**Case study**

**TITLE :** Hyperferritinemia in a case of Soft Tissue Sarcoma

Abstract-

An elderly male presented with symptoms suggestive of anemia .During workup for the same he was found to have very high levels of serum Ferritin along with a normocytic, normochromic peripheral blood film and no other apparent cause for hyperferritinemia .A swelling which incidentally found on his shin was further investigated by FNAC confirmed presence of soft tissue sarcoma.

Keywords-

Anemia, Hyperferritinemia, Soft tissue sarcoma

Introduction -

Anemia is the most common hematological abnormality in cancer patients.it has been assumed that over 40% of all cancer patients are anemic at the time of diagnosis and rate increases up to 80% in patients with advanced disease. [(1)] The reason for cancer related anemia is multifactorial as it can occur due to dysfunction of iron metabolism, inadequate production of the erythropoietin , bone marrow suppression due to infiltration , peripheral red blood cell destruction.[(4)(5)(6)]

Ferritin is an iron storage protein, small amount of which is found in blood called serum ferritin.it is a surrogate marker of stored iron. its level increases with age, liver disease and malignancies.[(7)]

The authors are hereby presenting a case of an elderly man presenting with painless swelling, anemia and high levels of serum Ferritin who was later diagnosed with soft tissue sarcoma.

Case report

A 70 year old male presented with complaints of exertional dyspnea and generalized weakness from past 6 months, were of gradual onset and progressive course. He was a known case of Hypertension on erratic treatment and had a history of bleeding from external hemorrhoids and had received one unit of blood transfusion in last one year but there was no active bleed per rectum since then .There was no history of fever ,joint pains ,rashes ,bony tenderness, hypertension ,Diabetes Mellitus ,jaundice, any other overt blood loss, melena or aspirin intake.

On general physical examination patient was averagely built and poorly nourished .Pallor was present while there was no icterus ,lymphadenopathy ,edema or clubbing .An ill-defined ,round , swelling was present over the right thigh on the medial aspect just below the inguinal region .It was 5cmX 5cm in size ,hard in consistency ,non-tender and non-mobile

.According to the patient this swelling had been present since 2 years but had progressively increased to current size .Another swelling was observed on right shin (image 1) dorsum of right foot .Pulse -72bpm,BP-170/90mm Hg,RR-15bpm. .Systemic Examination was normal except for a soft systolic murmur in the pulmonary area.

