

## Background

- CIC*-rearranged sarcoma is an aggressive malignancy that most commonly affects adolescents and young adults.
- CIC* is a gene encoding a transcriptional repressor that normally suppresses gene expression. In *CIC*-rearranged sarcoma, gene fusions disrupt its regulatory function, resulting in dysregulated transcription and aberrant activation of oncogenic pathways that promote tumor growth.
- CIC*-rearranged sarcoma is a soft tissue tumor arising from non-bony tissues, including muscle, fat, fibrous connective tissue, or peripheral nerves of the extremities and trunk.
- Features that should raise concern for a malignant neoplasm rather than a benign reactive vascular lesion include rapid or progressive enlargement, hemorrhage, and a friable appearance.
- Persistent or indeterminate lesions warrant imaging and biopsy to exclude rare malignant entities.

## Clinical History

- A 27-year-old male presented with a vascular lesion initially believed to be benign that progressively enlarged and was ultimately diagnosed as *CIC*-rearranged sarcoma.
- The patient, years prior, first noticed a nail plate lesion with a melanonychia beneath the left thumbnail, prompting removal, followed by partial nail disruption.
- The patient underwent emergency partial nail removal involving the dorsal aspect of the left thumb.
- The patient subsequently sustained repeated traumatic injuries to the same thumb, which initiated the development of the hemorrhagic, friable tumor, progressively increased in size. No pathology evaluation was performed.
- There were no signs of active infection, and neurovascular status of the hand remained intact.

**References:** Antonescu CR, Owosho AA, Zhang L, Chen S, Deniz K, Huryn JM, Kao YC, Huang SC, Singer S, Tap W, Schaefer IM, Fletcher CD. Sarcomas With *CIC*-rearrangements Are a Distinct Pathologic Entity With Aggressive Outcome: A Clinicopathologic and Molecular Study of 115 Cases. *Am J Surg Pathol*. 2017 Jul;41(7):941-949. doi: 10.1097/PAS.0000000000000846. PMID: 28346326; PMCID: PMC5468475. Link: <https://pmc.ncbi.nlm.nih.gov/articles/PMC5468475/>

2. Connolly EA, Bhadri VA, Wake J, Ingley KM, Lewin J, Bae S, Wong DD, Long AP, Pryor D, Thompson SR, Strach MC, Grimison PS, Mahar A, Bonar F, Maclean F, Hong A. Systemic treatments and outcomes in *CIC*-rearranged Sarcoma: A national multi-centre clinicopathological series and literature review. *Cancer Med*. 2022 Apr;11(8):1805-1816. doi: 10.1002/cam4.4580. Epub 2022 Feb 17. PMID: 35178869; PMCID: PMC9041083.

