Author's response to reviews

Title: Bladder irrigation and urothelium disruption: a reminder apropos of a case of fatal fluid absorption.

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Author's response to reviews: see over
Dear Editor,

BMC Urology

I sent you the new revised version of the paper “Bladder irrigation and urothelium disruption: a reminder apropos of a case of fatal fluid absorption”.

According to review’s suggestion we modified the paper; in red we addressed the changes.

In particular, we have added a few sentences in the case presentation trying to clarify the review 3’s doubts. Moreover in the conclusion we added some sentences according to the suggestion of the other reviews.

According to the editorial points, we modified the consent statement since written consent was obtained from the son of the deceased. We attached the written consent form. This is in Italian;
if you need an English translation, please do not hesitate to contact me.

A native speaker further revised the paper.

Thank you very much for your kind attention.

Emanuela Turillazzi, MD, PhD

3 September 2014
Response to review 1.

1. We perfectly agree with the take-home message focused by the review and, following his suggestion, we added a final sentence on the need of a close supervision of fluid balance.

2. Regarding the issue of brain edema we want to specify that brain edema is a very common autopsic finding regardless of the cause of death since the swelling of brain tissue is a common feature accompanying several pathological states. As underlined by forensic pathology literature, an histological examination of the particular sensitive brain does not yield any findings in which the causation can be determined with certainty. Since 1967 Klatzo's classification of brain edema into two distinct types, vasogenic and cytotoxic, has been commonly adopted. The former involves overall brain swelling due to fluid entry from the vasculature caused by openings in the blood-brain barrier (BBB), whereas the latter refers to cell swelling without any loss of the normal impermeability of the BBB. Many mechanisms may be underlying to the cerebral edema seen in this case. First of all, a terminal
oxygen deficiency could cause a swelling of the brain. This is the most common explanation of the brain edema that we usually observe during autopsy. Capillary permeability may be increased by a vast number of causes, weakening therefore the so-called 'blood-brain barrier' formed by the capillary endothelium and basement membrane, together with the astrocyte foot-plates. Cerebral edema, either traumatic or hypoxic, can develop with surprising rapidity.

Surely, a very suggestive one, is the creation of an osmotic gradient between brain and plasma with the onset of cerebral edema due to hemodialysis treatment. Dyalisis Disequilibrium Syndrom is a clinical syndrome that causes neurological symptoms due to the onset of cerebral edema. Different mechanisms have been proposed for cerebral edema during dialysis, including a reverse urea effect, cerebrospinal fluid acidosis, and idiogenic osmole produced by the brain. Animal studies have established that DDS is caused by cerebral edema that develops as a consequence of rapid hemodialysis and the creation of an osmotic gradient between the brain and the
plasma. The gradient is created by a difference in the urea concentration of the two compartments. The rapid dialysis treatment of the patient could be responsible for the creation of this osmotic gradient between brain and plasma with the onset of cerebral edema.

However, in the present case the absence of other neurological symptoms related to dialysis disequilibrium led us to believe that cerebral edema is an autoptic finding related to the terminal oxygen deficiency.

Finally, we changed macroematuria in macrohematuria at line 27 of the abstract.
Response to review 2

We perfectly agree with the observation of the review regarding the potential worsening role played in this case by the condition of chronic renal failure that affected the patient. Surely, the circulatory overload that occurred in the presented case may have been worsened by the coexisting chronic renal failure. In a very similar manner it is known that chronic renal failure has been implicated in transfusion – associated circulatory overload that is characterized by the occurrence of symptoms and signs of acute pulmonary edema. There is no doubt that associations with patient-related factors, including pre-existing congestive heart failure and chronic kidney disease, are also consistent. These factors are biologically plausible. Patients with cardiac dysfunction may not tolerate any increasing in preload and would be more likely to experience pulmonary edema. Patients with renal failure would be unable to generate an appropriate diuresis in case of increased blood volume and would be more susceptible to pulmonary edema even with a relatively preserved cardiac function.
We added a sentence following the suggestion of the review.
Response to review 3.

1. In this case no evidence of catheter blockage has ever been reported. No manual evacuation was performed on the patient.

2. No blood transfusion was performed at any point of the clinical course. HB >7 g/dl during all days of hospitalization.

3. Bladder distension was not present in this case. Neither the abdomen CT nor the autopsy demonstrated a bladder distension. We hypothesized that the shortness of breath and the breathing difficulties experienced by the patient were not related to a mechanical cause (massive bladder distension and elevation of the diaphragm); rather we hypothesize that a circulatory overload was caused by a massive fluid absorption.

4. As outlined at line 92 the gross examination of the bladder showed a certain amount of coagulated blood.

5. There was no blockage of the cathether.

6. There was no bladder distension in the case.
7. Usually 2.5/3 kg. He was not self feeding and fluid intake controlled.