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# Comprehensive Clinical and Pathological Analysis of *Chondroblastic* Osteosarcoma Masquerading as an Aneurysmal Bone Cyst in an Adolescent Patient: A Multidisciplinary Diagnostic Journey

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**Keywords**
Chondroblastic Osteosarcoma, Aneurysmal Bone Cyst, SATB2, Immunohistochemistry, Adolescent Oncology, Proximal Femur.

**Abstract**
Osteosarcoma is the most common primary malignant bone tumor, primarily affecting adolescents and young adults during periods of rapid skeletal growth. Chondroblastic osteosarcoma (COS) is a histological variant that poses a diagnostic challenge due to its extensive cartilaginous matrix, which can obscure the critical diagnostic feature: malignant osteoid production. This diagnostic complexity is further exacerbated when the tumor exhibits secondary aneurysmal bone cyst (ABC) changes, often leading to an initial misdiagnosis as a benign lesion. To analyze a case of chondroblastic osteosarcoma with secondary ABC changes, highlighting the importance of a multidisciplinary approach in diagnosing and managing high-grade bone tumors in adolescent patients. A case study of a 17-year-old male presenting with progressive pain and swelling in the right thigh. Diagnosis was confirmed through incisional biopsy, immunohistochemical profiling (positive for SATB2, P53, S100, and Osteocalcin), and MRI findings, which initially suggested an ABC. MRI findings indicated an aggressive bone tumor with fluid-fluid levels characteristic of ABC. However, after biopsy and immunohistochemical analysis, the final diagnosis was confirmed as high-grade chondroblastic osteosarcoma with secondary ABC changes. The patient underwent neoadjuvant MAP chemotherapy and limb-salvage surgery. This case underscores the importance of maintaining a high index of suspicion for malignancy in adolescent patients presenting with cystic bone lesions. A multidisciplinary approach involving clinical, radiological, and pathological correlation is crucial to prevent diagnostic delays and ensure the initiation of appropriate high-grade sarcoma therapy.

## INTRODUCTION

Osteosarcoma is a primary intramedullary high-grade malignant tumor characterized by the direct formation of bone or osteoid tissue by malignant mesenchymal cells. It is the most common non-hematopoietic primary bone malignancy, exhibiting a distinct bimodal age distribution (Autopsy and Case Reports, 2023). The first and most significant peak occurs in the second decade of life, specifically between ages 10 and 20, coinciding with the adolescent growth spurt and the highest rate of longitudinal bone growth at the metaphyseal plates (Autopsy and Case Reports, 2023). A smaller, secondary peak is observed in older adults, often

associated with pre-existing conditions such as Paget's disease of bone or prior radiation therapy.

The anatomical predilection of osteosarcoma is typically for the metaphysis of long tubular bones, with the distal femur, proximal tibia, and proximal humerus being the most common sites, collectively accounting for approximately 80% to 90% of cases (PubMed Central, 2024a). Conventional osteosarcoma is the most frequent histological variant, comprising approximately 90% of all cases. This category is further subdivided based on the predominant extracellular matrix into osteoblastic, *chondroblastic*, and fibroblastic subtypes (Autopsy and Case Reports, 2023). *Chondroblastic* osteosarcoma (COS) represents approximately 10% to 15% of conventional osteosarcomas and is defined by a dominant hyaline cartilage component that may obscure the underlying malignant osteoid (Autopsy and Case Reports, 2023).

A significant diagnostic dilemma arises when these malignant tumors present with secondary Aneurysmal Bone Cyst (ABC) changes (Kim et al., 2020). Primary ABC is a benign but locally aggressive lesion characterized by blood-filled cystic spaces separated by connective tissue septa (Kim et al., 2020). However, secondary ABC changes can occur as a complication of various benign and malignant bone tumors, including Giant Cell Tumor (GCT), fibrous dysplasia, and telangiectatic or *chondroblastic* osteosarcoma (Kim et al., 2020). The presence of fluid-fluid levels on Magnetic Resonance Imaging (MRI), while highly characteristic of ABC, can lead to the "masquerading" of a high-grade sarcoma as a benign lesion, thereby delaying appropriate oncological intervention.

