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Case Report

Heterotopic Ossification with Classical Hodgkin Lymphoma in a Surgical Incision: A Case Report

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Abstract: Heterotopic ossification (HO) is the formation of bone tissue in areas where bone does not normally exist. It most commonly affects soft tissues after orthopedic surgeries involving major joints and is a rare complication of abdominal surgeries. When heterotopic ossification is excised, histopathological and immunohistochemical studies are essential to assess and rule out neoplastic tissue. Hodgkin lymphoma (HL) is a lymphoproliferative neoplasm characterized by the proliferation of morphologically and immunophenotypically altered cells, derived from the malignant transformation of germinal center B lymphocytes. Less commonly, patients with classical HL may also present with other very rare manifestations, such as heterotopic ossification. This case report aims to present a heterotopic ossification found in the preperitoneal space of a midline incision during laparotomy for retroperitoneal lymph node biopsy due to suspected lymphoproliferative disease, with a rare immunohistochemical result consistent with classical Hodgkin lymphoma.

Keywords: Hodgkin lymphoma; Heterotopic ossification; Heterotopic calcification.

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1. Introduction

Heterotopic ossification (HO) is the formation of bone tissue in locations where bone does not normally exist. It most commonly affects soft tissues following orthopedic surgeries involving major joints and is considered a rare complication of abdominal surgeries [1,2]. The exact pathogenesis of HO remains unclear, and the fact that blood calcium and phosphorus levels remain unchanged during its development highlights the need for further studies and investigation into the condition [3,4]. Its pathogenesis is likely multifactorial, with several theories having been proposed.

Older studies suggest that midline incisions near the xiphoid process or pubic symphysis may facilitate the inoculation of periosteal or perichondrial cells into the surgical wound [5]. Kim et al. reported a 25% incidence of HO development in midline incisions [2]. This inoculation of activated osteoprogenitor cells could thus induce the formation of heterotopic bone. However, there are reports of HO occurring even without midline incisions, such as in patients with burn scars or non-healing ulcers [6]. The incidence of HO formation appears to be higher in trauma-related amputees; one theory is that in these patients, larger bone fragments are more likely to be left behind in the wound after debridement in an already compromised area [7].

The clinical presentation of patients with HO is variable. Some patients are asymptomatic, and HO is only identified during clinical examination or incidentally on imaging while investigating other conditions. However, when symptomatic, HO typically presents as a painful mass in the region of a surgical scar on the abdominal midline, potentially associated with localized edema and tenderness [8]. Heterotopic ossification in abdominal incisions is rare, but occasional reports document the presence of trilineage hematopoiesis in such areas. Even more exceptional is documented neoplastic infiltration, as described in this article. There are reported associations between HO and tumors such as gastric carcinoma, metastatic osteosarcoma, and central nervous system tumors, but to date, there are no reports in the literature of Hodgkin lymphoma associated with HO in the abdominal wall [9–11].

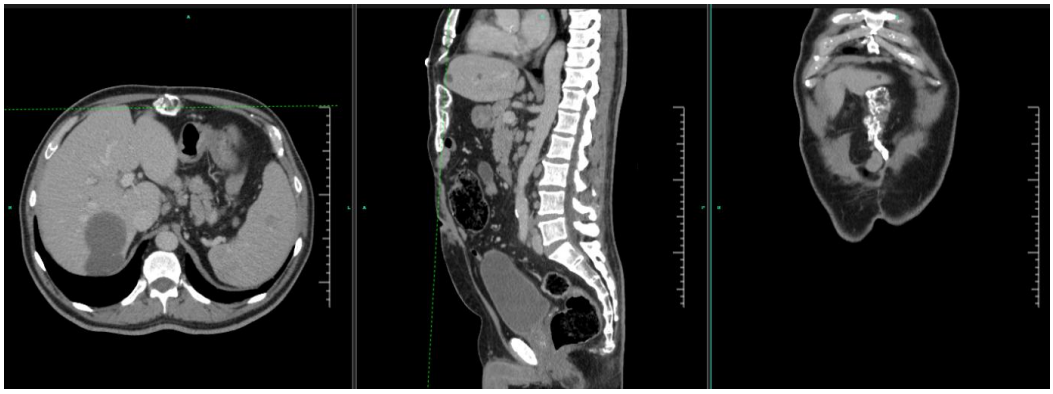
2. Case Report

A 64-year-old man, with a history of two midline laparotomies due to complicated acute diverticulitis in 2017—initially undergoing Hartmann's procedure followed by a second laparotomy for intestinal transit reconstruction in 2018—was referred to a specialized hospital for investigation of a wasting syndrome associated with daily fevers and lymphadenopathy for the past four months. The attending team requested a diagnostic biopsy of an intra-abdominal lymph node in collaboration with the General Surgery team, justified by the presence of B symptoms.

