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Letter to the Editor

Before blaming Legionella for severe rhabdomyolysis, consider alternative triggers

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We read with interest the article by Gopalakrishna *et al.* about a 58 years-old female who developed severe rhabdomyolysis requiring hemodialysis, mechanical ventilation, and treatment on the intensive care unit (ICU) during a pulmonary infection with legionella (Pontiac fever) [1]. Legionella infection was identified as the underlying cause of rhabdomyolysis and azithromycin was given resulting in partial recovery at discharge [1]. After two months, ambulatory hemodialysis could be discontinued as well [1]. The study is appealing but raises concerns that should be discussed.

Although infections with Legionella are well-known as triggers of rhabdomyolysis, alternative triggers or cofactors should be considered more thoroughly. The patient had a serum potassium of 3mEq/L on admission [1], which according to our reference limits, is a severe hypokalaemia. Since hypokalemia can trigger rhabdomyolysis [2], it should be considered as a trigger or co-trigger of the condition. The patient also had hyponatremia of 126mEq/L [1]. Hyponatremia is also well-known for its potential to trigger rhabdomyolysis [3]. Even losartan carries a risk of rhabdomyolysis [4], particularly in combination with bezafibrate [5]. We should also know if losartan was given in monotherapy or together with a diuretic drug, as diuretics carry an increased risk of rhabdomyolysis due to their potassium-lowering effect [6]. We should not forget that the Janus kinase inhibitor tofacitinib can increase serum creatine-kinase levels [7].

The patient was lethargic and only partially orientated [1]. However, an explanation other than fever was not provided. We should be told if a non-convulsive status epilepticus, a post-ictal phenomenon, and encephalitis were ruled out. Particularly, we should be informed about the results of cerebral MRI with contrast medium and electroencephalography (EEG). A cerebral CT scan without contrast medium as has been carried out in the index patient may easily miss encephalitis, embolic stroke, or venous sinus thrombosis. Tofacitinib carries an increased risk of thrombosis.

Creatine-kinase values further increased under after administration of azithromycin [1]. We should know if it was considered that azithromycin itself can cause rhabdomyolysis [8]. In a patient with rhabdomyolysis, administration of any new drug should be carefully considered whether it is beneficial or not.

A further limitation of the study is that an infection with SARS-CoV-2 was not ruled out as a trigger of rhabdomyolysis. The manuscript had been submitted in April 2021 [1]. Therefore, an infection with SARS-CoV-2 must be ruled out before attributing rhabdomyolysis exclusively to Legionella.

Another limitation is that the infection with Legionella was not confirmed by culture of endotracheal secretions during intubation. The gold standard of confirming a pulmonary infection with Legionella is culture from pulmonary secretions, as mentioned in the discussion [1].

Overall, the interesting study has limitations that challenge the results and their interpretation. Clarifying these weaknesses would strengthen the conclusions and could improve the study. Before attributing the cause of rhabdomyolysis to an infection with Legionella, alternative triggers should be thoroughly ruled out.

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