

Pathological fracture of primary lymphoma of bone: A case report on diagnosis and novel surgical management

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Received November 4, 2025; Accepted April 2, 2026

DOI: 10.3892/ol.2026.15717

Abstract. Primary lymphoma of bone (PLB) is an uncommon malignancy, representing ~4-5% of primary malignant bone tumors and 1% of all malignant lymphomas. Diffuse large B-cell lymphoma (DLBCL) is the most common subtype, accounting for ~80% of cases, and is highly curable with appropriate treatment. Therefore, accurate and timely diagnosis is crucial for favorable outcomes. The current study presents a 42-year-old male with primary DLBCL of the proximal humerus. The initial diagnosis was challenging due to overlapping morphological features with other small round cell tumors like Ewing's sarcoma and small cell osteosarcoma, particularly on small, decalcified biopsy samples. However, a definitive diagnosis was achieved through specific immunohistochemical markers. Following standard chemo-radiotherapy, the patient suffered a persistent, non-healing pathological fracture, resulting in severe functional shoulder impairment. This report details successful surgical management using a novel technique: A reverse shoulder mega-prosthesis combined with a liquid nitrogen-treated autologous bone graft. This case report underscores PLB's diagnostic challenges and highlights a significant treatment-related complication. It presents a novel and effective surgical solution for

managing pathological fractures in this context, emphasizing the necessity of a multidisciplinary, individualized approach to cure the disease, restore function and preserve the limb.

Introduction

Lymphomas are malignant lymphoproliferative disorders that can manifest in lymph nodes or extra-nodal sites. They are broadly categorized as either Hodgkin's lymphoma, arising from pre-B-cells, or non-Hodgkin's lymphoma (NHL), arising from the monoclonal development of malignant B- and T-cells (1,2). Primary lymphoma of bone (PLB), first described in 1928, is a rare form of extra-nodal NHL, accounting for just 1% of all malignant lymphomas and 4-5% of primary malignant bone tumors (2,3). Approximately 80% of PLB cases are the diffuse large B-cell lymphoma (DLBCL) subtype, which responds well to immunochemotherapy regimens such as R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone) (4).

While PLB is a curable disease, its diagnosis can be complex (5). Its histopathological appearance, characterized by sheets of small round cells, can mimic other primary bone tumors, including Ewing's sarcoma, small cell osteosarcoma and neuroblastoma (6). Immunohistochemistry is therefore an indispensable tool for differentiating these entities and ensuring an accurate diagnosis. The present case is unique, as it illustrates PLB's diagnostic challenges and the management of a significant, long-term complication following standard therapy. While pathological fractures are known to occur in PLB, this report details a novel surgical reconstruction for a non-healing fracture post-treatment, employing a reverse shoulder megaprosthesis with a cryo-treated autograft to restore function. This combination is rarely, if ever, used to treat this specific and complex diagnosis.

Case report

A 42-year-old male with no significant past medical history presented to the Vietnam National Cancer Hospital (Hanoi,

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Abbreviations: PLB, primary lymphoma of bone; DLBCL, diffuse large B-cell lymphoma; MRI, magnetic resonance imaging; CT, computed tomography

Key words: primary lymphoma of bone, diffuse large B-cell lymphoma, immunohistology

Vietnam) in November 2022 with a 5-month history of persistent pain in the proximal left humerus. The patient did not report any B symptoms, such as fever, night sweats or weight loss. Initial X-rays revealed an aggressive bone lesion in the proximal humerus with mixed lytic and sclerotic areas, a moth-eaten pattern and a wide zone of transition. The lesion exhibited cortical destruction and extended from the humeral head to the middle third of the humeral shaft, with suspected soft-tissue involvement. An open biopsy was performed and pathology results confirmed NHL.

The patient was diagnosed with Stage IV NHL of the left humerus (Ann Arbor staging system) (7). The patient was treated with 6 cycles of R-CHOP chemotherapy (Rituximab 375 mg/m² on day 1, Cyclophosphamide 750 mg/m² on day 1, Doxorubicin 50 mg/m² on day 1, Vincristine 1.4 mg/m² on day 1, Prednisolone 100 mg on day 1-5) from January to August 2023, followed by 36 Gy of radiotherapy in September and October 2023. However, follow-up X-rays revealed a pathological fracture at the anatomical neck of the humerus (Fig. 1). Despite pain resolution following primary treatment, radiographic assessment consistently demonstrated absence of callus formation and no progression toward union over a six-month observation period, leaving the patient with a significant functional impairment, unable to move his shoulder.