On physical examination, the patient presented with a hardened mass located in the epigastric region beneath the midline scar from previous laparotomies. The patient had noticed this mass as a slowly and progressively growing lesion over the past four years, with no clinical repercussions or further investigation until the current hospitalization. No enlarged lymph nodes were found in the cervical, axillary, or inguinal regions on examination. No other abnormalities were identified.

During hospitalization, diagnostic workup included computed tomography (CT) (Figure 1) and magnetic resonance imaging (MRI) of the abdomen and pelvis. Imaging revealed numerous retroperitoneal lymphadenopathies along chains near the bilateral common iliac, external and internal iliac, and left obturator arteries, measuring up to 8 cm, raising suspicion for neoplastic involvement. CT also confirmed the presence of a calcified structure along the midline of the abdominal wall, in the subcutaneous tissue of the epigastric region, located beneath a previous surgical incision.

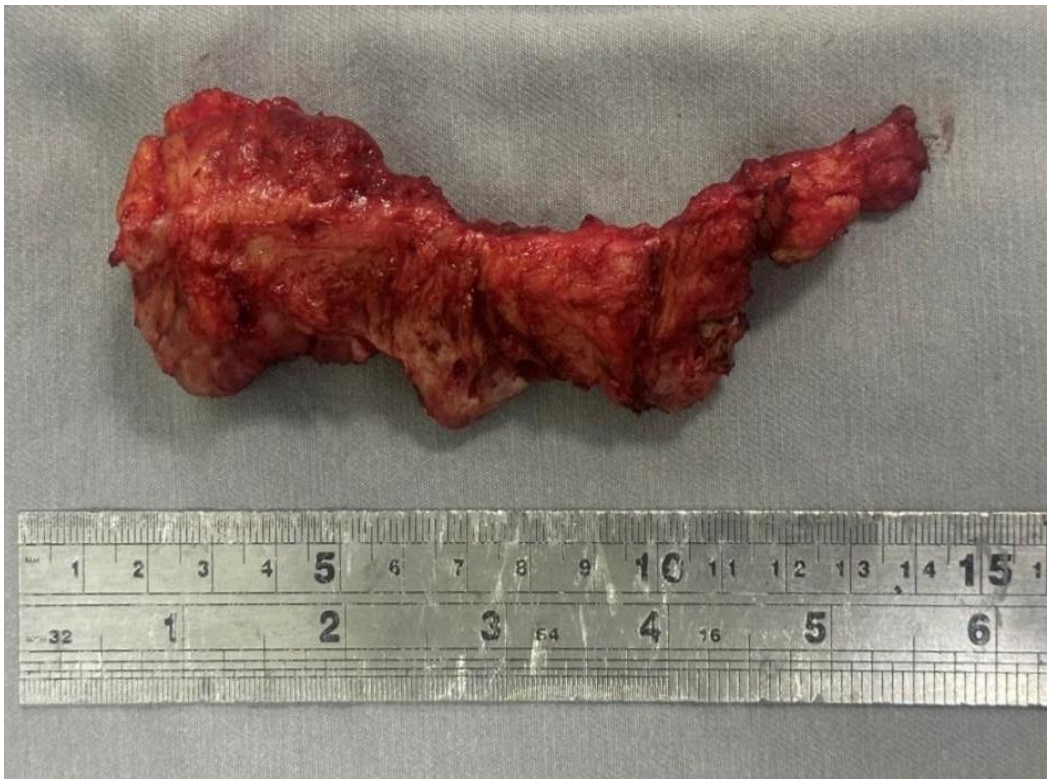
Figure 1. Abdominal computed tomography (CT) in three views (axial, sagittal, coronal) showing epigastric calcification in subcutaneous tissue.



