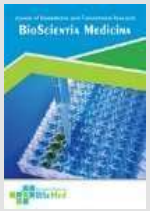
eISSN (Online): 2598-0580



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Malignant Lesion on Intraoperative Frozen Section with Histopathology Feature Alveolar Soft Part Sarcoma: A Case Report

Sri Wildanur[1*], Aswiyanti Asri[1], Pamelia Mayorita[1]

[1]Department of Pathological Anatomy, Faculty of Medicine, Universitas Andalas/Dr. M. Djamil General Hospital, Padang, Indonesia

ARTICLE INFO

Keywords:
Alveolar soft part sarcoma
Case report
Histopathology
Malignant lesion

***Corresponding author:**
Sri Wildanur

E-mail address:
sriwildanur28@gmail.com

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v8i6.1003

A B S T R A C T

Background: Alveolar soft part sarcoma (ASPS) are slow-growing inert soft tissue masses, but fast-growing masses are also reported. Because the cancer tissue is rich in blood vessels, distant metastasis is easy to occur through the blood tract, and lung metastasis is the most common. The diagnosis of ASPS should be combined with histopathology examination because of its rarity and often misdiagnosed, especially in unusual sites. **Case presentation:** A 22-year-old female came to the oncology surgery polyclinic at Dr. M. Djamil General Hospital Padang with a chief complaint of a lump in her left thigh since 1 year ago and has been getting enlarged in the last 6 months. The lump has been painful for the last 2 months. Upon an intraoperative frozen section examination, it was concluded that the lesion was malignant. Then, the tissue was prepared from formalin fixed paraffin embedded (FFPE), and the lesion was diagnosed as alveolar soft part sarcoma. **Conclusion:** In the case of ASPS, surgical management has an important role. The goal of the intraoperative frozen section of this patient is to determine whether the lesion is benign or malignant. There is a need for histological examination, collaboration, and optimal communication between pathologists and surgeons to avoid limitations and pitfalls examination.

1. Introduction

Alveolar soft part sarcoma (ASPS) is a rare histological subtype of sarcoma, accounting for approximately 0.5–1% of all soft-tissue sarcomas. ASPS primarily affects younger patients, with a peak incidence age of 15–35 years, and female predominance is well documented. ASPS commonly originates from deep soft tissues of the extremities, predominantly the lower extremities. Molecular studies have identified a specific translocation that results in ASPSCR1-TFE3 gene fusion.[1,2] Most of the clinical symptoms of ASPS are slow-growing inert soft tissue masses, but fast-growing masses are also reported. Because the cancer tissue is rich in blood vessels, distant metastasis is easy to occur through the blood tract. Lung metastasis is the most common. The diagnosis of ASPS should be combined with histopathology examination because of its rarity and often misdiagnosed, especially in unusual sites.[3] Grossly, ASPS is usually characterized by a well-circumscribed lesion that has a soft and rubbery consistency and can vary in color from yellow to gray to tan. Areas of necrosis and hemorrhage can also be demonstrated.[4] Microscopically, ASPS is characterized by an alveolar-like pattern with the growth of large, discohesive polygonal epithelioid cells bearing eosinophilic cytoplasm, forming organoid nests surrounded by delicate capillary channels that were further separated by broad fibrous septa into various compartments.[5] Diagnosis of ASPS is challenging because of morphological overlap with other tumors, particularly on small biopsies and uncommon sites of

occurrence. Difficulties are further confounded by the occurrence of rare morphologic features, particularly in biopsies, such as solid patterns, clear cytoplasm, and unusual nuclear features. Due to their highly vascular nature and feeder vessels, they are often misdiagnosed as arteriovenous malformations (AVMs).[6] The first choice for the treatment of ASPS is extensive surgical resection to obtain a tumor-free edge.[3]

The intra-operative frozen section plays an important role in the management of surgical patients, and it must be used prudently to avoid the indiscriminate use of this important technique as it is subjected to many limitations compared to the paraffin-embedded tissue sections. Establishing whether a lesion that needs to be resected is benign or malignant is very important to the operating surgeon, as this will decide the type of operative procedure or further sampling that he has to make.[7] Histopathology plays an integral role in the multidisciplinary approach of treating patients with alveolar soft part sarcoma, the accuracy of which has important therapeutic implications. Intraoperative frozen section consultation is particularly challenging. Indications for the frozen section include making a diagnosis, evaluating margin status, determining tumor extent/spread, and obtaining an adequate sample for diagnosis.[8] In the following, we report a case of alveolar soft part sarcoma (ASPS) in 22-year-old women. In this case, an intraoperative frozen section procedure was performed with the result of a malignant lesion. The patient's final diagnosis of formalin fixed paraffin embedded (FFPE) tissue was alveolar soft part sarcoma.