The team conducted a staging workup, including positron emission tomography (PET)/CT and chest CT. The PET/CT scan revealed high ¹⁸F-fluorodeoxyglucose (FDG) uptake in the humeral tumor (maximum standardized uptake volume (SUV_{max}), 30) (Fig. 2). Chest CT showed a new 6.3-mm diameter solid nodule in the left lower lobe of the lung with mild uptake on PET/CT (SUV_{max} 2.2) (Fig. 3). These results indicated a partial response to chemo-radiotherapy rather than complete remission. Given its small size, low and non-specific metabolic activity, and the absence of other extra-nodal sites of disease, it was most consistent with an inflammatory or incidental finding rather than a metastatic deposit or synchronous primary malignancy. The team decided to pursue active radiologic surveillance rather than immediate biopsy. Serial chest CT examinations were performed at 3-month intervals over the 1-year follow-up period. The nodule demonstrated no increase in size or FDG avidity, lending further support to a benign etiology. No dedicated biopsy was performed, given the nodule's stable radiologic behavior.

Magnetic resonance imaging (MRI) of the humerus confirmed an extensively destructive bone lesion ~15 cm in length, invading surrounding tendons and muscles, but not the neurovascular bundle (Fig. 4). Taken together, these findings suggested a case of primary bone lymphoma with a partial treatment response, which was complicated by a pathological fracture following radiotherapy. MRI and PET/CT findings were consistent with residual lymphomatous disease after therapy completion.

Histopathological examination of the initial biopsy revealed a diffuse pattern of cells with round nuclei, scant cytoplasm and frequent mitoses, suggestive of lymphoma. Due to the rarity of PLB, a differential diagnosis, including Ewing sarcoma and small cell osteosarcoma, was considered. The diagnosis was confirmed by immunohistochemical staining,

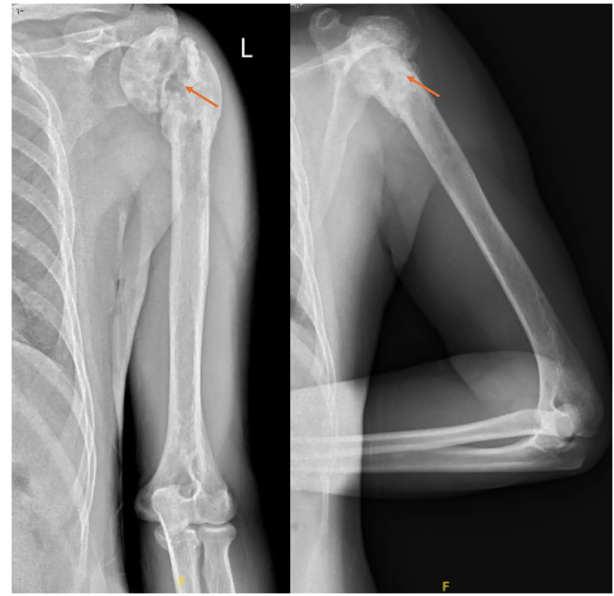


Figure 1. An X-ray exhibiting the complex bone lesion with lytic and sclerotic areas, irregular borders and an old fracture at the level of the anatomical neck (arrow). Left: AP view; Right: Lateral view.

which showed strong CD20 positivity, and positivity for BCL6 (>30%) and multiple myeloma oncogene 1 (MUM1) (>30%), and a high proliferation index with Ki67 (>90%). These markers confirmed DLBCL diagnosis, non-germinal center B-cell type (Fig. 5).

The multidisciplinary tumor board of our hospital recommended surgery, given the non-healing fracture and persistent functional deficit post-treatment. Pre-operative planning was facilitated using a 3-dimensional (3D) printed model of the patient's proximal humerus, constructed from CT imaging data, to guide implant selection and simulate the surgical reconstruction (3D Technology in Medicine Center, College of Health Sciences, Vin University) (Fig. 6A). The patient underwent a 20 cm-wide resection of the proximal humerus (Fig. 6B), and a 6-cm segment of the resected humeral diaphysis was treated with liquid nitrogen to serve as a devitalized cortical autograft (Fig. 6C). The liquid nitrogen protocol followed established oncological bone recycling principles: The bone segment was immersed in liquid nitrogen at -196°C for 20 min, then allowed to thaw at room temperature for 15 min, followed by thawing in sterile normal saline for 15 min. This freeze-thaw cycle ensured complete devitalization of residual tumor cells while preserving the cortical bone's structural integrity (8).