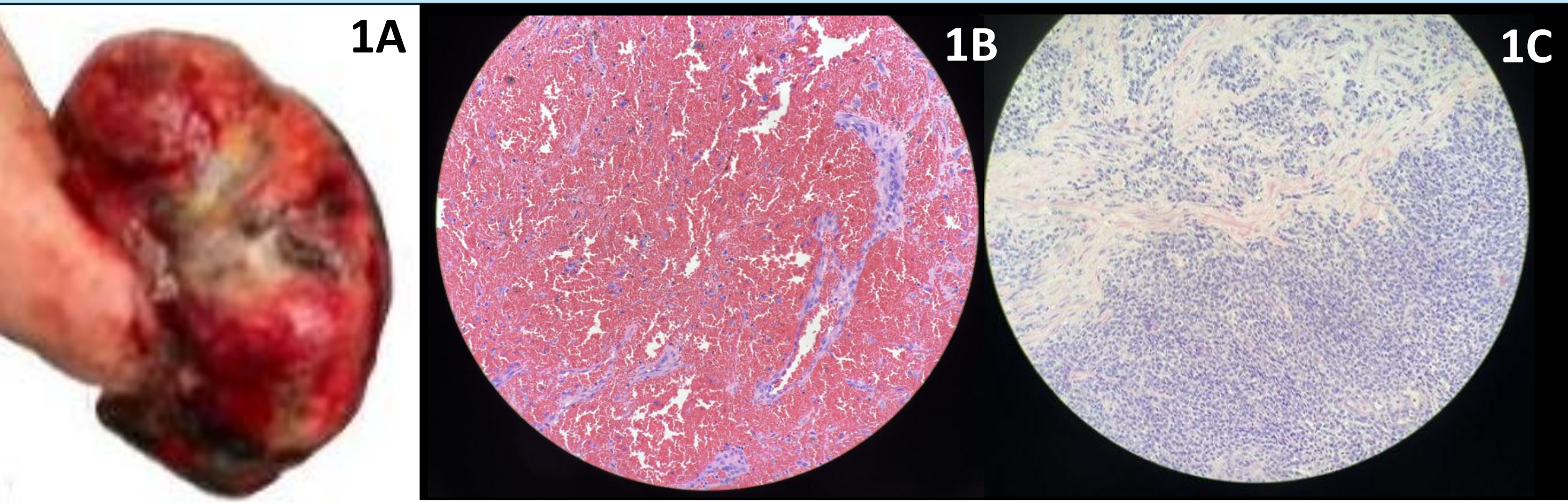
3. Maaita W, Hasasna N, Yaser S, Saleh Y, Abu-Hijli R, Asha W, Halalshah H, Abdel Al S, Al-Hussaini M, Jaber O. *CIC*-Rearranged Sarcoma: A Clinical and Pathological Study of a Peculiar Entity. *Diagnostics (Basel)*. 2025 Jul 11;15(14):1758. doi: 10.3390/diagnostics15141758. PMID: 40722508; PMCID: PMC12293365.

4. Makise N, Yoshida A. *CIC*-Rearranged Sarcoma. *Surg Pathol Clin*. 2024 Mar;17(1):141-151. doi: 10.1016/j.path.2023.06.003. Epub 2023 Aug 1. PMID: 38278603.

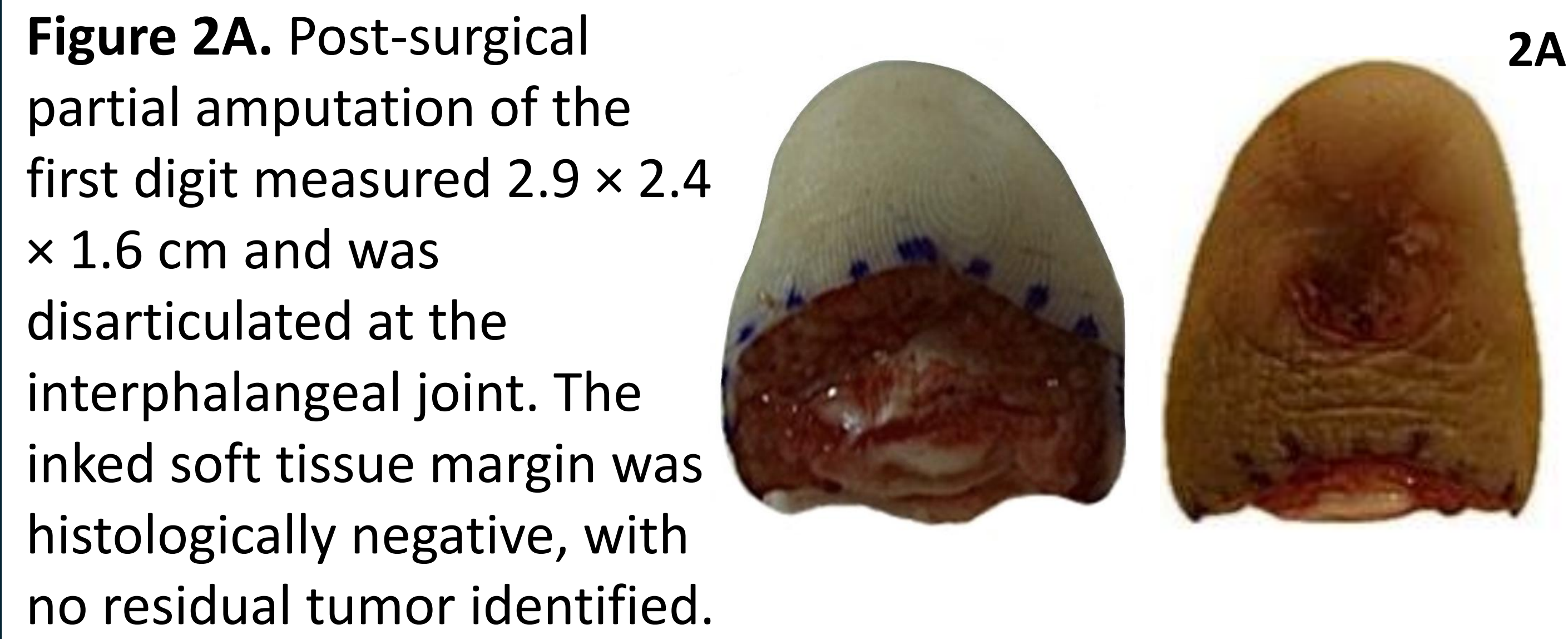
5. Mancarella C, Carrabotta M, Toracchio L, Scotlandi K. *CIC*-Rearranged Sarcomas: An Intriguing Entity That May Lead the Way to the Comprehension of More Common Cancers. *Cancers (Basel)*. 2022 Nov 2;14(21):5411. doi: 10.3390/cancers14215411. PMID: 36358827; PMCID: PMC9657047.