2. Case Presentation

A 22-year-old female came to the oncology surgery polyclinic at Dr. M. Djamil General Hospital Padang on August 2nd, 2023, with a chief complaint of a lump in her left thigh since 1 year ago and has been getting enlarged in the last 6 months. The lump has been painful for the last 2 months. From the previous medical history, the patient had no history of tumors in the family, no history of radiation and no history of previous treatment. Physical examination revealed that the patient was in moderate general condition and compos mentis state, with a blood pressure of 111/80 mmHg, a pulse of 79x/minutes, respiratory rate of 17x/minutes, and body temperature of 36,6°C. Examination from the left proximal of the femur region showed that there was a mass measuring 10x7x5cm, solid consistency, and fixed. A laboratory test resulted in hemoglobin levels of 10,9 g/dL, leukocytes 12.800/mm^3, and hematocrit 33%. The patient was temporarily diagnosed with a soft tissue tumor of the left femur. This patient underwent an AP-lateral chest X-ray with normal impression results. On July 26th, 2023, a lower extremity CT-Scan with IV contrast was conducted with suggestive of soft tissue (muscle) hemangioma in the proximal region of the left femur (anteromedial), an intact femoral bone (Figure 1). On August 10th, 2023, a CT angiography examination of the lower extremities showed the impression of a soft tissue AVM in the proximal vastus medial muscle region of the left femur (from the superficial femoral artery and left external iliac vein) (Figure 2). The patient was planned to undergo a tumor excision procedure with a frozen section.

The tissue from surgery was received in the anatomical pathology laboratory on September 1st, 2023, with the coding PJ 3489-23. Macroscopic examination showed a reddish brown, dense ruberry, with a size of 10,5 x 7 x 5 cm. The cross-section showed a white mass with a reddish brown part with a diameter of 10 cm (Figure 3). In smear preparations from imprinted tumors in the femur region, microscopically, there was a distribution and grouping of cells with an increased N/C ratio, large, round-oval nuclei, irregular nuclear membranes, prominent nuclei, eosinophilic cytoplasm. There were also cells with multinucleoli, in which mitosis can be found. The distribution of lymphocytes and macrophages was visible (Figure 4).

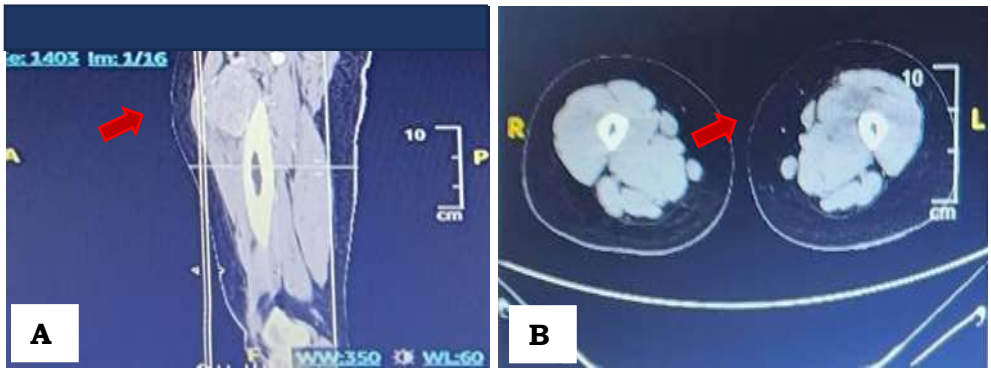


Figure 1. Lower extremity CT-Scan. A soft tissue mass with isodense density in the proximal region of the left femur with a tortuous and tubular vascular shape (red arrow) (A) Sagital-coronal (B) Axial.

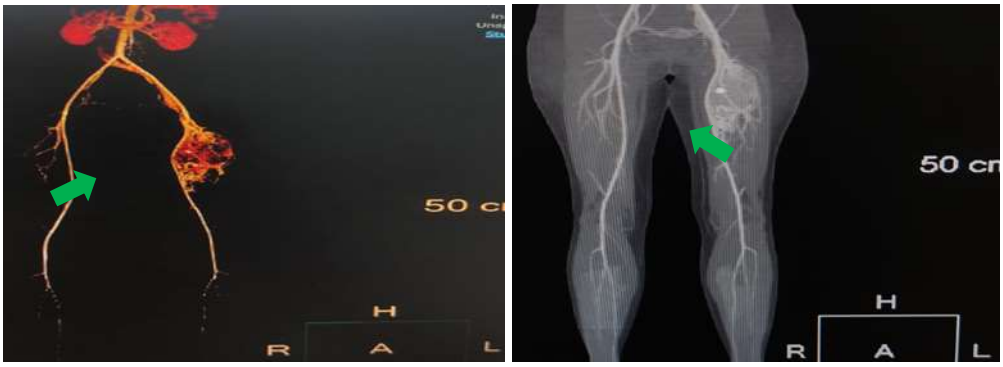


Figure 2. CT Angiography results showed a mass in the proximal region of the left femur with vascular malformation of the branch of the left superficial femoral artery (green arrow).