Reconstruction was performed using a modular reverse shoulder megaprosthesis (Beijing Chunli Zhengda Medical Instrument Co., Ltd.) with a 10.5-cm intramedullary stem. The devitalized autograft was then secured to the prosthetic stem using polymethylmethacrylate cement and fixed to the remaining humeral diaphysis using a plate and screws to achieve rotational stability (Fig. 6D). Soft-tissue reconstruction was critical to optimize reverse shoulder construct function. As the rotator cuff tendons had been resected *en bloc* with the specimen, the remaining deltoid muscle was meticulously sutured to pre-designed holes of the humeral prosthetic

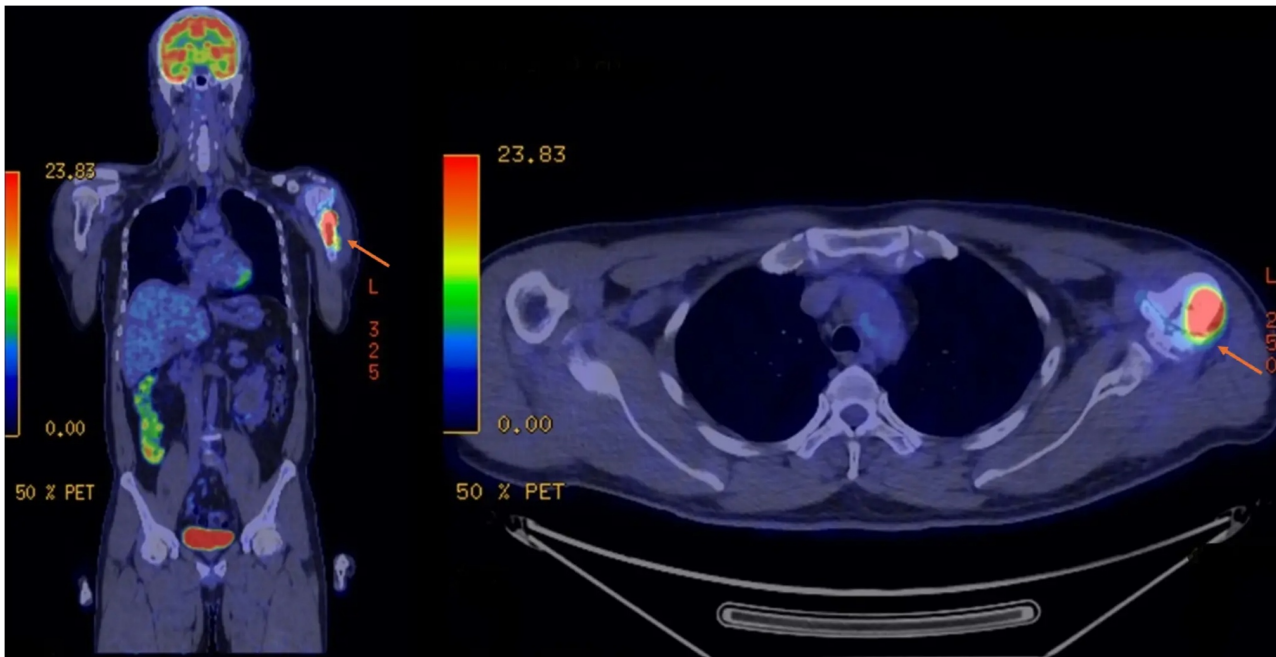


Figure 2. The bone tumor on the PET/CT scan has an SUV_{max} of 30 (arrow) (left: Coronal; right: Axial). SUV_{max} , maximum standardized uptake volume; PET/CT, positron emission tomography/Computed Tomography.