The management of osteosarcoma has evolved significantly from the era of radical amputation to the current standard of multimodal therapy (Kementerian Kesehatan RI, 2019). Modern protocols involve neoadjuvant chemotherapy (typically the MAP regimen: Methotrexate, Adriamycin/Doxorubicin, and Cisplatin) followed by surgical resection with wide margins—ideally through limb-salvage techniques and subsequent adjuvant chemotherapy (American Cancer Society, 2026). The histological response to neoadjuvant treatment, quantified by the percentage of tumor necrosis, remains the most critical prognostic indicator for long-term survival (Autopsy and Case Reports, 2023).

In regions where traditional medicine remains prevalent, such as Southeast Asia, diagnostic delay is a common hurdle. Patients often seek alternative therapies, such as "*Sangkal Putung*" (traditional bone setting), which can mask the symptoms of an underlying malignancy until it reaches an advanced stage with cortical breach and soft tissue involvement. This report details the comprehensive diagnostic and clinical management of a 17-year-old male whose *chondroblastic* osteosarcoma was initially mistaken for an ABC, illustrating the pivotal role of immunohistochemistry and multidisciplinary Clinical-Pathological Conferences (CPCs) in resolving complex orthopedic oncology cases.

The purpose of this study is to analyze the clinical presentation, radiological features, histopathological findings, and immunohistochemical characteristics of *chondroblastic* osteosarcoma with secondary ABC changes in an adolescent patient. In addition, this study aims to evaluate the role of multidisciplinary collaboration in resolving diagnostic uncertainty and determining the optimal therapeutic strategy for aggressive bone tumors.

The benefits of this study are expected to contribute both clinically and academically. Clinically, this report may increase physician awareness regarding malignant bone tumors that

mimic benign cystic lesions, thereby reducing the risk of delayed diagnosis and inappropriate treatment. Academically, this study enriches the existing literature on rare presentations of *chondroblastic* osteosarcoma and highlights the diagnostic value of SATB2, Osteocalcin, and integrated clinicopathological evaluation. Furthermore, this report may serve as a reference for future research and educational material for orthopedic oncology, radiology, and pathology practitioners in developing healthcare settings.

## RESEARCH METHOD

### Patient Identity and Clinical History

The patient, identified as a 17-year-old male student residing in Kediri, East Java, was referred to the Orthopedic and Traumatology Department at Rumah Sakit Umum Daerah (RSUD) Dr. Saiful Anwar (RSSA) Malang. He presented with a primary complaint of persistent and progressive pain in his right upper thigh and groin area, which had been worsening over the previous three months. The patient described the pain as a deep, dull ache that was exacerbated by physical activity, particularly walking, and partially relieved by rest.

The patient's clinical history was notable for a significant trauma event three years prior to his current presentation, occurring during a soccer match. Following the injury, he was taken to a traditional bone setter, a practice locally known as "*Sangkal Putung*," for alternative treatment. While he remained ambulatory, he began to notice a small, firm lump in the groin area that progressively increased in size over time, eventually interfering with his daily activities and gait. He denied any systemic symptoms such as fever, unintentional weight loss, chronic cough, or night sweats. There was no relevant family history of malignancy or similar orthopedic conditions.

### Physical Examination and Status Lokalis

Upon physical examination on March 5, 2024, the patient appeared in stable condition with no signs of acute distress. His vital signs were within normal physiological limits for his age:

**Table 1.** Vital Signs

| Vital Sign | Measurement |
|---|---|
| Blood Pressure | 120/80 mmHg |
| Pulse Rate | 76x/minute |
| Respiratory Rate | 20x/minute |
| Body Temperature | 36,3$^{O}$C |

Source: Patient medical record, RSUD Dr. Saiful Anwar Malang (2024)

General status assessment showed no anemia, jaundice, or peripheral lymphadenopathy. Cardiovascular and respiratory examinations were unremarkable, with normal heart sounds (S1-S2 single) and vesicular breath sounds without added wheezing or crackles. The abdominal examination was flat, soft, and showed no organomegaly or masses Local Status of the right thigh (Regio Thigh Dextra) revealed:

1. Inspection (Look): Significant swelling was observed in the proximal third of the thigh. No skin venectasia, redness, or hyperpigmentation was noted.

2. Palpation (Feel): A firm, fixed mass was palpable in the proximal femoral region. The area was notably warm and demonstrated significant tenderness upon deep palpation. The mass felt solid and was fixed to the deeper structures.
3. Measurements: The circumference of the affected right thigh was measured at 54 cm, while the healthy left thigh measured 52 cm, indicating a 2 cm discrepancy.
4. Mobility (Move): The range of motion (ROM) of the right hip joint was significantly limited in all planes due to pain and mechanical obstruction by the tumor mass.