Histopathological evaluation from the frozen section resulted in tissue pieces that contained the proliferation of tumor cells that grow infiltratively between the connective tissue stroma to form lobulated with thick fibrous septae, nest, organoid pattern, and solid structures. Some appeared to have discohesive and alveolar patterns. These cells have large, pleomorphic, partly hyperchromatic, partly vesicular, coarse chromatin, and prominent nuclei; the cytoplasm was eosinophilic and clear. There was a distribution of lymphocytes, plasma cells, hyperemic capillaries, and bleeding foci. The frozen section concludes a malignant lesion and will be confirmed with formalin fixed paraffin embedded (FFPE) for definitive diagnosis (Figure 5).

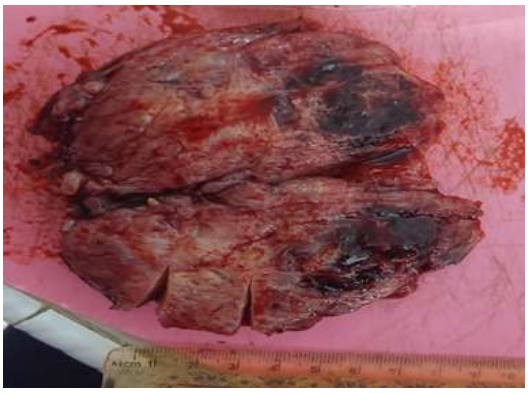


Figure 3. Macroscopic examination from the frozen section. A reddish brown with a cut surface with a white mass.

Histopathological evaluation with a paraffin block showed a feature of connective tissue section containing a proliferation of polygonal cells that grow infiltratively between the connective tissue stroma to form lobed structures with thick fibrous septae, nest, organoid pattern, and solid sheets; some appeared discohesive and alveolar pattern. These cells were found with large, round-oval, pleomorphic, partly hyperchromatic, partly vesicular nuclei, coarse chromatin, prominent nucleoli, and atypical mitoses. The granular cytoplasm was eosinophilic and clear, with visible rhabdoid cells. Tumor cell emboli were seen in the blood vessels. There was a distribution of lymphocytes, plasma cells, hyperemic capillaries, and bleeding. Microscopic examination of FFPE concluded that diagnosis of alveolar soft part sarcoma, minimal staging pT2NxMx, and periodic acid-schiff (PAS) histochemical examination is recommended to confirm the diagnosis (Figure 6).

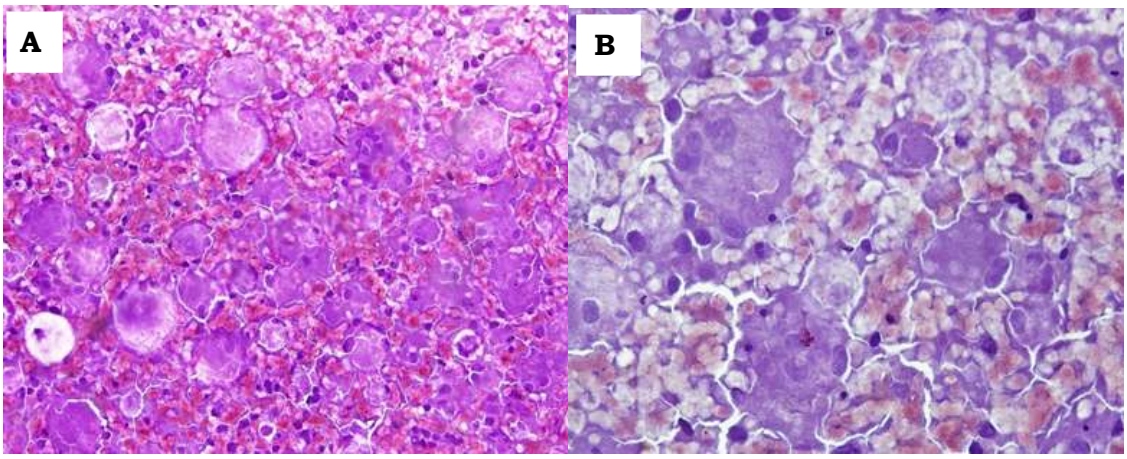
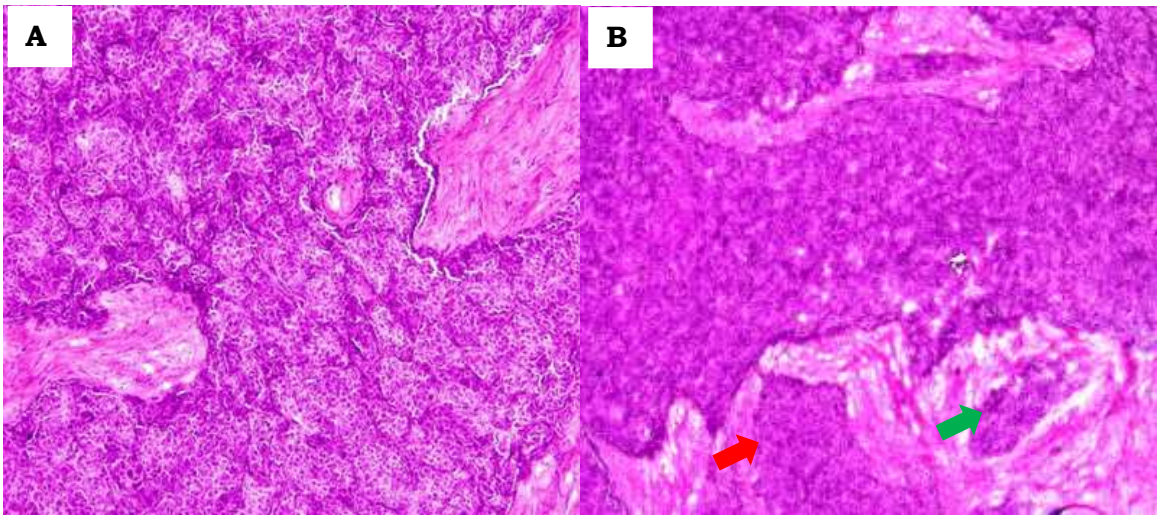