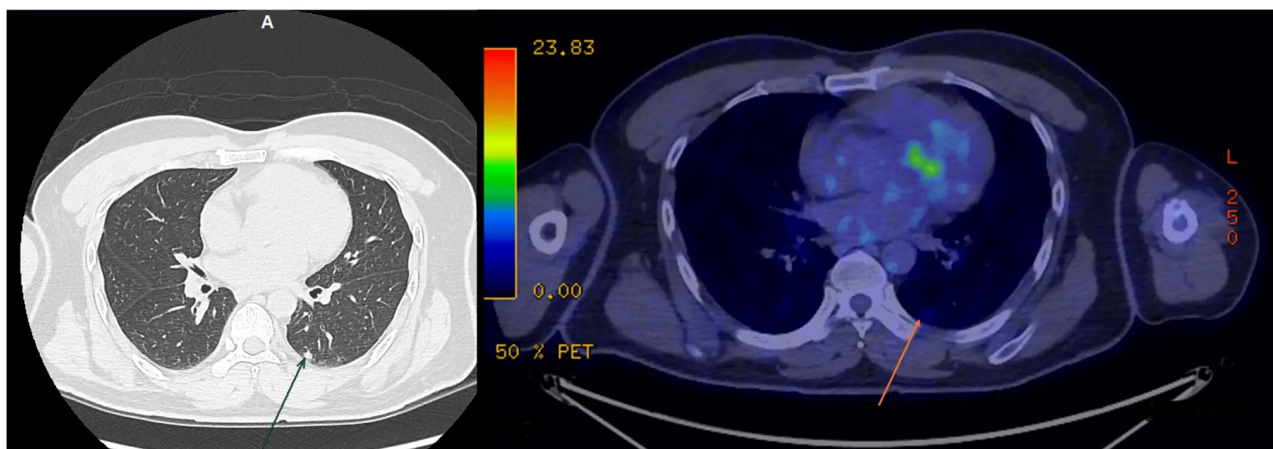


Figure 3. Chest CT revealing a solid nodule in the left lower lobe of the lung (arrow) (left), corresponding to the SUV_{max} of 2.2 on PET/CT (right).

component, and the residual musculature was re-approximated to the autograft using non-absorbable sutures. This soft-tissue envelope reconstruction was essential for reverse shoulder megaprosthesis function to provide dynamic stability and prevent dislocation (9).

Postoperatively, the patient followed a structured rehabilitation program beginning with passive range-of-motion exercises at 2 weeks and progressing to active-assisted exercises at 6 weeks. At the 1-year follow-up, the patient was assessed using the Musculoskeletal Tumor Society (MSTS) scoring system (10). The preoperative MSTS score was 8/30, reflecting severe functional impairment, and improved to 22/30 at the 1-year follow-up. The patient continues to be monitored every 3 months and remains stable with no signs of local recurrence or distant metastasis on imaging (Fig. 6E).

Discussion

This case is notable for two primary reasons: The diagnostic challenge presented by a rare tumor and, more significantly, the management of a severe post-treatment complication with a novel surgical technique. Primary lymphoma of bone is rare, predominantly affecting males, with a median diagnostic age in the 7th decade (11), but the patient of the present study was considerably younger. While local pain is a common presenting symptom, pathological fractures occur in a substantial number of cases (25-30%) and are prognostically significant (12).

Diagnosing PLB can be difficult, as its morphology overlaps with other round cell tumors. As demonstrated in the present case, small or decalcified biopsy samples can further complicate diagnosis. The present findings underscore immunohistochemistry's pivotal role in reaching a definitive

