Persistent Coma in Strongyloides Hyperinfection Syndrome Associated With Persistently Increased Ivermectin Levels

To the Editor—We share an interesting clinical case that impacts on the treatment of Strongyloides hyperinfection syndrome. A 64-year-old man was admitted to our intensive care unit for postoperative care after aortic valve replacement. His previous medical history was relevant for giant cell arteritis for which he was using prednisone. Three days postoperatively, severe sepsis with multiorgan failure developed. Sputum was collected, and high numbers of mobile Strongyloides stercoralis larvae were observed and a diagnosis of S. stercoralis hyperinfection syndrome with dissemination was made. Ivermectin therapy, first orally and later subcutaneously, was initiated. Although numbers of live Strongyloides decreased rapidly and his clinical condition improved, he remained in a persistent vegetative state and the patient died. Given the fact that other causes for a persistent coma were excluded, we suspected that neurotoxicity of ivermectin might have been responsible for the persistent coma.

Ivermectin is generally a safe drug that does not accumulate even in high dosages when given to healthy volunteers [1]. However, cases of encephalopathy have been reported [1, 2], which is associated with coma in animals [3, 4]. To analyze whether drug accumulation was present

Figure 1. Time curve of ivermectin levels in serum. Ivermectin serum levels are shown. Day 1 indicates first day of ivermectin treatment. Patient was treated from days 1–8 with ivermectin. Days of ivermectin administration, per oral (po) or subcutaneous (sc), are shown above the arrows. Curve indicates corresponding ivermectin serum levels. Last ivermectin level was measured 11 days after the last administration. From day 10 onward, no live larvae were observed in sputum. Patient died at day 25.
in our patient, we measured ivermectin levels in serum during and after treatment as well as in autopsy-derived brain tissue (Figure 1). A steady state of serum levels was reached after 5 days, but hereafter no diminishment of serum ivermectin levels was observed even after ivermectin treatment had been discontinued for 11 days. In line with this, the ivermectin level in brain tissue was still markedly elevated (30 ng/g brain tissue) at the time of death, 14 days after the last ivermectin treatment. Such a markedly elevated concentration may have been attributed to severe neurotoxicity. This high concentration of ivermectin in brain long after ivermectin treatment was discontinued might be related to loss-offunction mutations in the multidrug-resistant mdr1/abcb1 gene encoding for P-glycoprotein, which excretes ivermectin out of the systemic compartment as well as the central nervous system. We investigated the most common single-nucleotide polymorphisms associated with decreased abcb1 expression and found that none were present in our patient. Secondly, after careful review of all comedications used during treatment, no probable relation between these and decreased ivermectin elimination was observed. This report illustrates that ivermectin treatment may lead to persistently elevated levels of ivermectin in serum and abnormal drug brain level during treatment of S. stercoralis hyperinfection syndrome, potentially leading to severe neurotoxicity even in the absence of genetic or iatrogenic factors known to decrease ivermectin elimination. Our report is of significance as it shows that generally reported treatment schemes, which advocate daily treatment with ivermectin for extended periods during hyperinfection syndrome, may do harm. Treatment should be closely guided by serum levels, and once appropriately effective serum levels are obtained, no further dosages of ivermectin should be given unless the infection is still uncontrolled and serum levels are decreasing significantly.

Note

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References


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