Given these findings, a laparoscopic biopsy of the retroperitoneal lymph nodes was chosen, while a conservative approach was initially adopted regarding the calcification due to its asymptomatic and indolent nature. However, during the laparoscopic procedure, a large number of intra-abdominal adhesions were observed. Due to the high risk

of inadvertent visceral injury, it was decided to convert the procedure to a midline laparotomy along the previous incision site. During the incision, a calcified structure was identified in the subcutaneous tissue within the pre-aponeurotic space of the epigastric region. The structure had a hardened consistency, measured approximately 12 cm in length, and had an irregular shape (Figure 2). Complete resection of the newly formed bone tissue was performed, and the specimen was sent for histopathological and immunohistochemical analysis. A biopsy of retroperitoneal lymphoid tissue was also performed. The surgery was completed without complications. Postoperatively, the patient experienced a prolonged postoperative ileus but no other complications. He was discharged on postoperative day 10 and referred for outpatient follow-up with both the surgical and medical teams.

Figure 2. Resected fragment of heterotopic bone tissue from the pre-aponeurotic space of the anterior abdominal wall, measuring approximately 12 cm at its longest axis, with irregular surface and hardened consistency. The image shows the specimen placed next to a millimeter ruler for scale.



On the histopathological examination, the resected specimen measured 12.0 × 4.0 × 3.0 cm, weighed 42 grams, and was described as irregular and firm. Histological sections stained with Hematoxylin and Eosin (Figures 3 and 4) revealed the presence of bone tissue with atypical cellular proliferation of pleomorphic cells, intermixed with hematopoietic elements and fibrosis. Immunohistochemical analysis (Table 1, Figures 5 and 6) involved overnight incubation with the primary antibody, detection using the HRP-Polymer method, and chromogenic development with diaminobenzidine (DAB). The results showed positive and increased expression in atypical cells for the markers Ki67 (clone SP6), CD15 (clone C-arb-3), and CD30 (clone Ber-H2), consistent with a diagnosis of Classical Hodgkin Lymphoma involving bone tissue. Histopathological examination of the retroperitoneal lymph node revealed no evidence of neoplasia, with findings of a lipoma and a lymph node showing reactive changes.

Figure 3. Abrupt transition between the lesion and adjacent bone marrow (Hematoxylin and Eosin, 40x).

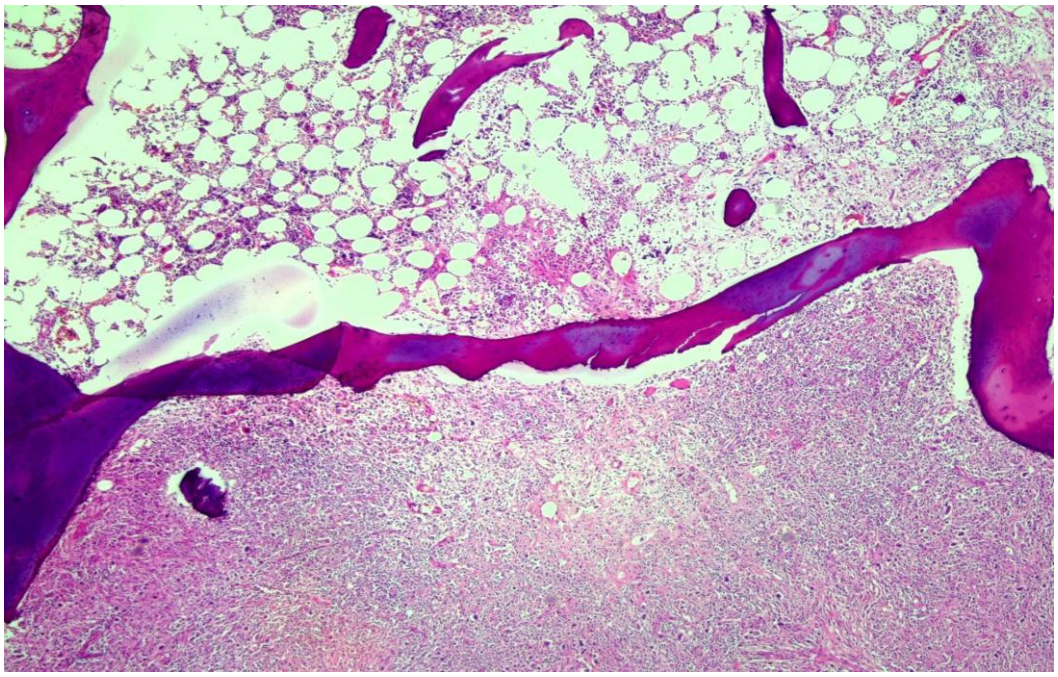
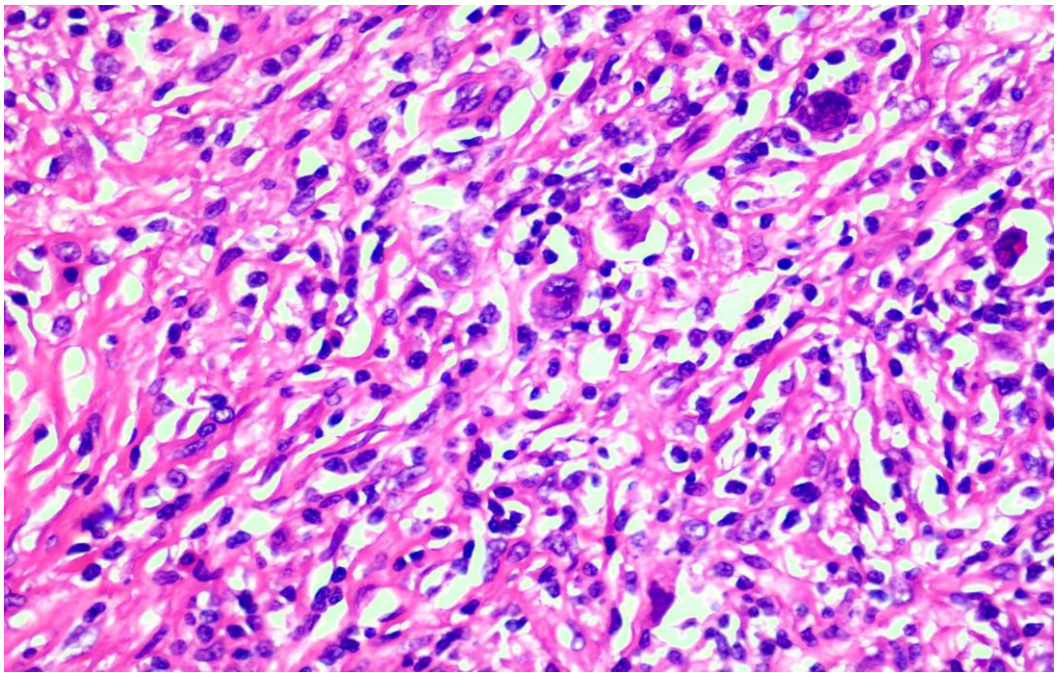


