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# Shiga toxin–producing *Escherichia coli*–associated hemolytic uremic syndrome in solid organ transplant recipients



**To the editor:** Shiga toxin–producing *Escherichia coli*–associated hemolytic uremic syndrome (STEC–HUS) has been very rarely documented in solid organ transplantation patients.<sup>1</sup> We report a series of 5 solid organ transplantation recipients diagnosed with STEC–HUS between January 2017 and March 2019 in 2 French nephrology centers (Table 1). One patient had 2 episodes of STEC–HUS. All had severe acute kidney injury (requiring hemodialysis in 2).

**Table 1 | Characteristics of 5 solid organ transplant recipients with STEC–HUS**

STEC–HUS features															
Pt	Sex, age (y)	SOT (primary disease)	Time since SOT (mo)	IS <sup>a</sup>	Baseline SCr (mg/dl)/eGFR (ml/min per 1.73 m <sup>2</sup> )	Maximal SCr (mg/dl)	Plt (g/l)	Hb <sup>b</sup> (g/dl)	LDH (xULN)	U P/Cr (g/g)	Extrarenal manifestations	<i>E coli</i> serotype	Stx <sup>c</sup>	Treatment	Outcome
1	M, 51	Kidney (polycystic kidney disease)	19	Tac [3.3] + MMF	1.8/42	5	128	7.9	2	4.1	Watery diarrhea	NA	Stx2	Switch MMF/AZA Ecu (4)	Chronic dialysis
2	F, 49	Pancreas (type 1 diabetes)	41	Tac [2.2] + AZA + Cs	1.6/36	8.5/HD	20	8.1	7	21	Watery diarrhea, confusion/tremor, myocardial ischemia	O157H7	Stx2	Tac + AZA discontinuation PI + Ecu (4)	Partial renal recovery (SCr 2.1 mg/dl) <sup>d</sup>
3	M, 43	Heart, lung, and kidney (cystic fibrosis)	186	Tac [NA] + AZA + Cs	1.9/41	3.5	99	10.9	1.9	4.7	Watery diarrhea, generalized seizures	NA	Stx2	No specific treatment	Decrease of SCr to baseline values (2.2 mg/dl) <sup>d</sup>
4	F, 38	Lung (cystic fibrosis)	21	Tac [10] + MMF + Cs	2.2/27	4.6	39	7.2	2.8	1	Pancolitis, myoclonia/coma	NA	Stx2	Switch Tac/CSA Ecu (2)	Decrease of SCr to baseline values (2.5 mg/dl) <sup>d</sup>
5	F, 25	Lung (cystic fibrosis)	57	Tac [NA] + MPA + Cs	1.8/36	7.2	99	8.3	3.5	0.7	Watery diarrhea, colitis, confusion/generalized seizures	O156	Stx1	Transient Tac withdrawal (3 d)	Decrease of SCr to baseline values (mg/dl) <sup>d</sup>
			64	Tac [3.4] + MPA + Cs	1.8/36	4.3/HD	83	7.5	3.3	8.8	Diarrhea/pancolitis, confusion/generalized seizures	NA	Stx1	Switch Tac/CSA Ecu (4)	Chronic dialysis

AZA, azathioprine; Cs, corticosteroids; Ecu, eculizumab (number of infusions; dosage was 900 mg/wk); eGFR, glomerular filtration rate estimated using the Modification of Diet in Renal Disease formula; F, female; Hb, hemoglobin; HD, hemodialysis; IS, immunosuppressors; KB, kidney biopsy; LDH, lactate dehydrogenase; M, male; MMF, mycophenolate mofetil; NA, not available; PCR, polymerase chain reaction; PI, plasma infusion; Plt, platelet count; Pt, patient; SCr, serum creatinine; SOT, solid organ transplantation; STEC–HUS, Shiga toxin–producing *Escherichia coli*–associated hemolytic uremic syndrome; Stx, Shiga toxin; Tac, tacrolimus; TMA, thrombotic microangiopathy; U P/Cr, urinary protein/creatinine ratio.

<sup>a</sup>Tacrolimus trough levels (ng/ml) at the time of STEC–HUS diagnosis are indicated in brackets.