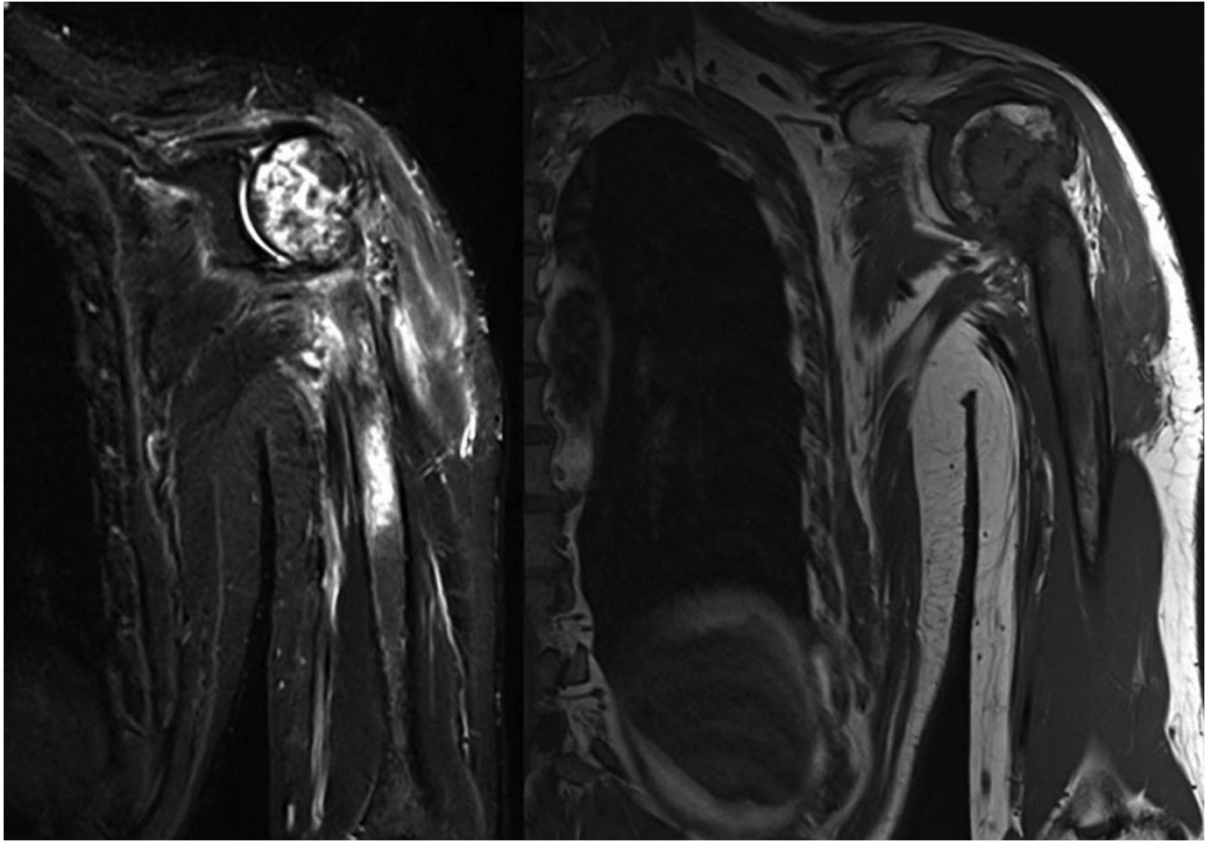


Figure 4. MRI demonstrating the lesion extending from the humeral head to the middle third of the shaft, with invasion of the surrounding soft tissues.