Figure 4. Scattered atypical cells among numerous lymphocytes (Hematoxylin and Eosin, 400x).



Currently, after an uneventful post-operative follow-up, the patient has been discharged from the General Surgery Department. In a follow-up consultation with the Hematology-Oncology service, the patient was referred to a specialized Oncology center for treatment and follow-up of Classical Hodgkin Lymphoma with an atypical site of involvement.

Figure 5. Immunohistochemistry (CD3). CD3 immunopositivity highlights non-neoplastic T lymphocytes in the background of the lesion (100x).

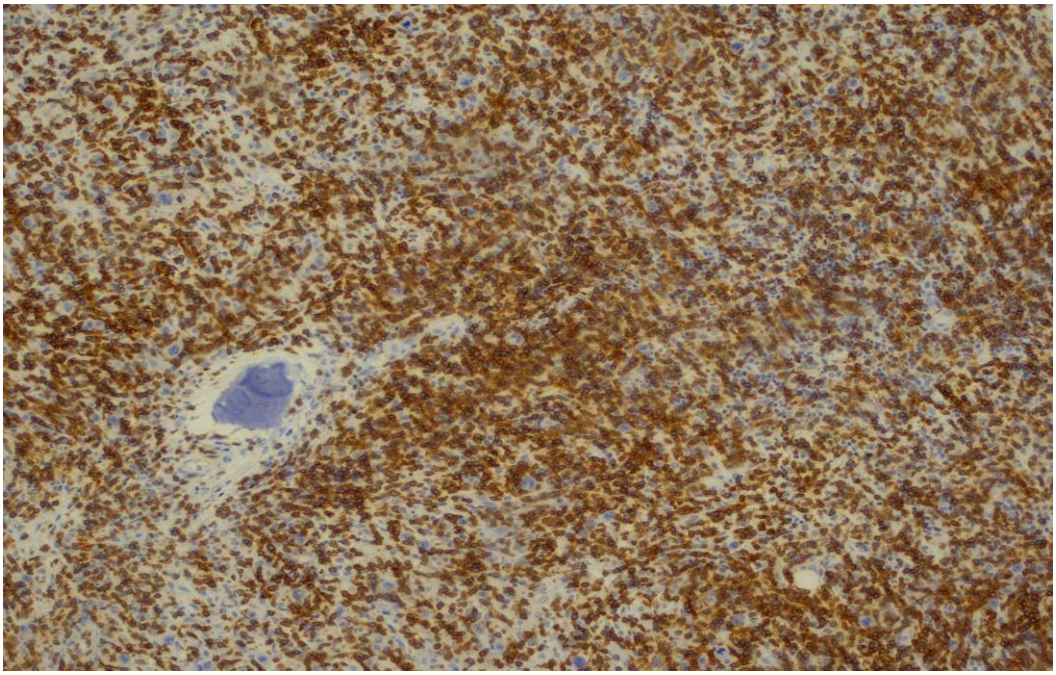


Figure 6. Immunohistochemistry (CD30) shows strong CD30 expression in neoplastic cells (Hodgkin and Reed-Sternberg cells) (400x).

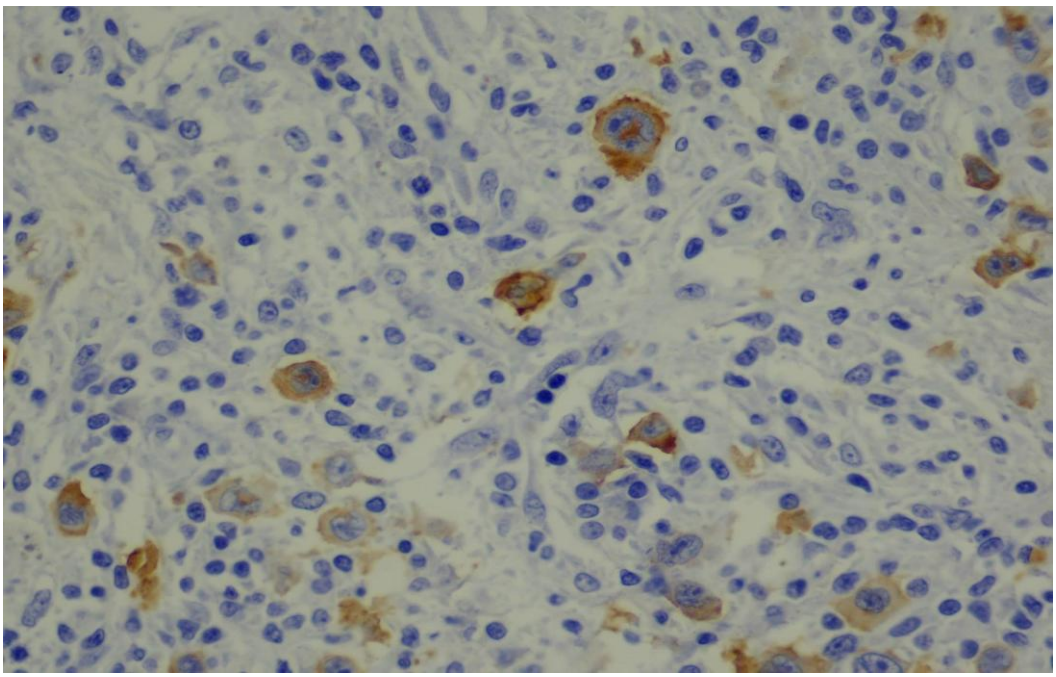


Table 1. Immunohistochemical evaluation results of the surgical specimen found in the epigastric region. Identification of antibodies used, their clones, and observed results.

Antibody	Clone	Result
CD34	QBend10	Negative in atypical cells.
Myeloperoxidase	Polyclonal	Negative in atypical cells.
CD31	JC70A	Negative in atypical cells.

E-Cadherin	EP700Y	Negative in atypical cells.
CD117	EP10	Negative in atypical cells.
Ki67	SP6	Increased in atypical cells.
CD3	Polyclonal	Negative in atypical cells.
CD15	C-arb-3	Positive in atypical cells.
CD20	L26	Negative in atypical cells.
CD30	Ber-H2	Positive in atypical cells.
PAX5	—	Inconclusive.

3. Discussion

Heterotopic ossification (HO) can be defined as a pathological process in which bone tissue forms outside the skeletal system, such as in muscles, subcutaneous tissue, skin, and scars [1,2]. HO may be understood as an abnormal tissue repair process and commonly arises in regions affected by musculoskeletal trauma. The literature shows a higher prevalence of HO in patients undergoing orthopedic surgeries, especially hip arthroplasties, acetabular and elbow fractures, as well as in patients with traumatic spinal cord and central nervous system injuries and burn victims [3,4]. In patients undergoing abdominal surgeries, HO formation is a rare complication, more frequently observed in midline laparotomy scars, particularly after upper abdominal procedures [5].