<sup>b</sup>All patients had schizocytes on a blood smear and an undetectable serum haptoglobin level.

<sup>c</sup>In all cases, STEC infection was confirmed by multiplex PCR (commercial assay) for *stx1* (*n* = 1) and *stx2* (*n* = 4).

<sup>d</sup>SCr at last follow-up.

In all patients, C3, C4, and CH50 serum levels were normal, and ADAMTS13 plasma activity was > 10%. None had donor-specific antibodies or detectable cytomegalovirus plasma replication. Kidney biopsy performed in patients 1 (renal graft) and 5 (second episode) disclosed extensive lesions of TMA (thrombi in arterioles and glomerular capillaries). No patient had genetic testing for variants in complement genes.

Neurological involvement was noted during 5 episodes: seizures ( $n = 4$ ) and confusion/coma ( $n = 4$ ). Patient 2 (Table 1), with type 1 diabetes but no history of coronaropathy, had acute elevation of serum level of troponin T (8119 ng/l; normal <14) with normal coronary angiography. All patients had detectable (>10%) serum ADAMTS13 activity. After STEC-HUS diagnosis, the immunosuppressive regimen was amended in 4 patients. Four patients were treated with eculizumab because of severe renal and/or extrarenal manifestations. One patient had a partial renal recovery, 2 regained their baseline renal function, and 2 progressed to end-stage renal disease.

To the best of our knowledge, this is the first case series of STEC-HUS in solid organ transplantation patients. STEC-HUS is probably underdiagnosed in this setting because diarrhea and thrombotic microangiopathy are usually attributed to causes other than STEC infections (immunosuppressive drugs, non-STEC infections, recurrence of atypical HUS, humoral rejection). Clinicians should be aware that STEC-HUS is a potential severe form of thrombotic microangiopathy in solid organ transplantation patients. Systematic screening for Shiga toxin in stool using preferentially polymerase chain reaction<sup>2</sup> is recommended even in the presence of only mild digestive symptoms. Several issues regarding the management of STEC-HUS in these patients warrant further assessment, especially the discontinuation of anticalcineurin and mammalian target of rapamycin inhibitors and the potential use of complement inhibitors. The use of eculizumab during 4 episodes in our series was empirical. In contrast to atypical HUS, STEC-HUS has not been linked to a constitutional or acquired dysregulation of the complement alternative pathway,<sup>3</sup> and screening for variants in complement genes is not usually performed in STEC-HUS patients (as in the present series). The available clinical experience with eculizumab in STEC-HUS has yielded contrasting results.<sup>4</sup> The relevance of this complement inhibitor in STEC-HUS is currently assessed in a prospective trial (NCT01410916).

#### DISCLOSURE

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## Measuring systolic and diastolic blood pressure in rodents



**To the editor:** The recently conducted debate on tail-cuff versus telemetry blood pressure (BP) measurements helps both clinicians and basic scientists place reporting of BP in experimental studies in perspective.<sup>1–3</sup>

What I would like to add is that the tail-cuff is certainly useful for systolic BP under the conditions stipulated by Drüeke and Devuyt,<sup>3</sup> but the diastolic BP reading is much less reliable.<sup>4</sup> So tail-cuff BP data should, in my opinion, be restricted to systolic BP. This is well known to basic scientists as reflected by hits in PubMed: 782 for “systolic tail cuff pressure rats” versus 129 for “diastolic tail cuff pressure rats” and 122 for “systolic tail cuff pressure mice” versus 27 for “diastolic tail cuff pressure mice.”

A thin, polyvinyl chloride, fluid-filled catheter with an external pressure transducer (often used in terminal experiments) tends to dampen the pulse, so the “mean” arterial pressure is fine, but systolic BP tends to be underestimated and diastolic BP overestimated. This also means that the mean arterial pressure value thus obtained is not the same as the conventionally calculated mean arterial pressure from the Riva-Rocci method.

Telemetry catheters have transducers at their tip and give reliable systolic BP and diastolic BP recordings in rats and mice.<sup>5,6</sup> They are indispensable for analysis of complex phenomena such as circadian rhythms.<sup>7</sup>

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