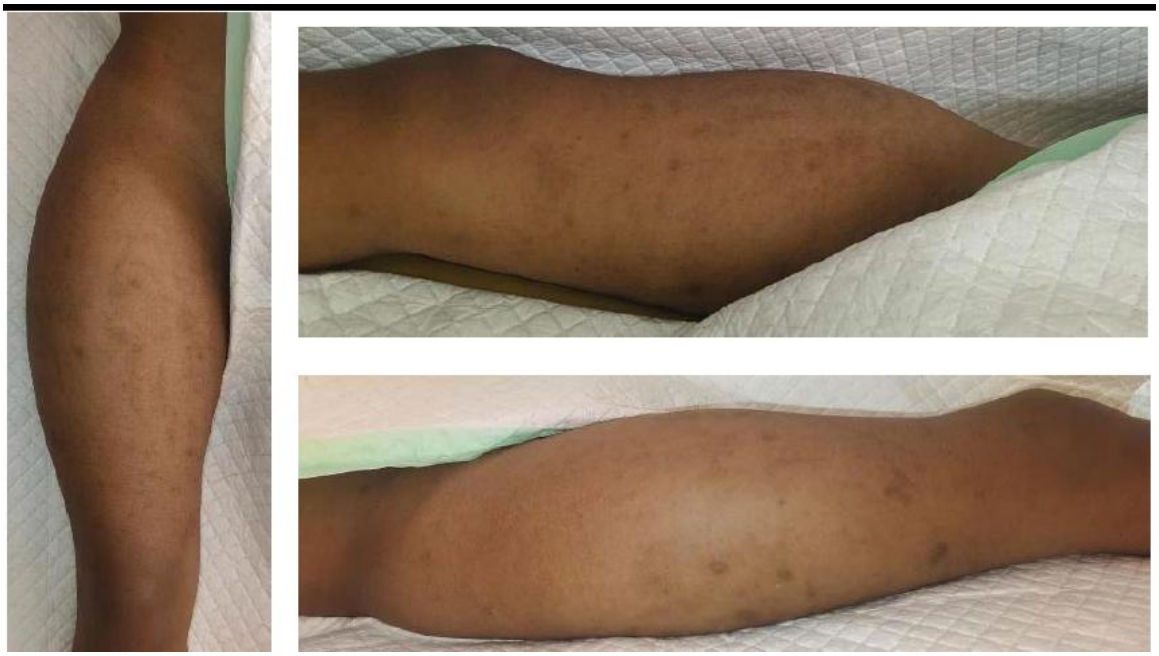

**Figure 1.** Local Status

Source: Patient clinical documentation, Department of Orthopedic and Traumatology, RSUD Dr. Saiful Anwar Malang (2024)

**Table 2.** Hematology Results (December 11, 2023)

| Examination Type | Result | Unit | Reference Value |
|---|---|---|---|
| Hemoglobin (HGB) | 15.10 | g/dl | 13.4 – |
| Erythrocytes (RBC) | 5.00 | Million | 4.74 – |
| Leukocytes (WBC) | 9.08 | 103/mm | 5.07 – |
| Hematocrit | 44.1 | % | 39.90 – |
| Platelets (PLT) | 285.0 | 103/mm | 185.00 – |
| MCV | 88.2 | $\mu m^3$ | 73.40- |
| MCH | 30.20 | $pg$ | 24.20- |
| MCHC | 34.20 | $g/dL$ | 31.90- |
| RDW | 12.10 | % | 11.30- |
| MPV | 9.7 | $fL$ | 7.2- |

Source: Clinical Pathology Laboratory, RSUD Dr. Saiful Anwar Malang (2023)

**Table 3.** Biochemistry (December 2023 - February 2024)

| Parameter | Result | Unit | Reference Range |
|---|---|---|---|
| Alkaline Phosphatase (ALP) | 415 | U/L | 35 - |
| Lactate Dehydrogenase (LDH) | 201 | U/L | 135 - |
| Urea | 13.9 | Mg/dl | 16.6 - |
| Creatinine | 0.67 | Mg/dl | 0.67 - |

Source: Clinical Pathology Laboratory, RSUD Dr. Saiful Anwar Malang (2023–2024)

The significantly elevated ALP (415 U/L) provided an early biochemical indication of high osteoblastic activity, which is a common finding in malignant bone-forming tumors like osteosarcoma.