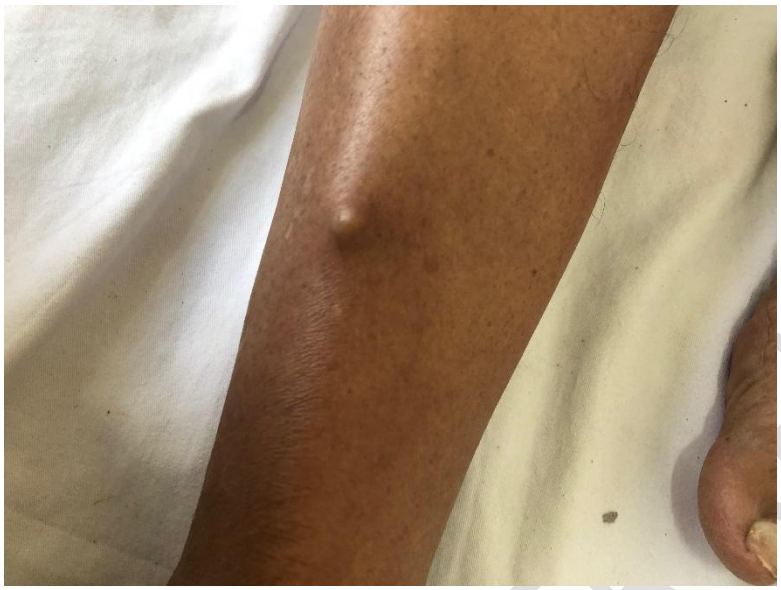


IMAGE 1.Small nodule present over the right shin

Investigations :Patient had a Hemoglobin of 5.6gm%,TLC -8400/cmm with DLC-P68%L30%,E00%,M02%.Platelet count -2,04000/cmm.TRBC-1.79million/cmm,PCV-17.4%,MCV-88.3FL,MCH-28.4Pg,MCHC-32.2gm%.RDW-SD 53.2FL,RBS-98mg%.KFT-blood Urea 43mg%.s creatinine-1.32mg%.LFT-T Bil-0.21mg%,direct-0.13mg%SGOT12U/L,SGPT16U/L. Serum Alkaline phosphatase 286IU/ml, Total protein-6.8gm%,Albumin-1.6gm%.HIV,HBsAG,HCV antibody was negative .PBF-RBCs Normocytic and normochromic .No hemoparasites ,no immature cells .Urine r/e was showing1 + albumin .Stool was negative for ova ,cyst and occult blood .Iron studies-Serum Iron-27mcg/dl,TIBC-110mcg/dl, Transferrin saturation24%.Serum Ferritin-1650 ng /ml.PSA-0.39g%

FNAC –taken from lump on right thigh and also right shin-similar cytopathlogical features with moderate to highly blood mixed smears showing tumor cells arranged in dispersed pattern with focal areas of clustering and pseudoacinar pattern. The cells were large and round with irregular nuclear margins and coarse chromatin having prominent macronuclei and fragile scant cytoplasm .Large bizarre multilobulated cells with intranuclear inclusions and a background of necrotic debris .Impression-poorly differentiated Ca /malignant melanoma/NHL.

Histopathology sections of biopsy from the site revealed partially encapsulated tumor with spindle cells arranged in fascicles and intervening areas showing sheets of epitheloid cells with moderate amount of pale eosinophilic cytoplasm and prominent nucleoli .Tumor was

reaching up to the capsule .Atypical mitosis(>30/hpf) and multiple areas of necrosis were noted .Impression :high grade sarcoma.(Images 2,3 and 4)

