A fifty-seven-year-old male presented with cervical mass and B symptoms for the last two months. The patient had a history of stage II diffuse large B-cell lymphoma (DLBCL), which had a complete response after six cycles of rituximab-cyclophosphamide-doxorubicin-vincristine-prednisone (RCHOP) chemotherapy in 2010. At the time of diagnosis the International Prognostic Index score was low-intermediate. Three years after RCHOP treatment, the patient suffered from cervical mass again. Excisional lymph node biopsy confirmed the relapse of DLBCL. After three cycles of rituximab-ifosfamide-carboplatin-etoposide (R-ICE) chemotherapy, the patient achieved a second complete response and underwent autologous stem cell transplantation. Five years after the transplantation, the disease relapsed. Excisional lymph node biopsy revealed a relapse of nongerminall type of DLBCL. The patient presented with the signs, symptoms and laboratory findings of tumor lysis syndrome and paraneoplastic hypercalcemia. PET-CT imaging demonstrated widespread FDG uptake in skeletal system (SUVmax: 23.5), liver (SUVmax:16.2), mediastinal lymph nodes (SUVmax:7.4), abdominal lymph nodes (SUVmax:26.6), cervical lymph nodes (SUVmax:23.8), and left maxillary sinus (SUVmax:29.5). The patient received six cycles of polatuzumab vedotin (1.8 mg/kg/day), rituximab (375 mg/m2/day), bendamustine (90 mg/m2/day) every 21 days. After three cycles of polatuzumab-rituximab-bendamustine, the patient was evaluated by PET-CT scan, which demonstrated disappearance of all FDG uptakes except those in costal bones, which decreased significantly (SUVmax:23.5 to SUVmax:5.1). This new drug can be effective and promising in this difficult to manage group of patients.