Figure 4 Microscopic of imprint. (A) Cells with an increased N/C ratio, large, round-oval nuclei, regular nuclear membranes, prominent nuclei, and eosinophilic cytoplasm (HE, 200x). (B) There were also cells with multinucleoli (HE, 400x).



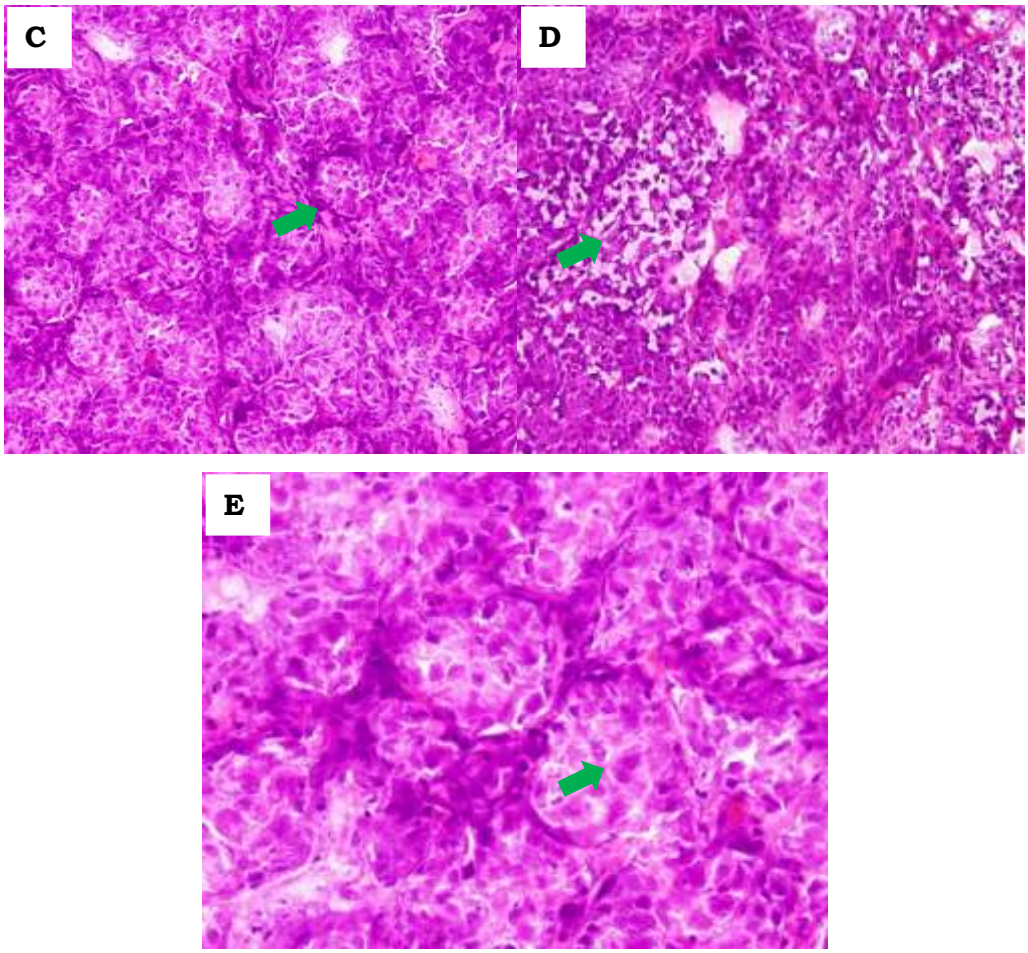
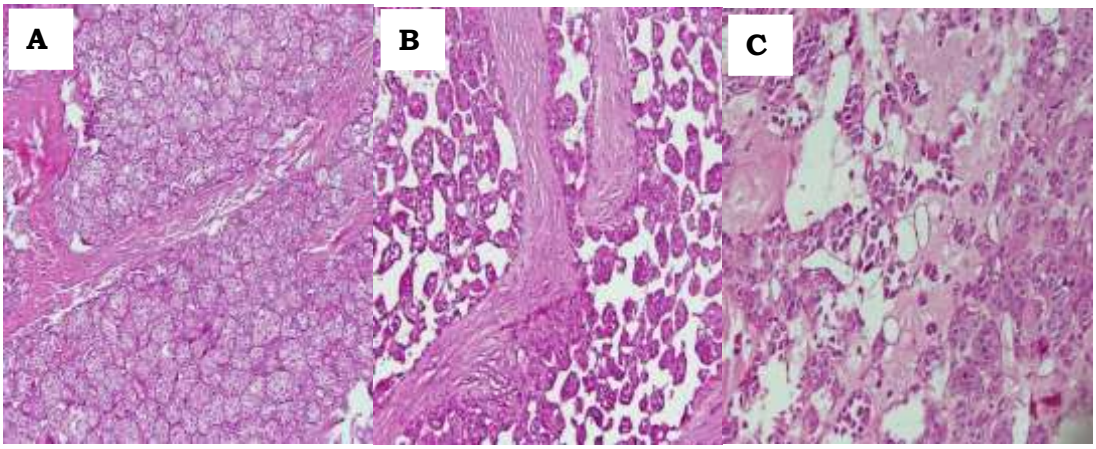