***Plain Radiographs***

X-rays of the pelvis and femur (December 2023) showed a large osteolytic lesion with a narrow zone of transition in the proximal third of the right femur, involving the meta-diaphysis. The lesion appeared multiloculated with some internal septations.1 By July 2024, follow-up radiographs suggested a Shepherd's crook-like deformity and a visible cortical break on the lateral diaphysis.

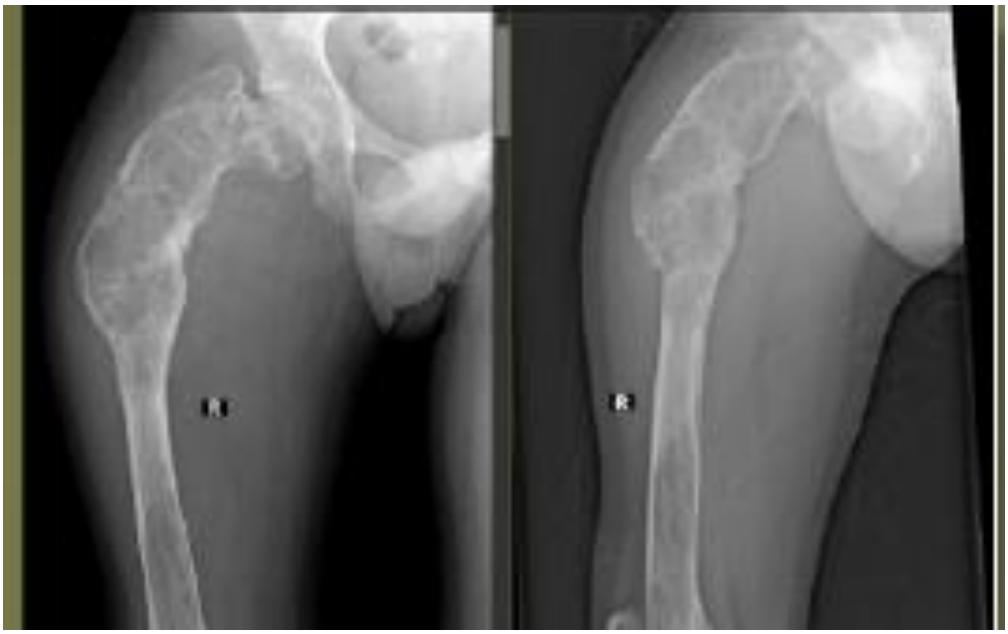

**Figure 2.** X-rays of the pelvis and femur (December 2023)
Source: Department of Radiology, RSUD Dr. Saiful Anwar Malang (2023)

**Magnetic Resonance Imaging (MRI)**

MRI of the right femur with contrast (March 2, 2024) revealed:

1. Tumor Characteristics: A large, primary aggressive bone tumor involving the epi-meta-diaphysis of the proximal femur.
2. Internal Composition: The lesion exhibited multiple fluid-fluid levels, highly characteristic of blood-filled cystic spaces typically associated with Aneurysmal Bone Cyst (ABC).

3. Cortical Integrity: There was significant cortical thinning and a clear cortical breach on the lateral side.
4. Soft Tissue Extension: The tumor extended into the adjacent musculature, specifically the rectus femoris.
5. Conclusion: The initial radiological impression was primary aggressive bone tumor suggestive of an Aneurysmal Bone Cyst.