Although risk factors for HO development are known, its etiology remains poorly understood [6]. In abdominal incisions, it is believed that HO formation may be associated with intraoperative injury to the xiphoid process or pubis in surgeries involving upper or lower midline incisions, respectively, allowing bone-forming cells to be deposited at the wound site [7]. The present case brings attention to the rare occurrence of lymphomatous infiltration in heterotopic bone. There is scarce literature linking hematological malignancies to heterotopic ossification and its pathophysiology, although some cases of trilineage hematopoiesis and even leukemic infiltration in HO have been described [6,7]. Immunologic and microenvironmental hypotheses have been proposed in other contexts, suggesting that chronic inflammation and wound healing may attract hematopoietic or neoplastic stem cells. This abnormal microenvironment could act as a permissive ectopic niche for the homing and seeding of Hodgkin lymphoma cells, especially in a context of chronic postoperative inflammation [16].

From a diagnostic perspective, it is essential to differentiate HO from other postoperative complications such as infection, foreign body reaction, or neoplasia [11]. Histologically, HO is composed of mature lamellar bone, cartilage, and hematopoietic bone marrow [9,12]. Although there are reports of trilineage hematopoiesis in HO, hematolymphoid neoplastic infiltration in ectopic bone remains extremely rare, and to date, there have been no previous reports of Classical Hodgkin Lymphoma (cHL) involving HO tissue, making this case unique [10].

In this report, the identification of atypical cellular proliferation within the ectopic bone tissue, with immunohistochemical positivity for CD15, CD30, and Ki-67, confirmed the diagnosis of cHL. The leading hypothesis is that the inflammatory microenvironment of HO, combined with active vascularization and the possible presence of functional marrow, may have facilitated the homing and infiltration of Reed-Sternberg cells [11]. The literature reports bone involvement in up to 6.5% of cHL cases, typically involving axial or medullary bones, but never before in heterotopic ossification [12,13,15].

Differentiating between reactive HO with hematopoiesis and neoplastic infiltration is challenging. Immunohistochemistry was crucial in this case: CD15 and CD30 are characteristic markers of Classical Hodgkin Lymphoma and are expressed by Reed-Sternberg

cells. Elevated Ki-67 indicated proliferative activity, further supporting the neoplastic nature of the infiltration. The absence of markers for other lineages excluded differential diagnoses such as sarcomas or non-Hodgkin lymphomas. The discrepancy between the negative retroperitoneal lymph node and the malignant infiltration in the HO raises discussions regarding tumor heterogeneity, sampling limitations, and the possibility of an early-stage disease. Cases of isolated bone involvement in cHL are rare and require complementary investigation with PET-CT for accurate staging and therapeutic planning [14], which had not yet been performed in this case.

Treatment for HO depends on the patient's clinical condition. In asymptomatic or mildly symptomatic individuals, conservative management is preferred. In symptomatic patients—particularly those with pain or complications such as fractures or visceral perforation—surgical resection of the HO with wide margins is recommended to reduce the risk of recurrence [9]. In addition to surgery, other strategies have been used to prevent recurrence, especially in orthopedic contexts, including disodium etidronate, anti-inflammatory drugs, radiotherapy, and corticosteroids. However, for preventing HO after abdominal surgeries, these strategies remain controversial and require further study [10].

4. Conclusion

This report presents a novel case of Classical Hodgkin Lymphoma diagnosed in heterotopic ossification tissue, identified incidentally during abdominal surgery. The possibility of neoplastic cells being present in ectopic bone, as reported here, underscores the importance of individualized decision-making regarding histological evaluation of masses, even when asymptomatic or located in unusual sites, especially in patients with a surgical history or undergoing neoplastic investigation.

The integration of clinical, imaging, histopathological, and immunohistochemical findings was essential for establishing this rare diagnosis. This case highlights the importance of awareness regarding heterotopic ossification, the need to maintain a high index of suspicion for hematologic malignancies even in seemingly benign lesions, and the relevance of proper staging in cases of atypical bone involvement to guide treatment and follow-up.

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Research Ethics Committee Approval: Written informed consent was obtained from the patient for the publication of anonymized clinical data and images. The study followed the ethical guidelines established by the Declaration of Helsinki.

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Conflicts of Interest: None.

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