Figure 5. Microscopic examination in frozen section. (A) (B) Proliferation of tumor cells that grows infiltratively between the connective tissue stroma to form lobulated with thick fibrous septae. (HE, 100x). (B) Nest (green arrow) and solid pattern (red arrow) (HE, 40x). (C) Organoid pattern (green arrow) (HE, 200x). (D) Some was appeared discohesive and alveolar pattern (green arrow). (HE, 200x). (E) These cells have large, pleomorphic, partly hyperchromatic, partly vesicular, coarse chromatin, and prominent nuclei; the cytoplasm was eosinophilic and clear (green arrow). (HE, 400x).



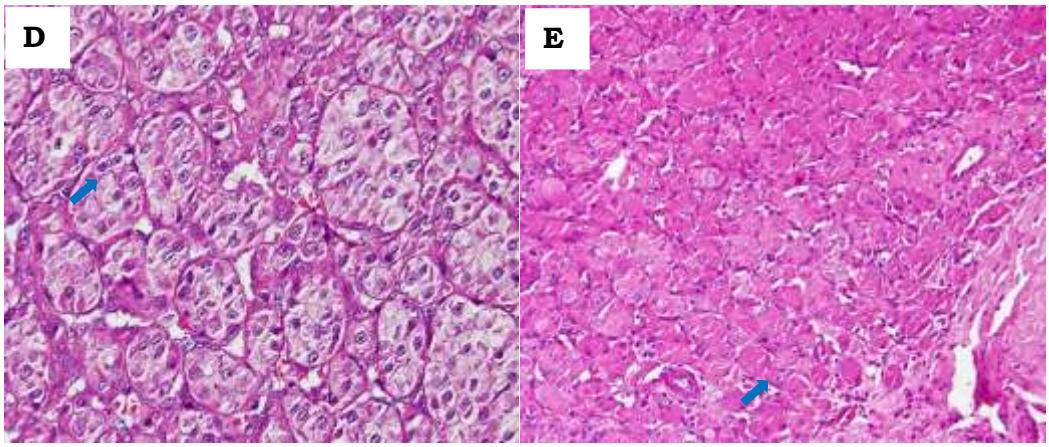


Figure 6. Microscopic examination in FFPE. (A) The proliferation of polygonal cells that grow infiltratively between the connective tissue stroma to form lobed structures with thick fibrous septae, nest, and organoid pattern (HE, 100x). (B) Some appeared to have discohesive and alveolar patterns. (B. HE, 100x and C. HE, 200x). (D) These cells were found with large, round-oval, pleomorphic, partly hyperchromatic, partly vesicular nuclei, coarse chromatin, prominent nucleoli, and atypical mitoses (blue arrow) (HE, 400x). (E) The granular cytoplasm was eosinophilic and clear, with visible rhabdoid cells (blue arrow) (HE, 400x).