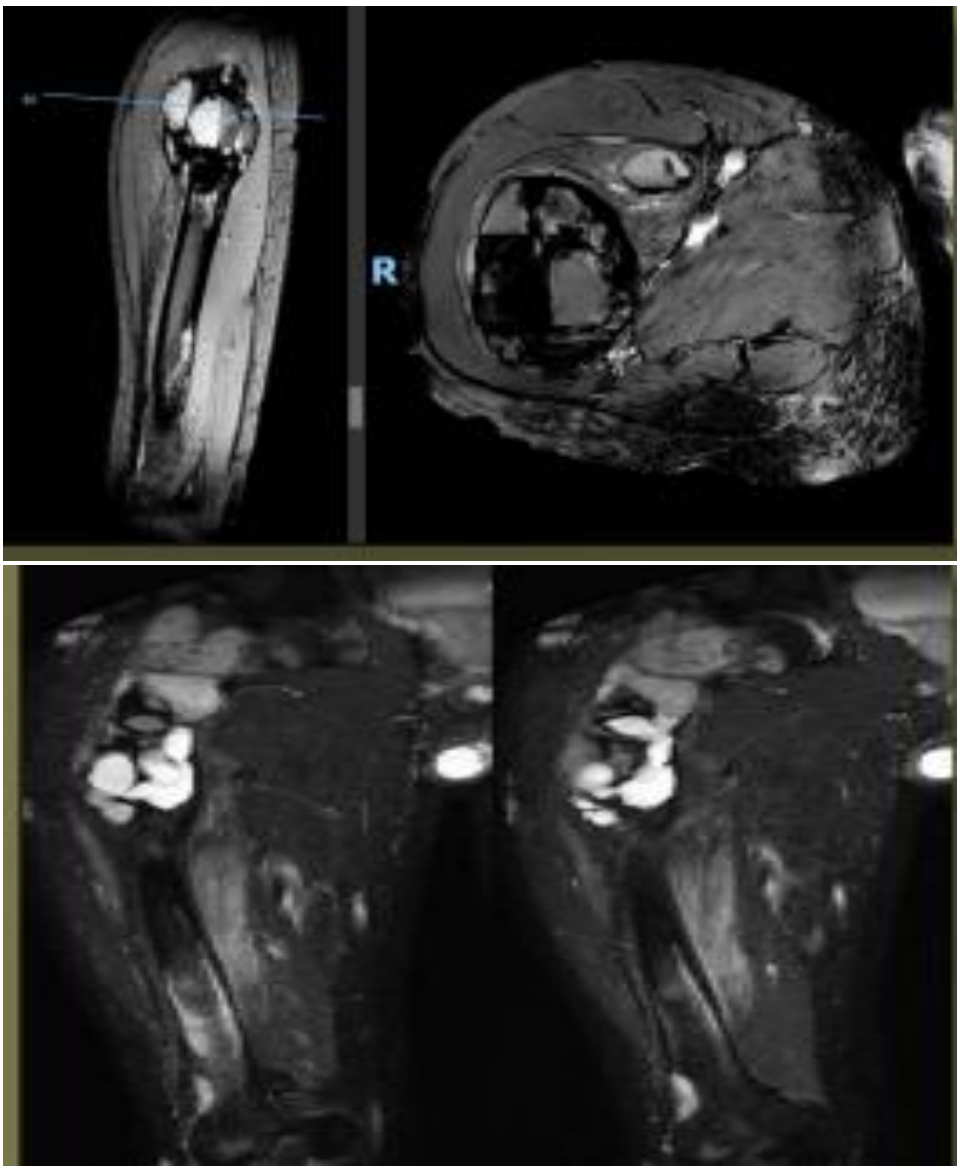


**Figure 3.** MRI of the right femur with contrast
Source: Department of Radiology, RSUD Dr. Saiful Anwar Malang (2024)

**Staging Studies**

A Thorax PA X-ray (March 8, 2024) showed that the heart and lungs were within normal limits, with no evidence of pulmonary nodules or bone metastasis, which is critical for staging high-grade sarcomas.

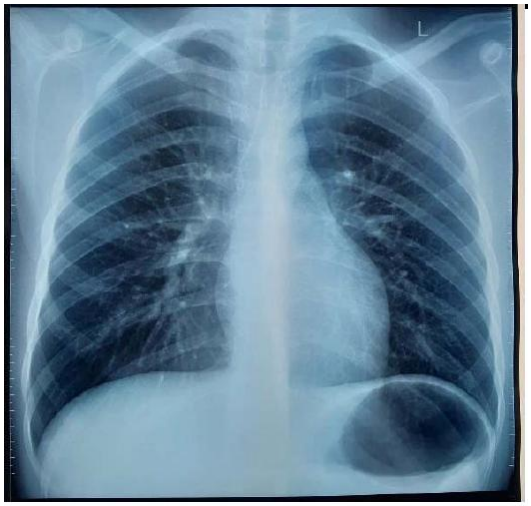

**Figure 4.** Thorax PA X-ray
Source: Department of Radiology, RSUD Dr. Saiful Anwar Malang (2024)

**Histopathological Analysis**

To resolve the diagnostic ambiguity, an incisional biopsy was performed on April 3, 2024.

