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Nephrotic syndrome as possible adverse drug reaction in patients using dasatinib

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A boy between 10 and 18 years with Ph+ common acute lymphoid leukemia, developed nephrotic syndrome (edema, proteinuria with protein creatinine ratio 126.7 mg/mmol, blood albumin 12 g/L and), 27 days after starting dasatinib, once daily 60 mg/m^2. Dasatinib was withdrawn and fluid intake restricted. One week after withdrawal of dasatinib the patient had recovered from the nephrotic syndrome. Previous treatment included cytarabine and mercaptopurine. Scientific literature describes at least another four patients with nephrotic syndrome associated with dasatinib. These patients concern two children and two adults, three females and one male. Daily doses were 60 mg/m^2 (child), 100 mg (adult), 140 mg (adult) and not reported in one case. Latencies were 26 days, two weeks after dose increase and not reported in two cases. All the patients recovered from the nephrotic syndrome after withdrawal or dose reduction (in one patient) of dasatinib, in two cases within a week. A possible mechanism is disruption of the vascular endothelial growth factor (VEGF) signaling pathway through inhibition of the SRC family kinases, one of the targets of dasatinib. VEGF expression occurs in human podocytes, and therapy targeting VEGF or inhibiting VEGF receptors is associated with proteinuria. Concerning other tyrosine kinase inhibitors sorafenib and sunitinib, both drugs with therapeutic targets that include VEGF receptors, nephrotic syndrome is described as adverse reaction in the Summary of Product Characteristics (SmPC). It is important to realize when a patient develops nephrotic syndrome while on therapy with dasatinib, this might concern an adverse drug reaction of dasatinib.