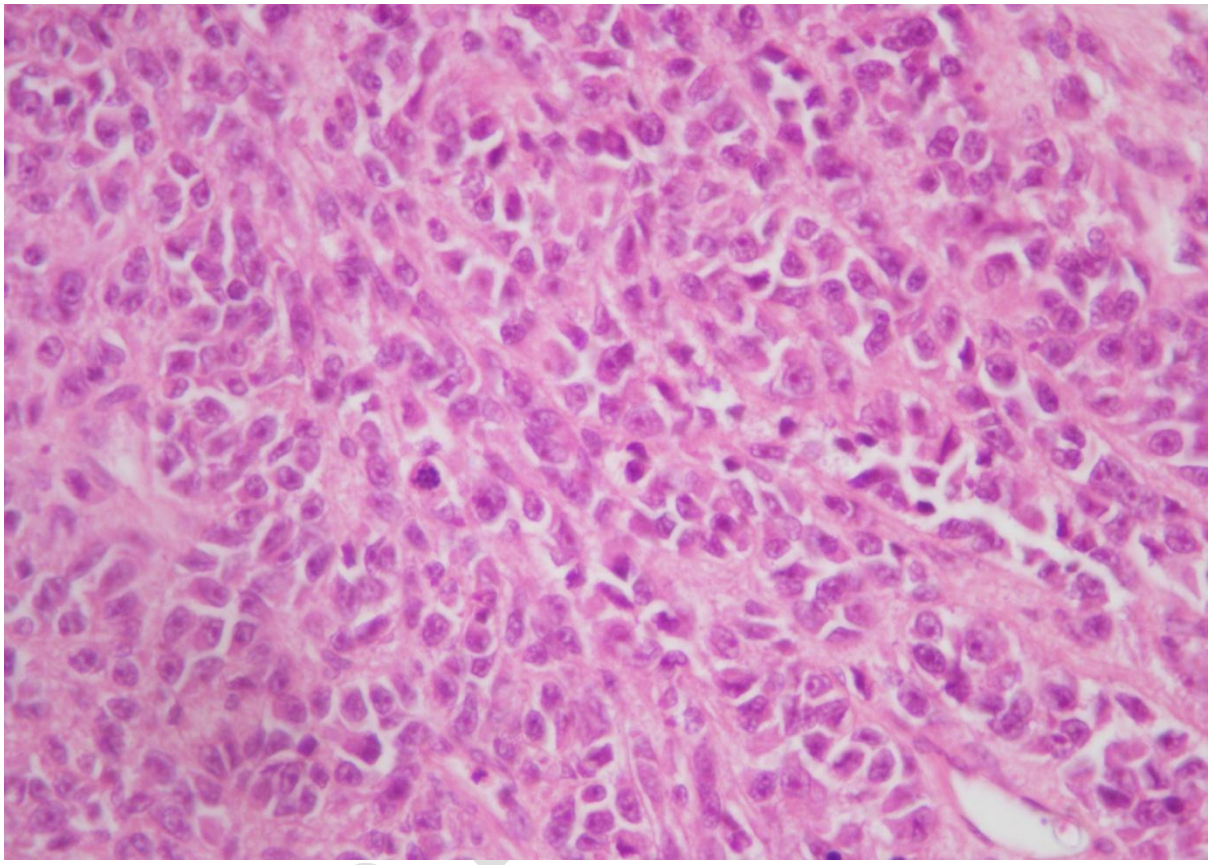


IMAGE 2

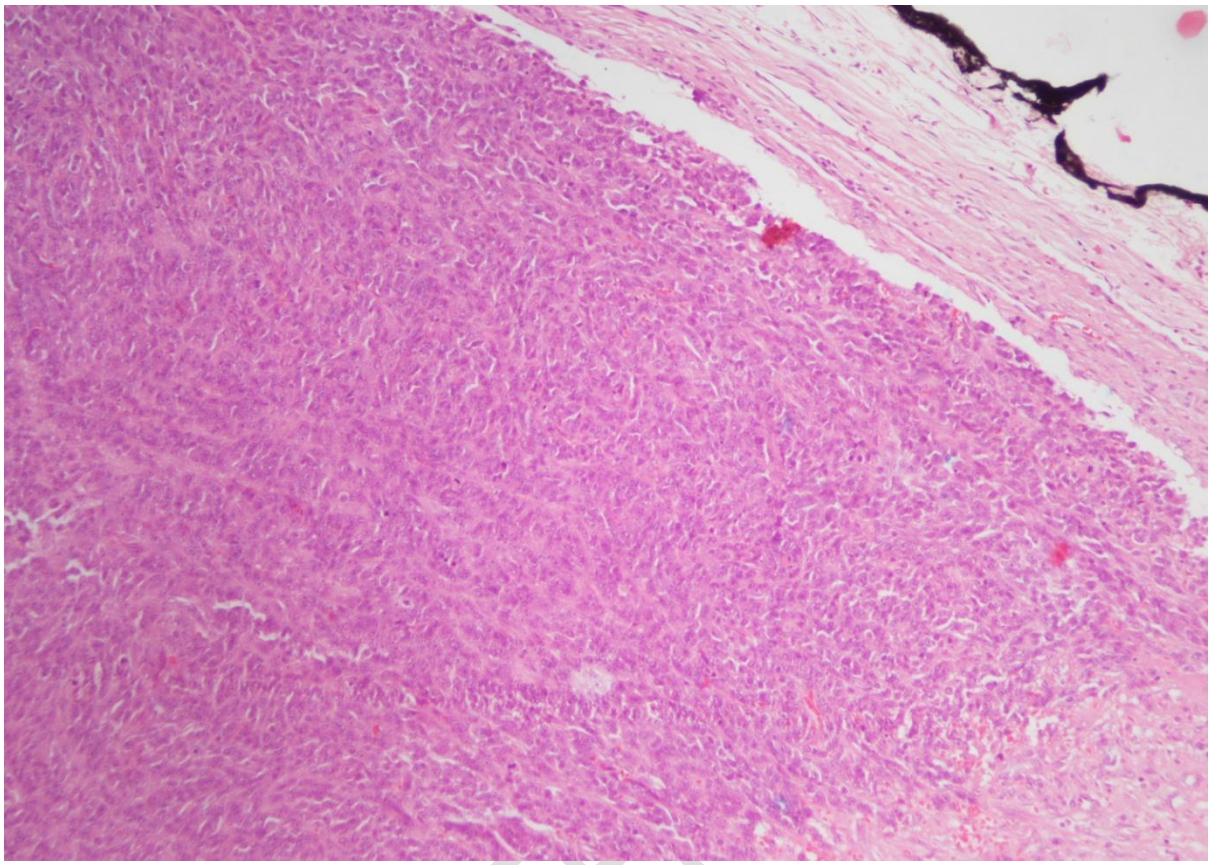
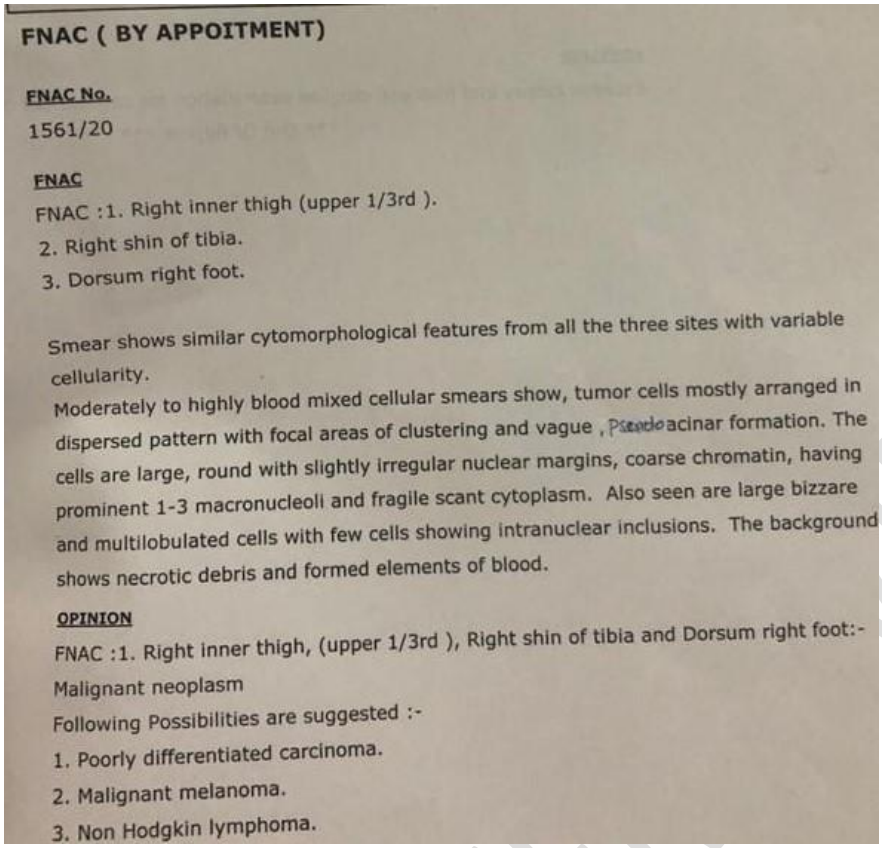


IMAGE 3

**DISCUSSION**

Sarcomas are a rare and heterogeneous group of malignant tumors of mesenchymal origin that comprise less than 1 percent of all adult malignancies and 12 percent of pediatric cancers. Approximately 80 percent of new cases of sarcoma originate from soft tissue, and the rest originate from bone.

A markedly elevated serum ferritin level has been associated with inflammatory conditions such as adult-onset Still's disease, systemic juvenile idiopathic arthritis, and hemophagocytic lymphohistiocytosis/macrophage activation syndrome and malignancy



**FNAC ( BY APPOITMENT)**

**FNAC No.**
1561/20

**FNAC**
FNAC :1. Right inner thigh (upper 1/3rd ).
2. Right shin of tibia.
3. Dorsum right foot.

Smear shows similar cytomorphological features from all the three sites with variable cellularity.
Moderately to highly blood mixed cellular smears show, tumor cells mostly arranged in dispersed pattern with focal areas of clustering and vague , Pseudo acinar formation. The cells are large, round with slightly irregular nuclear margins, coarse chromatin, having prominent 1-3 macronucleoli and fragile scant cytoplasm. Also seen are large bizzare and multilobulated cells with few cells showing intranuclear inclusions. The background shows necrotic debris and formed elements of blood.