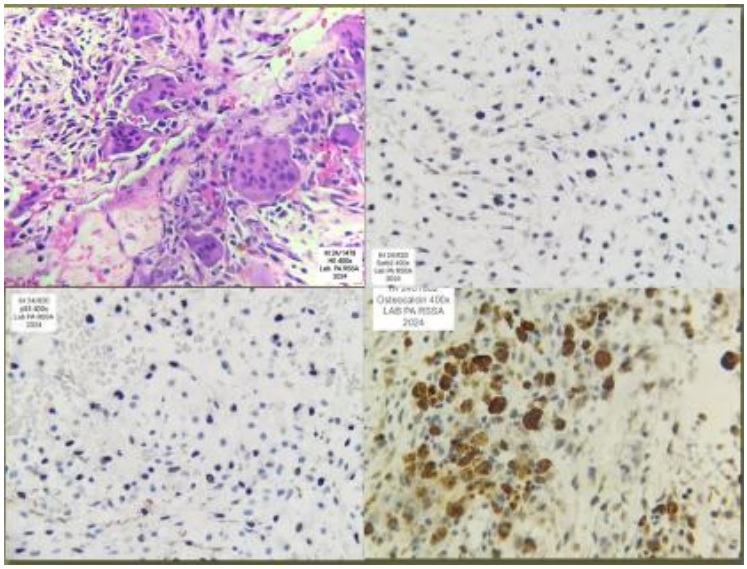

**Figure 5.** Histopathological Examination of Incisional Biopsy (April 3, 2024)
Source: Anatomical Pathology Laboratory, RSUD Dr. Saiful Anwar Malang (2024)

**Immunohistochemical Profiling**

Due to the histological overlap with other chondroid lesions, a comprehensive IHC panel was performed.

**Table 4. Immunohistochemical Profiling**

| IHC Marker | Result | Interpretation |
|---|---|---|
| **SATB2** | Positive (patchy, 30% nuclei) | Confirms osteoblastic differentiation |
| **P53** | Positive (patchy, 30% nuclei) | Surrogate for TP53 mutation |
| **Osteocalcin** | Positive (80% cytoplasm) | Indicates active bone matrix |

| IHC Marker | Result | Interpretation |
|---|---|---|
| | | production |
| **S100** | Positive (nuclei) | Consistent with *chondroblastic* cells |
| **Ki67** | Positive (patchy) | Reflects high proliferative activity |

Source: Anatomical Pathology Laboratory, RSUD Dr. Saiful Anwar Malang (2024)

The positivity for SATB2 and Osteocalcin was instrumental in distinguishing this high-grade sarcoma from purely cartilaginous tumors like chondroblastoma or chondrosarcoma.

## RESULTS AND DISCUSSION

### Clinical Presentation and Diagnostic Dilemmas

The diagnostic journey of this 17-year-old male highlights the significant challenges inherent in the identification of high-grade bone sarcomas that exhibit cystic features. Osteosarcoma often presents with vague symptoms, such as deep-seated bone pain that may be initially dismissed as "growing pains" or sports-related injuries. In this case, the patient's three-year delay in seeking professional medical help, largely due to the use of traditional *Sangkal Putung* therapy, allowed the tumor to progress from an intramedullary lesion to one with significant cortical breach and soft tissue invasion. This socio-cultural aspect of healthcare in Indonesia remains a major barrier to the early diagnosis and successful treatment of pediatric bone cancers.

### Radiological Masquerade: ABC vs. Osteosarcoma

The most deceptive aspect of this case was the MRI finding of multiple fluid-fluid levels, which initially pointed toward a diagnosis of Aneurysmal Bone Cyst (ABC). Fluid-fluid levels occur when there is sedimentation of blood products within cystic spaces, a feature classically associated with the benign ABC (Kim et al., 2020). However, as noted in the medical literature, this finding is not pathognomonic and can be seen in several other bone lesions, most notably telangiectatic and *chondroblastic* osteosarcoma (PubMed Central, 2026a).

A key differentiating feature in this case was the presence of a cortical break and soft tissue mass, which are much more common in high-grade sarcomas than in benign ABCs (PubMed Central, 2026a). Additionally, the significantly elevated Alkaline Phosphatase (ALP) provided a biochemical "red flag". ALP is an enzyme involved in bone mineralization, and its elevation in a patient with a suspected bone tumor often correlates with high osteoblastic activity and aggressive tumor growth.