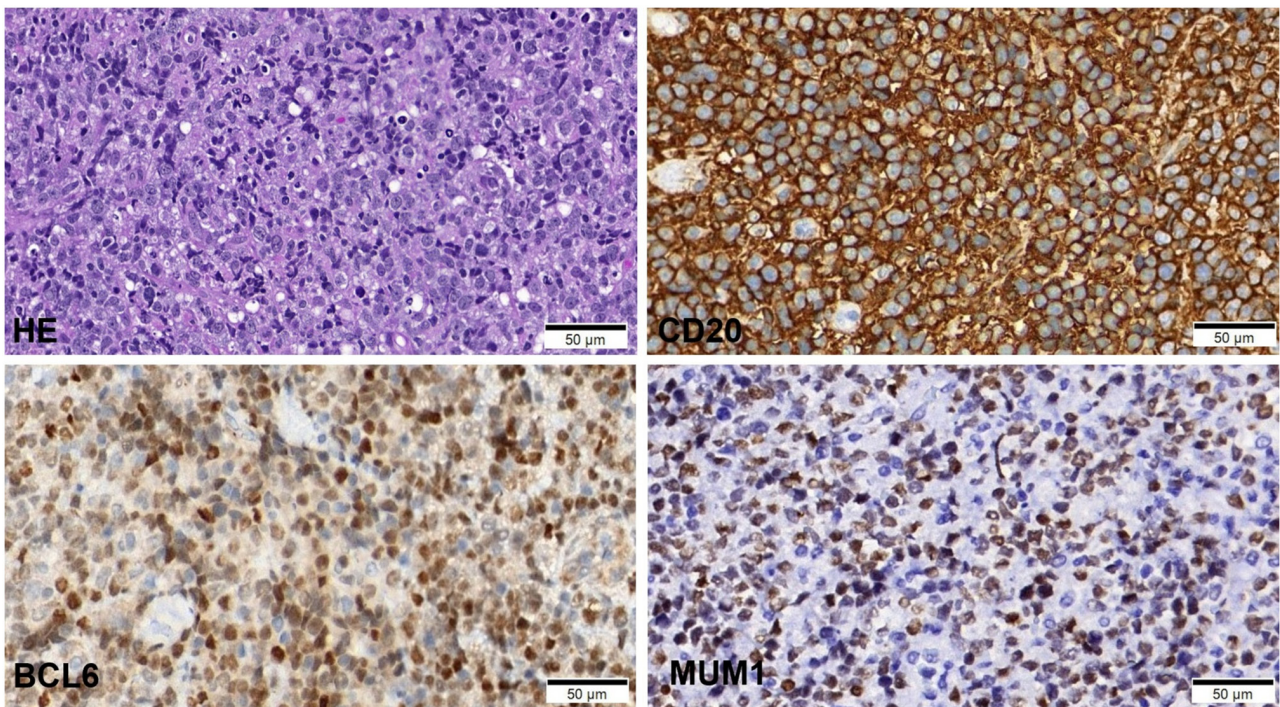


Figure 5. Histopathological examination of HE-stained sections revealed diffuse, round tumor cells with scant cytoplasm. Immunohistochemical staining exhibited tumor cell positivity for CD20, BCL6 and MUM1 (scale bars, 50 μ m). HE, hematoxylin and eosin; MUM1, multiple myeloma oncogene 1.

diagnosis. The sample's strong positivity for B-cell markers CD20 and CD45 (13), along with the specific profile of BCL6,

MUM1 and a high Ki-67 index, was crucial in confirming DLBCL and excluding mimics like Ewing sarcoma.

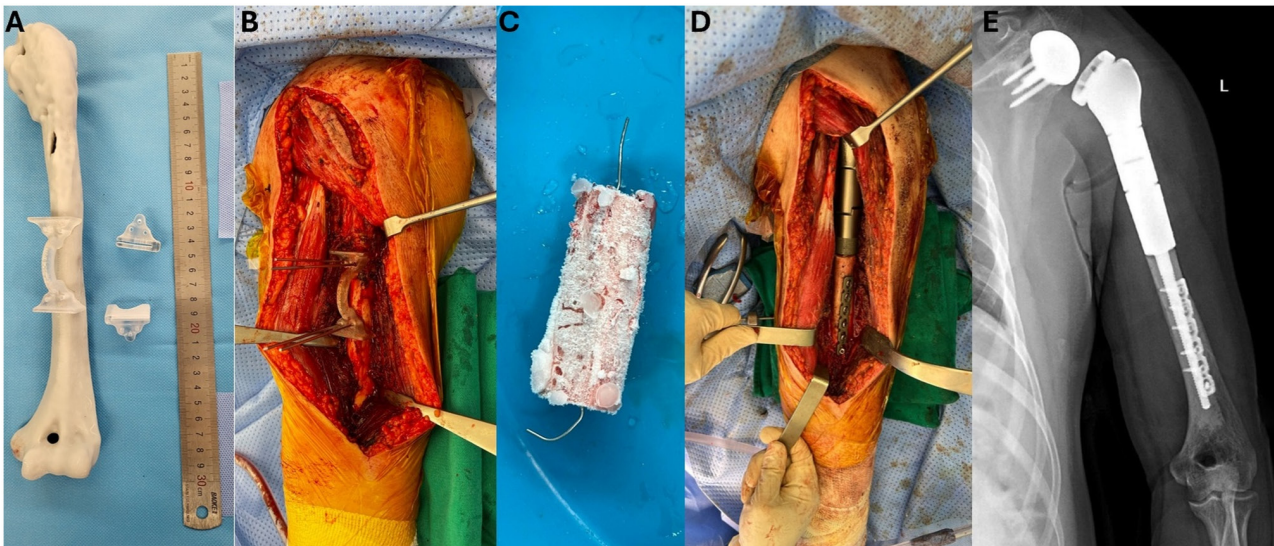


Figure 6. Hybrid limb salvage reconstruction using a modular reverse shoulder megaprosthesis combined with a liquid nitrogen-treated, devitalized autograft for a large proximal humeral defect. (A) A 3-dimensional printed pre-operative planning model derived from CT imaging, used to guide implant selection and simulate the reconstruction. (B) Patient-specific instrumentation was used to precisely cut bone segments. (C) The 6-cm recycled tumor-bearing humeral autograft after treatment with liquid nitrogen. (D) The devitalized cortical autograft segment was fixed to the stem with cement and to the remaining humeral diaphysis with plate and screws. (E) One-year follow-up X-ray.