**OPINION**
FNAC :1. Right inner thigh, (upper 1/3rd ), Right shin of tibia and Dorsum right foot:-
Malignant neoplasm
Following Possibilities are suggested :-
1. Poorly differentiated carcinoma.
2. Malignant melanoma.
3. Non Hodgkin lymphoma.

Pic 1. FNAC report : sample taken from all the above mentioned lesions

Sarcomas are a rare and heterogeneous group of malignant tumors of mesenchymal origin that comprise less than 1 percent of all adult malignancies and 12 percent of pediatric cancers. Approximately 80 percent of new cases of sarcoma originate from soft tissue, and the rest originate from bone.

A markedly elevated serum ferritin level has been associated with inflammatory conditions such as adult-onset Still's disease, systemic juvenile idiopathic arthritis, and hemophagocytic lymphohistiocytosis/macrophage activation syndrome and malignancy

.

Table I. Causes of raised serum ferritin.

| Increased ferritin synthesis due to iron accumulation | Increase in ferritin synthesis not associated with significant iron accumulation | Increased ferritin as a result of cellular damage |
|---|---|---|
| Hereditary (genetic) haemochromatosis | Malignancies | Liver diseases including: liver necrosis, chronic viral hepatitis, alcoholic and non-alcoholic steatohepatitis* |
| Hereditary acaeruloplasminaemia | Malignant or reactive histiocytosis | Chronic excess alcohol consumption |
| Secondary iron overload from blood transfusion or excessive iron intake/administration | Hereditary hyperferritinaemia with and without cataracts | |
| Ineffective erythropoiesis: sideroblastic anaemia, some myelodysplastic syndromes (e.g. refractory anaemia with ring sideroblasts) | Gaucher disease | |
| Thalassaemias | Acute and chronic infections | |
| Atransferrinaemia | Chronic inflammatory disorders | |
| Perroportin disease | Autoimmune disorders | |

REFERENCES

Szkandera, J., Gerger, A., Liegl-Atzwanger, B., Stotz, M., Samonigg, H., Ploner, F., … Pichler, M. (2014). Pre-Treatment anemia is a poor prognostic factor in soft tissue sarcoma patients. *PLoS ONE*, *9*(9). https://doi.org/10.1371/journal.pone.0107297

Fletcher CDM, Bridge JA, Hogendoorn P, Mertens F (2013) WHO Classification of Tumours of Soft Tissue and Bone. In: WHO Classification of Tumours. 4th edn, Vol. 5. Lyon, France: IARC Press.

Hh

De Rienzo DP, Saleem A (1990) Anemia of chronic disease: a review of pathogenesis. Tex Med 86: 80–83.
Miller CB, Jones RJ, Piantadosi S, Abeloff MD, Spivak JL (1990) Decreased erythropoietin response in patients with the anemia of cancer. N Engl J Med 322: 1689–1692.
Ludwig H, Fritz E (1998) Anemia in cancer patients. Semin Oncol 25: 2–6.)

Song, A., Eo, W., Kim, S., Shim, B., & Lee, S. (2018). Significance of serum ferritin as a prognostic factor in advanced hepatobiliary cancer patients treated with Korean medicine: A retrospective cohort study. *BMC Complementary and Alternative Medicine*, *18*(1), 1–10. https://doi.org/10.1186/s12906-018-2240-7

S0304419X13000395 (1).txt

Serum Ferritin_ Past, Present and Future.html

Richardson DR. Iron and neoplasia: serum transferrin receptor and ferritin in prostate cancer. J Lab Clin Med. 2004 Oct;144(4):173-5. doi: 10.1016/j.lab.2004.05.016. PMID: 15534986.

Deshpande UR, Nadkarni GD, Samuel AM. Serum ferritin in thyroid cancer. Thyroid. 1993 Winter;3(4):301-3. doi: 10.1089/thy.1993.3.301. PMID: 8118224.