### Histological and Immunohistochemical Integration

*Chondroblastic* osteosarcoma is a histological subtype of conventional osteosarcoma defined by the presence of significant chondroid matrix (Yakushiji et al., 2009). It can be easily confused with chondroblastoma or chondrosarcoma on small biopsy samples because the malignant osteoid—the diagnostic hallmark of osteosarcoma—may be sparse or localized (Autopsy and Case Reports, 2023).

The introduction of SATB2 (Special AT-rich sequence-binding protein 2) as an IHC marker has revolutionized the diagnosis of these tumors (ResearchGate, 2025a). SATB2 is a sensitive nuclear marker for osteoblastic differentiation and is positive in over 90% of osteosarcomas, including the *chondroblastic* and small-cell variants (ResearchGate, 2016). In

our patient, the patchy nuclear positivity for SATB2, combined with the cytoplasmic expression of Osteocalcin, provided definitive proof of the tumor's bone-forming nature. Furthermore, the p53 positivity served as a surrogate for TP53 mutation, a frequent genetic aberration in high-grade osteosarcomas that is associated with chromosomal instability and poor prognosis.

**Management Protocols: The Multi-Step Approach**

The treatment of high-grade osteosarcoma requires a coordinated multidisciplinary approach, as recommended by both the Indonesian National Guidelines (PNPK) and international standards such as NCCN and ESMO.

*Neoadjuvant Chemotherapy (MAP Regimen)*

Neoadjuvant chemotherapy is administered to shrink the primary tumor, facilitate surgical resection, and treat potential micro metastatic disease (American Cancer Society, 2026). The MAP regimen (Methotrexate, Adriamycin, and Cisplatin) remains the global standard for the pediatric and adolescent population (American Cancer Society, 2026). High-dose Methotrexate requires intensive monitoring of renal function and urine pH, along with Leucovorin rescue, to mitigate severe systemic toxicity.

**Surgical Strategy and Limb Salvage**

The surgical objective is wide resection, removing the tumor with a margin of healthy tissue to minimize the risk of local recurrence (PubMed Central, 2024b). Historically, amputation was the only option, but modern limb-salvage surgery (LSS) using modular mega prostheses now offers equivalent oncological outcomes with significantly better functional and psychological results for the patient (PubMed Central, 2024b). In the case of this 17-year-old male, the involvement of the proximal femur necessitated a mega prosthesis to restore gait and hip stability.

**Prognostic Considerations in *Chondroblastic* Osteosarcoma**

Chondroblastic osteosarcoma is often associated with a slightly less favorable prognosis compared to the osteoblastic or fibroblastic subtypes (MDPI, 2025). Research indicates that COS may exhibit a poorer response to neoadjuvant chemotherapy, with lower rates of tumor necrosis (<90%) (PubMed Central, 2024a). This highlights the need for rigorous post-operative monitoring and potential adjustments to adjuvant therapy if the histological response is suboptimal (Autopsy and Case Reports, 2023). Despite these challenges, multimodal therapy has improved the 5-year survival rate for localized osteosarcoma to approximately 60% to 70%.

## CONCLUSION

This case report of a 17-year-old male with *chondroblastic* osteosarcoma illustrates the diagnostic complexity and clinical masquerade presented by secondary aneurysmal bone cyst changes in a high-grade malignancy. The patient's initial presentation, influenced by socio-cultural reliance on traditional therapy, led to a diagnostic delay that was only resolved through advanced imaging and a comprehensive immunohistochemical panel. The successful identification of the tumor’s osteogenic nature through SATB2 and Osteocalcin staining was critical in redirecting the management strategy from a benign curettage plan to a multimodal sarcoma protocol. This case underscores the necessity for clinicians to maintain a high index of suspicion in adolescent patients with lytic bone lesions, especially when accompanied by "red flags" such as elevated ALP, cortical breach, and soft tissue invasion. A multidisciplinary

approach integrating radiology, pathology, and orthopedic oncology remains the gold standard for navigating such deceptive presentations and ensuring that patients receive timely, aggressive, and appropriate life-saving therapy. Future efforts should focus on early detection and public education to reduce the diagnostic delays associated with alternative medicine in the Southeast Asian context.

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