The primary PLB management is a combination of chemotherapy and radiotherapy. Surgery is typically reserved for obtaining a diagnosis or for managing complications like pathological fractures. The optimal surgical timing and method for these fractures are not well-established. Scoccianti *et al* (14) documented various approaches, including conservative management, fixation and resection, with the timing of surgery varying from pre- to post-chemotherapy.

In the present case, the decision to perform surgery after the completion of both chemotherapy and radiotherapy was based on the patient's specific clinical situation: A non-healing fracture causing significant functional loss, despite the patient being pain-free. This aligned with the principle of intervening to enhance function and quality of life. The present surgical technique addressed substantial bone loss and soft tissue involvement, consistent with recommendations to consider wide excision in such scenarios. Furthermore, complete resection was supported by evidence suggesting improved survival rates compared to incomplete resection (15). The uniqueness of the present surgical approach lies in the combination of a reverse shoulder arthroplasty with the use of a liquid nitrogen-treated autograft. This technique aimed to provide stability and improve shoulder function while preserving the patient's bone stock, representing an innovative evolution in our surgical practice for humeral cancers (16). Furthermore, Schmitz *et al* (15) reported that survival was significantly higher in patients who underwent complete resection compared to those who underwent incomplete resection. This supports our decision to proceed with wide excision followed by megaprosthesis replacement.

To contextualize the innovation of the proposed hybrid approach, it is useful to compare it directly to the principal alternatives: Structural allograft composite arthroplasty and megaprosthesis reconstruction alone. Osteoarticular or intercalary allografts offer biological reconstruction and the potential

for tendon reattachment to host tissue. However, they have high complication rates, including infection, fracture and non-union, and carry the additional risk of disease transmission (17). Furthermore, allografts are not universally available, particularly in resource-limited healthcare settings such as Vietnam, where the bone banking infrastructure remains underdeveloped. Additionally, reconstruction with megaprosthesis alone, while durable and immediately stable, sacrifices all residual bone stock. In many cases, this option is not feasible when there is not enough bone left to attach the implant stem.

The hybrid technique described in this report addresses these limitations by combining the immediate mechanical stability of the modular reverse shoulder prosthesis with the biological advantages of the patient's own devitalized cortical bone. The recycled autograft serves as a bridging scaffold that facilitates soft-tissue attachment, augments the bone-prosthesis interface and preserves the patient's residual cortical stock—all without the immunological concerns or availability constraints of an allograft. This approach represents a pragmatic and reproducible innovation particularly suited to centers where commercial allografts are unavailable.

In conclusion, this case of primary diffuse large B-cell lymphoma of the bone highlights the critical importance of immunohistochemistry for accurate diagnosis when faced with histopathological mimics. Additionally, the non-healing pathological fracture of the present patient required a highly specialized intervention. This case underscores that PLB treatment goals should extend beyond oncological control to include limb function preservation and improved quality of life, necessitating a creative and individualized multidisciplinary approach.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The data generated in this study may be requested from the corresponding author.

Authors' contributions

DTT and VKN conceived the study and wrote original manuscript. MQD and THL summarized data, operated on the patient and confirmed the authenticity of the raw data. TQSN operated on the patient and contributed to writing the manuscript. VAN reviewed the results of diagnostic imaging. TTHaT and VCT collected, validated and interpreted the patient's chemotherapy and radiotherapy treatment data. TTHiT and TDT followed up and interpreted the patient's outcome. All of the authors have read and approved the final manuscript.

Ethics approval and consent to participate

This study's procedures adhered to the tenets of the Declaration of Helsinki. Case reports are approved by the Joint Consultation for Approval of Surgery of Vinmec Times City International Hospital, Vinmec Healthcare System, 458 Minh Khai, Vinh Tuy, Hanoi and are exempt from requiring ethical approval at the Vinmec Healthcare System.

Patient consent for publication

Written informed consent was obtained from the patient for the publication of this case report, including clinical information and accompanying images.

Competing interests

The authors declare that they have no competing interests.

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