The patient was hospitalized for five days. During postoperative care, the patient received IVFD RL, ceftriaxone injection 2x1 g, 3x500 mg of mefenamic acid, and 3x500 mg of tranexamic acid. The patient was followed up for examination at the surgical polyclinic. Recently, the patient had no complaints, and the surgical wound improved.

3. Discussion

Alveolar soft part sarcoma (ASPS) is a rare, highly vascular, deep soft tissue mesenchymal malignancy that is classically seen in the lower extremities of young adults. They account for <1% of all soft tissue sarcomas. There is a slight female predilection in patients less than 30 years old. The molecular genetics aspect involves the recurrent unbalanced translocation der(17)t(X;17)(p11;q25).[9-15] Typically, ASPS is a slow-growing tumor and often comes to clinical attention late in the disease process. About 65% of adults and 30% of children present with metastatic disease in the lungs, brain, bone, and/or lymph nodes. From the assessment, this patient underwent an AP-lateral chest X-ray with normal impression results. This shows that there are no metastases in the lungs. Pathologists should look at radiological findings in cases, especially for soft tissue tumors. The patient was temporarily diagnosed with a soft tissue tumor of the left femur. A lower extremity CT scan with IV contrast was conducted with a suggestion of soft tissue (muscle) hemangioma in the proximal region of the left femur (anteromedial), which is an intact femoral bone. Hemangioma is another commonly confused entity with ASPS, which is a benign vascular tumor. However, hemangiomas are known to occur in a much younger age group than ASPS and are usually present since birth. These show characteristic involution with age and can often contain a fatty component on imaging. Also, they enhance in the early arterial phases compared with soft tissue tumors, which enhance later in the late arterial or early venous phases.[16,17]

A CT angiography examination of the lower extremities showed the impression of a soft tissue AVM in the proximal vastus medial muscle region of the left femur (from the superficial femoral artery and left external iliac vein). Due to their highly vascular nature and feeder vessels, they are often misdiagnosed as arteriovenous malformations (AVMs), but AVMs

usually lack any soft tissue component in contrast to sarcomas. Findings such as arterial feeders with prolonged staining of the tumor and late washout indicate soft tissue vascular tumor rather than an AVM.[17-23] The patient was planned to undergo a tumor excision procedure. Currently, complete surgical resection is the first-line treatment for ASPS, as it offers the greatest benefit. Based on research by Andrea et al. it was stated that the concordance between the results of intraoperative frozen sections and the final results of pathological examinations with paraffin block was 98%.[4,19] Frozen section was performed in this patient to differentiated benign or malignant lesion. The main purpose of the frozen section is to guide the surgical management immediately.

The tissue from surgery was received in anatomical pathology laboratory on September 1st, 2023. Macroscopic evaluation showed a reddish brown, dense ruberry tissue, with a size of 10,5 x 7 x 5 cm. The cross section showed a white-brown mass sorrounded by a reddish part with a diameter of 10 cm. Based on literature, ASPS has a soft consistency with encapsulated borders. The cut surface has a white to yellow–brownish color tinged with hemorrhagic spilling or central necrosis in large tumors.[24] The size of ASPS can range in presentation from 1,2 cm to 24 cm, with a mean size of 6,5 cm, and variability depends on the primary tumor site.[4]

In smear preparations from imprinted tumors in the femur region, microscopically there was a distribution and grouping of cells with an increased N/C ratio, large, round-oval nuclei, irregular nuclear membranes, clear nuclei, eosinophilic cytoplasm. There were also cells with multinucleoli, which mitosis can be found. Based on literature, cytologically, tumor cells were epithelioid or polygonal with abundant eosinophilic granular cytoplasm in 91% of the cases and predominantly clear cytoplasm in some cases. The classically described round to oval nuclei with vesicular chromatin and prominent eosinophilic nucleoli with anisonucleosis was a major feature.[6] Cytology preparations typically included touch imprint can enhanced the diagnosis in conjunction with frozen section.[20] Difficulty seeing cell morphology in frozen sections can be assisted by improving examination simultaneously. Intraoperative imprint cytology coincides with frozen section is very helpful in making diagnosis. Imprint has a simple, fast, and cost effective technique with a fairly good level of accuracy.[20] In this patient, the results of microscopic imprint examination give the impression of malignant. This result is also in accordance with the microscopic picture on the frozen section. The combination of frozen section examination with an improving will increase the accuracy of the diagnosis.

