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## **Acute, Haemorrhagic, Necrotizing Pancreatitis Associated with Riluzole Treatment in a Patient with Amyotrophic Lateral Sclerosis**

### **Case Report**

We report the case of a woman diagnosed with Amyotrophic Lateral Sclerosis (ALS) at the age of 71. ALS is a degenerative motor neuron disease, usually leading to death within 2-5 years due to respiratory failure. One month after starting Riluzole 50 mg bid *per os*, she was admitted to the hospital due to severe upper quadrant abdominal pain, nausea and fever. Physical examination, blood tests and CT scan confirmed a severe, acute, haemorrhagic, necrotizing pancreatitis with abdominal fluid collections, ileus, and bilateral pleural effusions, without any evidence of biliary obstruction. Riluzole treatment was immediately stopped, and therapy with crystalloids, Tramadol, Paracetamol (Acetaminophen), proton pump inhibitors and parenteral nutrition was started. The past medical history resulted negative for gallbladder stones, alcohol consumption, hypertriglyceridemia or hypercalcemia. Ultrasonography performed after partial recovery showed a dilated gallbladder with biliary sludge, but no bile ducts dilatation. Therapy with ursodeoxycholic acid (UDCA) was started, but it was soon after discontinued because of the onset of diarrhoea. The clinical course showed progressive improvement. One month after dismissal, magnetic resonance cholangiopancreatography (MRCP) and echoendoscopy revealed persistent dilation of the gallbladder, with sludge and wall thickening. Following studies with MRCP and abdominal CT angiography showed normal radiological images of gallbladder (without any evidence of sludge), bile ducts and pancreas, with some residual pseudocysts. After complete clinical recovery, we chose not to restart Riluzole treatment, since pancreatitis represented a life-threatening complication. No further episodes of pancreatitis have occurred along an 18-month follow up.

## Discussion

Riluzole represents the only drug approved for the treatment of ALS in Italy. Riluzole-induced pancreatitis is a rare adverse reaction, with an incidence of 0.5-1 case/1000 treated patients.<sup>1,2</sup>

Some case reports described moderately severe pancreatitis, sometimes followed by complications, with 1-6 month latency between the introduction of Riluzole and the onset of symptoms.<sup>1-4</sup> In our patient the timing of the adverse event suggested a possible association with the drug therapy. According to Naranjo Scale<sup>5</sup>, our case could be classified as *possibly* caused by Riluzole (score 4/13), if we consider biliary sludge as a possible causative factor for acute pancreatitis. In our patient, however, biliary sludge was interpreted as due to parenteral nutrition by gastroenterologists. Indeed, it resulted absent during radiological follow up after clinical recovery, even in the absence of therapy with UDCA. If we do not consider biliary sludge as a possible aetiologic factor, pancreatitis could be classified as *probably* caused by Riluzole (score 7/13 at Naranjo Scale).

Since acute pancreatitis was life-threatening, Riluzole was not readministered, also considering that in other case reports pancreatitis resulted reversible when therapy was withdrawn<sup>3</sup> and recurrent when therapy was restarted.<sup>2</sup>

In conclusion, acute pancreatitis must be kept in mind as possible adverse event during Riluzole treatment, particularly within the first 6 months, since it is a potentially life-threatening, although rare, complication. In the presence of known risk factors for acute pancreatitis, it would be reasonable to discuss with patients about the opportunity of a more careful monitoring of Riluzole treatment.

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