatric populations [2], but not among adults patients. The aim of the study was to describe the clinical and histopathological features of the IFO-associated nephrotoxicity.

PATIENTS AND METHODS

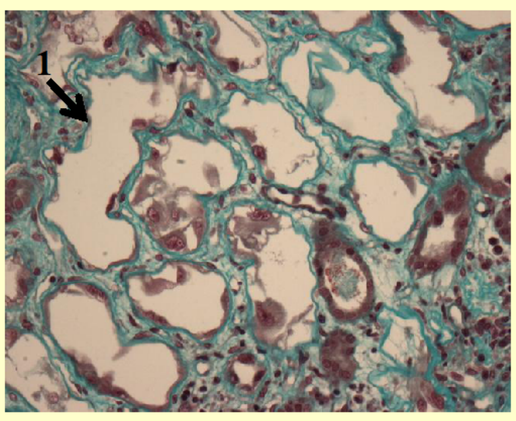
We conducted an observational, retrospective study in 4 Nephrology and Oncology centers. All adults patients admitted for kidney failure (eGFR [MDRD] < 60 ml/min/1,73m²) and/or tubular dysfunction after IFO therapy were included.

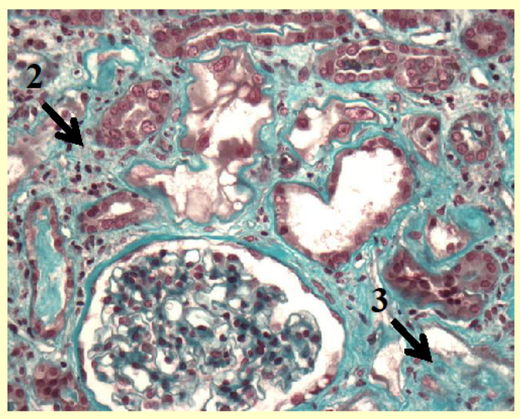
RESULTS

We have included 15 patients with a mean age of 54 (18-75). Ninety-three percent were treated for sarcoma. IFO mean cumulative dose was 18.4 g/m². Ten patients also received Cisplatin. Renal presentation was : AKI (n=6), CKD (n=6) and/or proximal tubulopathy (n=6), characterized by hypokaliemia (n=10), metabolic acidosis (n=6), hypophosphatemia (n=4), $TmPO4^{2-}$/eGFR < 0,8 (n=3), fractional excretion of uric acid > 10% (n=1) and low molecular weight proteinuria (n=6).

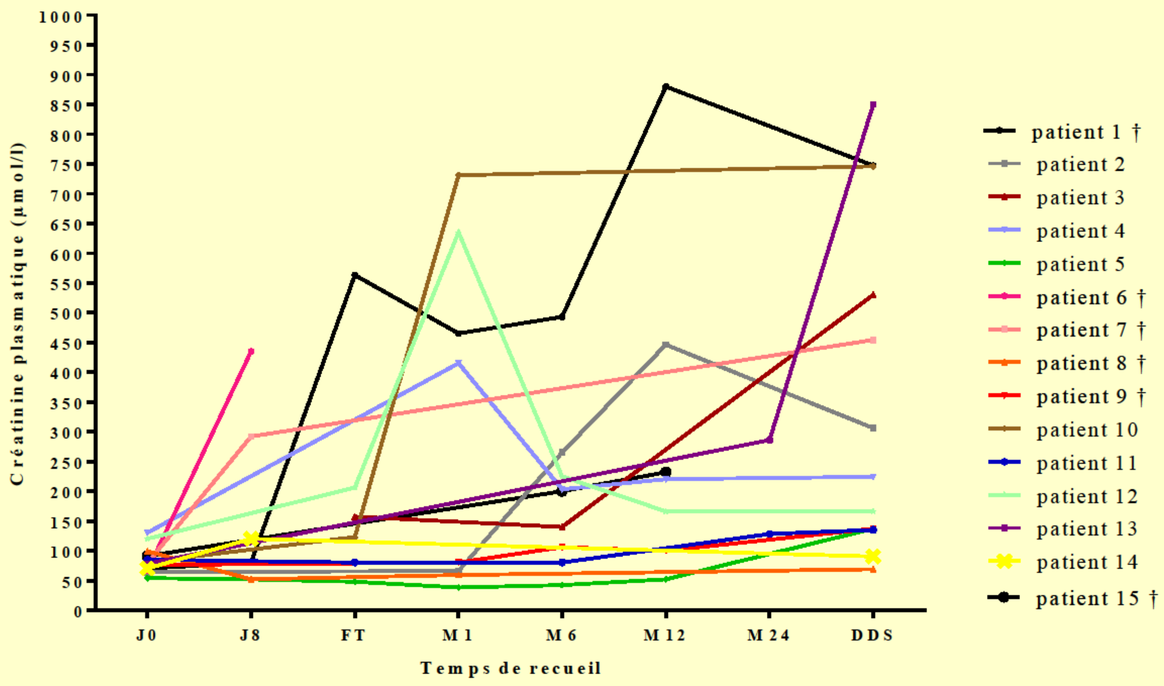


Kidney biopsy (n=5) showed : proximal tubular mitochondrial cytopathy (1) (n=4), interstitial inflammation (2) (n=2) and IF/TA (3) (n=2).





The mean eGFR at the initial IFO administration was 86 ml/min/1,73m² and decrease to 29 ml/min/1,73m² after a mean follow-up of 16 months. Three patients reached ESRD. One AKI patients (12) requiring hemodialysis experienced a progressive improvement of renal function.



Corticosteroids were used in 2 cases without improvement of CKD. In the absence of control group, no risk factor of IFO nephrotoxicity could be identified. Netherless, kidney toxicity occured with low IFO cumulative doses (< 20 g/m² for 67% of the patients), whereas children IFO nephrotoxicity is usually observed for cumulative doses of 60-100 g/m² [3].

CONCLUSION

In adults patients, IFO nephrotoxicity is secondary to tubulo-interstitial injury, presenting either as :

- AKI immediately following IFO administration,
- CKD diagnosed several months after chemotherapy, with progression to ESRD despite symptomatic or corticosteroid treatments, and/or,
- Proximal tubulopathy, due to probable mitochondrial cytopathy.

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L) Renal pathology. L1) Experimental pathology.
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