Histopathological evaluation from frozen section resulted with tissue pieces which contained proliferation of tumor cells that grows infiltratively between the connective tissue stroma to form lobulated with thick fibrous septae, nest, organoid pattern, solid structures, some was appeared discohesive and alveolar pattern. These cells have large, pleomorphic, partly hyperchromatic, partly vesicular, coarse chromatin, and prominent nuclei, the cytoplasm was eosinophilic and clear. There was a distribution of lymphocytes, plasma cells, hyperemic capillaries, and bleeding foci. Frozen section conclude a malignant lesion. Base on literature, ASPS shows a distinctive recognizable morphology in most cases with nests or trabeculae of large epithelioid round cells displaying an alveolar and sometimes dyscohesive appearance. The stroma has a delicate vasculature with frequent lymphovascular invasions. Typical cytoarchitectural aspects include individual monomorphic tumor cells with an abundant granular eosinophilic or clear glycogen-rich cytoplasm, sharp cytoplasmic borders, and an eccentric vesicular nucleus containing a prominent central nucleolus.[15]

Histopathologic diagnosis on routine paraffin section is used as the gold standard.[20] In this case, histopathological evaluation with a paraffin block concluded that diagnose of alveolar soft part sarcoma. Base on literature, errors can occur due to diagnostic interpretation errors, frozen section preparations are not representative or technical problems, such as the

folds of network or uneven staining parts, can prevent proper evaluation. Frozen section diagnosis accuracy can be assessed by comparing the diagnosis made in the frozen section with a final diagnosis made from paraffin blocks. The literature reports the level of discrepancy between the diagnosis of frozen section and histopathological diagnosis ranging from 1,4% to 12,9%.[24-26] The results of the frozen section examination are in accordance with the results of the paraffin block examination in patients. During surgical resection of tumors, intra-operative frozen section consultation is useful for obtaining an adequate specimen for diagnosis as well as for evaluating tumor extent and margin status, hence quiding a surgeon to achieve disease free margins. Thus, significantly reduces the chances of postoperative positive margins and primary recurrence of tumors. However, result of frozen sections are not 100% accurate and false negative results may still lead to positive margins and tumor recurrence.[25]

Role of intra operative frozen sections has been extensively studied for various cancers. However, there is considerable lack of literature evaluating the diagnostic accuracy of frozen sections in soft tissue tumors. An overall diagnostic accuracy of frozen sections has been shown to vary from 89 to 98% for various tissue types, however soft tissue tumors still pose a major challenge owing to their rare incidence rate and therefore limited exposure of pathologists to these tumors.[7] The distinctive alveolar pattern of ASPS and its moderate, sometimes clear cytoplasm are shared by other tumors including renal cell carcinoma (RCC), granular cell tumor (GCT), clear cell sarcoma. Immunohistochemistry is often performed to exclude other tumors in the differential diagnosis.[21]

In this case the incision margin were not taken, the clinician performs excision of the tumor to determined benign or malignant lesion. According to the literature that complete surgical resection is the first-line treatment for ASPS, as it offers the greatest benefit. The purpose of surgical intervention is to excise the tumor completely and to prevent disease relapse. Surgeons should remove the tumor with a sufficiently wide margin of the surrounding normal tissue, however it is also necessary to pay attention to maximizing postoperative physical function.[4] Alveolar soft part sarcoma (ASPS) is characteristically resistant to chemotherapy. Radiotherapy is currently used for incomplete surgical resection or when the surgical margin is questionable and is currently being evaluated for a role in preventing local recurrence.[4] In this case after surgical removal of the tumor and reconstruction, the patient should undergo radiotherapy. The five-year survival rate for ASPS is estimated at 86% for those without metastatic spread. Other predictors of a worse prognosis in ASPS include male sex, tumor size greater than 5 cm in local lesions, distant metastatic, and a primary site other than the extremity.[19] In this case the size of the tumor is 10 cm, the prognosis for this patient is likely to be poor because the tumor size is more than 5 cm based on predictors of a worse prognosis in ASPS.

4. Conclusion

A case of 22 year old woman who underwent an intraoperative frozen section was reported with a malignant lesion. These result were confirmed by formalin fixed paraffin embedded (FFPE) examination with a final diagnosis of alveolar soft part sarcoma (ASPS). In the case of ASPS, surgical management has an important role. The goal of intraoperative frozen section of this patient is to determine whether the lesion is benign or malignant. There is a need for histological examination, collaboration, and optimal communication between pathologist and surgeons to avoid limitations and pitfall examination.

