This study evaluated the outcome of patients with symptomatic bone Langerhans cell histiocytosis (LCH) treated with indomethacin alone, either at diagnosis or after reactivation (after recurrence with previous therapies). We evaluated the nonrandomized use of oral indomethacin (2 mg/kg/d) in patients with symptomatic single-system bone LCH. From 1997 to 2012, 38 sequential patients were treated for a median of 4 months. Criteria of nonactive disease (NAD) after initial treatment (8 wk) were: no pain, no soft tissue involvement, no increase of size, or no new bone lesions. Twenty-two patients were treated at diagnosis: 18 showed NAD after initial treatment (2 patients who had bone reactivations were retreated with indomethacin and remain with NAD). Three patients improved and they are with NAD after treatment with indomethacin, steroids, or radiotherapy. One patient developed progressive bone disease and he is with NAD after treatment with steroids and chemotherapy. Sixteen patients were treated after reactivation, and all were with NAD after initial treatment: 5 reactivated and 4 remain with NAD after retreatment with indomethacin. Toxicity was not significant. We conclude that indomethacin is a well tolerated and active drug in patients with symptomatic bone disease. The results support the concept that chemotherapy may not be necessary for limited bone disease.