

Opioid Antagonist for Pruritus of Cholestasis Unmasking Bony Metastases

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Sir,

Pruritus in cholestasis has been attributed to the accumulation of endogenous opioids (1). This theory is supported by elevated levels of endogenous opioids in patients with primary biliary cirrhosis (2) and successful treatment of pruritus of cholestasis with opioid antagonists (3, 4). Elevated endogenous opioids are believed to be anti-nociceptive, theoretically reducing awareness of painful stimuli. Naloxone-reversible anti-nociception has been demonstrated in cholestatic rats (5). We report here a case of pruritus of cholestasis where opioid antagonist therapy resulted in loss of anti-nociception, unmasking the pain of bony metastases.

CASE REPORT

A 73-year-old man presented with a 6-week history of intense generalized pruritus and a one-week history of painless jaundice. The itch so disturbed his sleep that he had resorted to lying in the snow overnight to obtain relief. He was on no analgesia. Liver profile revealed cholestasis and an ultrasound scan showed liver metastases. After the failure of topical treatments and cholestyramine, he was treated with an infusion of the opioid antagonist naloxone. The dose was gradually titrated upwards according to a modified standard regime (0.002 µg/kg/min doubled every 12 h up to 0.2 µg/kg/min) (6). After 2 days his pruritus began to improve. However, on the third day of the infusion, when he was receiving a dose of 0.128 µg/kg/min naloxone, he developed severe back pain. A coincident computed tomography (CT) scan demonstrated a primary bronchogenic carcinoma with a number of sclerotic bony metastases in the thoracic and lumbar spine. The naloxone infusion was stopped. Unfortunately, his condition deteriorated rapidly and he became too unwell to relate alteration of his symptoms of itch and pain. He died the following day.

DISCUSSION

We have found three reports in the literature of pain associated with opioid antagonism for pruritus of cholestasis. McRae et al. (7) described three patients with non-malignant pruritus of cholestasis who developed post-herpetic neuralgia, liver capsule pain and arthralgia between one and 3 months after starting opioid antagonists. In each case, the pain resolved on stopping the opioid antagonist. The other case reports described two patients with pruritus of cholestasis secondary to liver metastases (8, 9), which initially responded to opioid antagonists. However, after one month the first patient developed pain in the right upper abdomen, which was controlled with low-dose naloxone and opioid analgesia (buprenorphine) until her death.

The second patient developed diffuse abdominal and back pain after 6 months' treatment with naltrexone. Pain was exacerbated at higher doses of naltrexone. She developed intestinal obstruction, her pain became intolerable and she died 4 weeks later under terminal sedation. In these cases with liver metastases the delayed onset of the pain following the introduction of opioid antagonists makes it likely that the pain was largely attributable to disease progression, rather than opioid antagonism.

We report our experience to add weight to the role of endogenous opioids in pruritus of cholestasis and anti-nociception, but more importantly to urge caution in the use of opioid antagonists in the context of metastatic cholestasis, lest their use reveals metastatic pain. Use of the partial µ-opioid agonist, buprenorphine, might be a preferable option in the context of possible revealed metastatic pain (10, 11).

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