5. References

1. Fujiwara T, Nakata E, Kunisada T, Ozaki T, Kawai A. Alveolar soft part sarcoma: progress toward improvement in survival? A population-based study. BMC Cancer. 2022; 22(1): 891.
2. Mody DR, Thrall MJ, Krishnamurthy S. Diagnostic pathology cytopathology second

edition. US: Elsevier. 2018; 676.
3. Zhang Y, Wang Y, Wang H, Wen C, Wu X. Alveolar soft part sarcoma in childhood and adolescence: Report of three cases and review of literature. Front Pediatr. 2022; 10: 937112.
4. Palmer TM, Yu WM, Moenster JM. Alveolar soft part sarcoma of the nasolabial fold: a case report and literature review. Cureus. 2023; 15(4): e38310.
5. Huang SW, Huang HY, Lin H. Alveolar soft part sarcoma of the uterine corpus: a 13-year follow-up case report and review of the literature. Taiwan J Obstet Gynecol. 2023; 62(5): 769-73.
6. Kaur K, Gami A, Shah A, Gandhi J, Trivedi P. Clinico-pathological spectrum of alveolar soft part sarcoma: case series from a tertiary care cancer referral centre in india with a focus on unusual clinical and histological features. Turkish J Pathol. 2023; 1-12.
7. Jaafar H. Intra-operative frozen section consultation: concepts, applications and limitations. Malaysian J Med Sci. 2006; 13(1): 4-12.
8. Miwa S, Yamamoto N, Hayashi K. Diagnostic accuracies of intraoperative frozen section and permanent section examinations for histological grades during open biopsy of bone tumors. Int J Clin Oncol. 2021; 26(3): 613-9.
9. World Health Organization. WHO classification of tumours 5th edition: soft tissue and bone tumours. Switzerland: WHO; 2020; 297-9.
10. Wang B, Wei J, Qu L, Meng L, Xin Y, Jiang X. Alveolar soft part sarcoma of the right calf: a case report. Medicine (Baltimore). 2020; 99: e18952.
11. Stockwin LH. Alveolar soft-part sarcoma (ASPS) resembles a mesenchymal stromal progenitor: evidence from meta-analysis of transcriptomic data. PeerJ. 2020; 8: e9394.
12. Salarzaei O, Khoroushi F, Aminzadeh B, Jafarian AH, Ghodsi A, Soleimani Bami H. Primary alveolar soft part sarcoma of the chest wall: a case report. Clin case reports. 2022; 10(4): e05719.
13. Rafizadeh SM, Cheraqpour K, Amoli FA, Haydar AA. Alveolar soft part sarcoma of the superior rectus muscle: case report and review of literature. Am J Ophthalmol Case Reports. 2022; 27: 101645.
14. Asano Y, Kashiwagi S, Takada K. Alveolar soft part sarcoma metastatic to the breast: a case report. BMC Surg. 2019; 19(1): 30.
15. Robin YM. Pathology of alveolar soft part sarcoma. In: Arnouk H, ed. Advances in Soft Tissue Tumors. IntechOpen. 2022.
16. Akhtar K, Anees A. Alveolar soft part sarcoma : a rare cytological impression. 2016; 1(1): 1-4.
17. Gulati M, Mittal A, Barwad A, Pandey R, Rastogi S, Dhamija E. Imaging and pathological features of alveolar soft part sarcoma: analysis of 16 patients. Indian J Radiol Imaging. 2021; 31(3): 573-81.
18. Muthusamy RK, Mehta S. Alveolar soft-part sarcoma on the abdominal wall in an adult: a rare presentation with cytological and histological correlation. Indian J Med Paediatr Oncol. 2019; 40(2): 309-10.
19. Chang X, Li Y, Xue X, Zhou H, Hou L. The current management of alveolar soft part sarcomas. Medicine (Baltimore). 2021; 100(31): e26805.
20. Bui MM, Smith P, Agresta S V., Cheong D, Letson GD. Practical issues of intraoperative frozen section diagnosis of bone and soft tissue lesions. Cancer Control. 2008; 15(1): 7-12.
21. Nicolas MM, Nayar R, Abdul-Karim FW. Chapter 4 - soft tissue. In: Sidawy MK, Ali SZ, Goldblum JRBTFNAC, eds. Churchill Livingstone. 2007: 93-126.
22. Rekhi B, Ingle A, Agarwal M, Puri A, Laskar S, Jambhekar NA. Alveolar soft part sarcoma "revisited": Clinicopathological review of 47 cases from a tertiary cancer referral centre,

including immunohistochemical expression of TFE3 in 22 cases and 21 other tumours. Pathology. 2012; 44(1): 11-17.

23. Yam MKH, Chan KKK. Alveolar soft part sarcoma in a young woman: a case report from Hong Kong. Radiol Case Rep. 2022; 17(6): 1938-41.
24. Kumar A, Alrohmain B, Taylor W, Bhattathiri P. Alveolar soft part sarcoma: the new primary intracranial malignancy : a case report and review of the literature. Neurosurg Rev. 2019; 42(1): 23-29.
25. Fahad S, Umer M. Diagnostic accuracy of frozen section in musculoskeletal tumors. Int J Surg Oncol. 2021; 6(1): 10-17.
26. Mahe E, Ara S, Bishara M, Kurian A, Tauqir S. Intraoperative pathology consultation: Error, cause, and impact. Can J Surg. 2013; 56(3).