6. Murphy J, Resch EE, Leland C, Meyer CF, Llosa NJ, Gross JM, Pratilas CA. Clinical outcomes of patients with *CIC*-rearranged sarcoma: a single institution retrospective analysis. *J Cancer Res Clin Oncol*. 2024 Mar 4;150(3):112. doi: 10.1007/s00432-024-05631-7. PMID: 38436779; PMCID: PMC10912249. Link: <https://pmc.ncbi.nlm.nih.gov/articles/PMC10912249/>

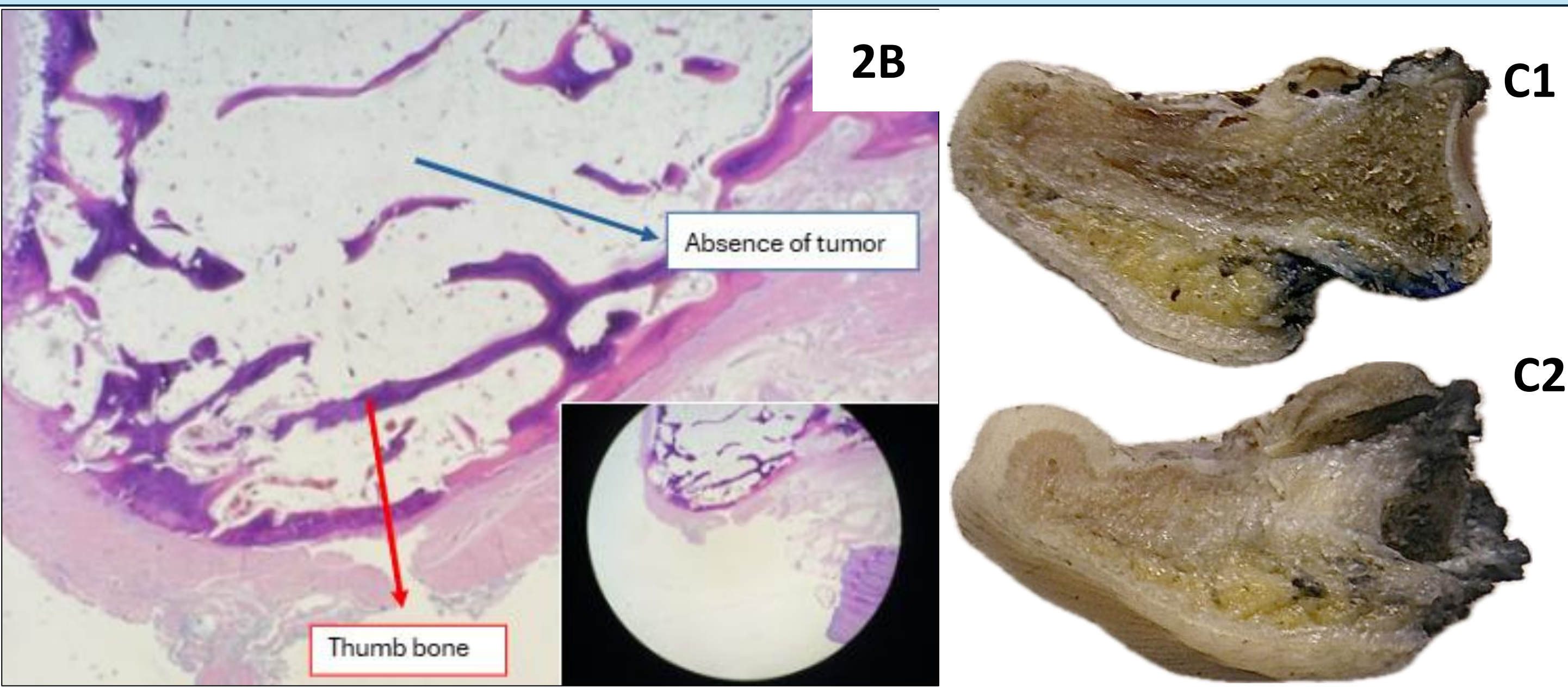
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**Figure 1A.** The exophytic thumb tumor excised specimen measured 5.5 × 4.5 × 2.8 cm. **Figure 1B.** The excised tumor histopathology demonstrated a highly vascularized stroma with fibrous connective tissue, consistent with the macroscopic grossly hemorrhagic appearance. **Figure 1C.** The histological image demonstrated tumor cells with intercalating collagen fibers.



**Figure 2A.** Post-surgical partial amputation of the first digit measured 2.9 × 2.4 × 1.6 cm and was disarticulated at the interphalangeal joint. The inked soft tissue margin was histologically negative, with no residual tumor identified.



**Figure 2B.** The histologic sections demonstrate typical bone mineralization and normal articulation, with no evidence of abnormal spindle cells or atypical cartilage. **Figure C1-2.** Clear surgical margins were achieved at the amputation site. The tumor was confined to soft tissue arising from the nail bed and overlying skin at the distal aspect of the left thumb. Extent of tissue involvement justified thumb amputation. Margins inked in black.

## Pathologic Findings

A rapidly growing, hemorrhagic exophytic tumor demonstrating features of a small round blue cell neoplasm. The diagnosis was confirmed by IHC, FISH and next-generation sequencing. Histologic examination demonstrated a small round blue cell neoplasm with nuclear pleomorphism, high mitotic activity, and myxoid stromal changes, supporting the diagnosis of an aggressive malignant neoplasm and ultimately leading to partial amputation of the thumb. *CIC*-rearranged sarcoma can resemble other small round blue cell tumors morphologically, making molecular studies necessary for definitive diagnosis.

## Discussion

- Accurate diagnosis requires histopathological assessment in conjunction with molecular genetic testing.
- Overall, the integrated diagnostic workup confirmed *CIC*-rearranged sarcoma, characterized as a small round blue cell neoplasm.
- The patient's tumor was initially considered a benign vascular lesion due to its subungual location, history of repeated trauma, and absence of neurovascular compromise.
- The significance of this case lies in the fact that *CIC*-rearranged sarcoma can arise in unusual anatomic locations such as the thumb.
- The tumor was subsequently managed with surgical excision achieving local control, with consideration of further oncologic evaluation and radiation therapy given its poor prognosis.
- Maintaining a broad differential diagnosis is essential, as delayed recognition of *CIC*-rearranged sarcoma may postpone treatment of a highly aggressive malignancy.

## Conclusion

*CIC*-rearranged sarcoma is a rare, highly aggressive soft tissue malignancy with a deceptively benign clinical presentation. Early recognition and multimodal diagnostic confirmation are essential for accurate diagnosis and appropriate management.

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