Lorenzi M, Lorenzi B, Vernillo R. Serum ferritin in colorectal cancer patients and its prognostic evaluation. Int J Biol Markers. 2006 Oct-Dec;21(4):235-41. doi: 10.5301/jbm.2008.2954. PMID: 17177162.

Akiba S, Neriishi K, Blot WJ, Kabuto M, Stevens RG, Kato H, Land CE. Serum ferritin and stomach cancer risk among a Japanese population. Cancer. 1991 Mar 15;67(6):1707-12. doi:

10.1002/1097-0142(19910315)67:6<1707::aid-cncr2820670638>3.0.co;2-c. PMID: 2001562.

Kuvibidila SR, Gauthier T, Rayford W. Serum ferritin levels and transferrin saturation in men with prostate cancer. J Natl Med Assoc. 2004 May;96(5):641-9. PMID: 15160979; PMCID: PMC2640669.

Zhang XZ, Su AL, Hu MQ, Zhang XQ, Xu YL. Elevated serum ferritin levels in patients with hematologic malignancies. Asian Pac J Cancer Prev. 2014;15(15):6099-101. doi: 10.7314/apjcp.2014.15.15.6099. PMID: 25124580.

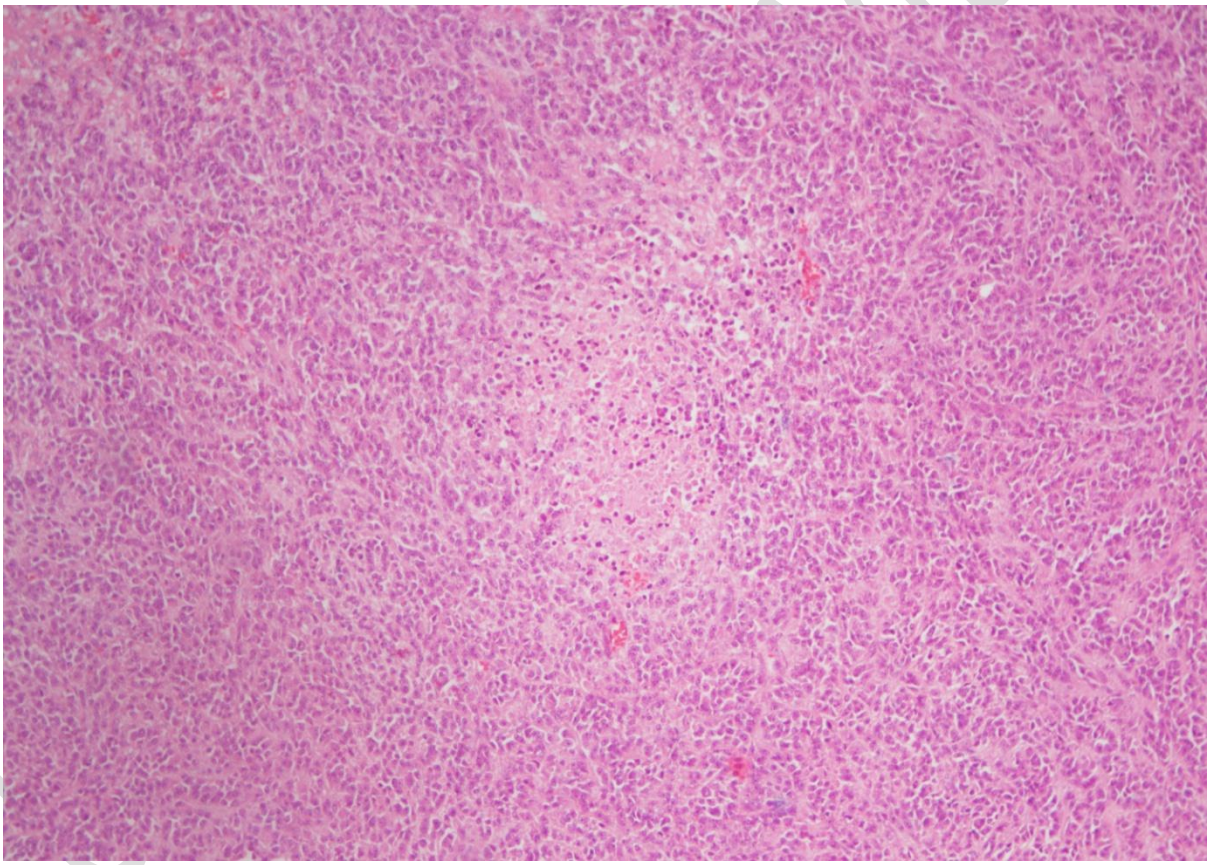


Image 4. X10 necrosis

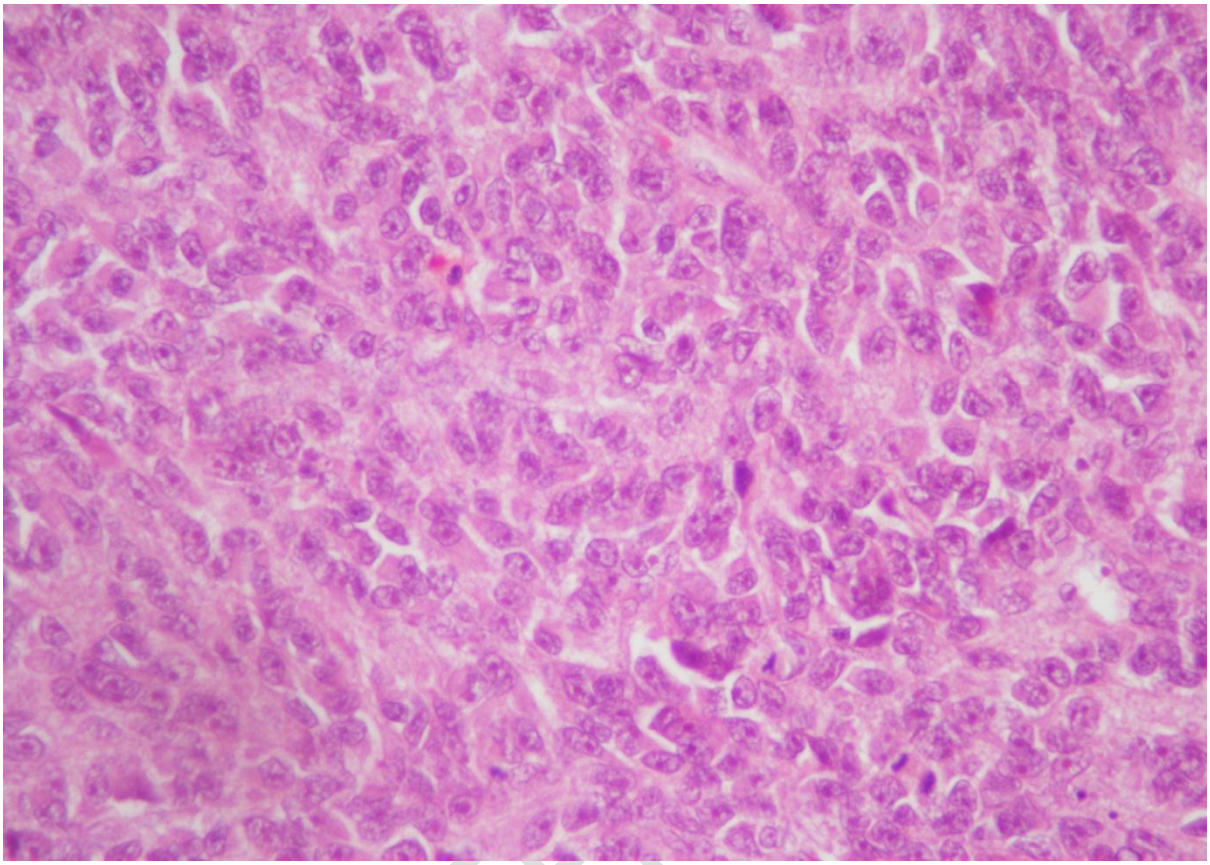


Image 5. Tumorx 40

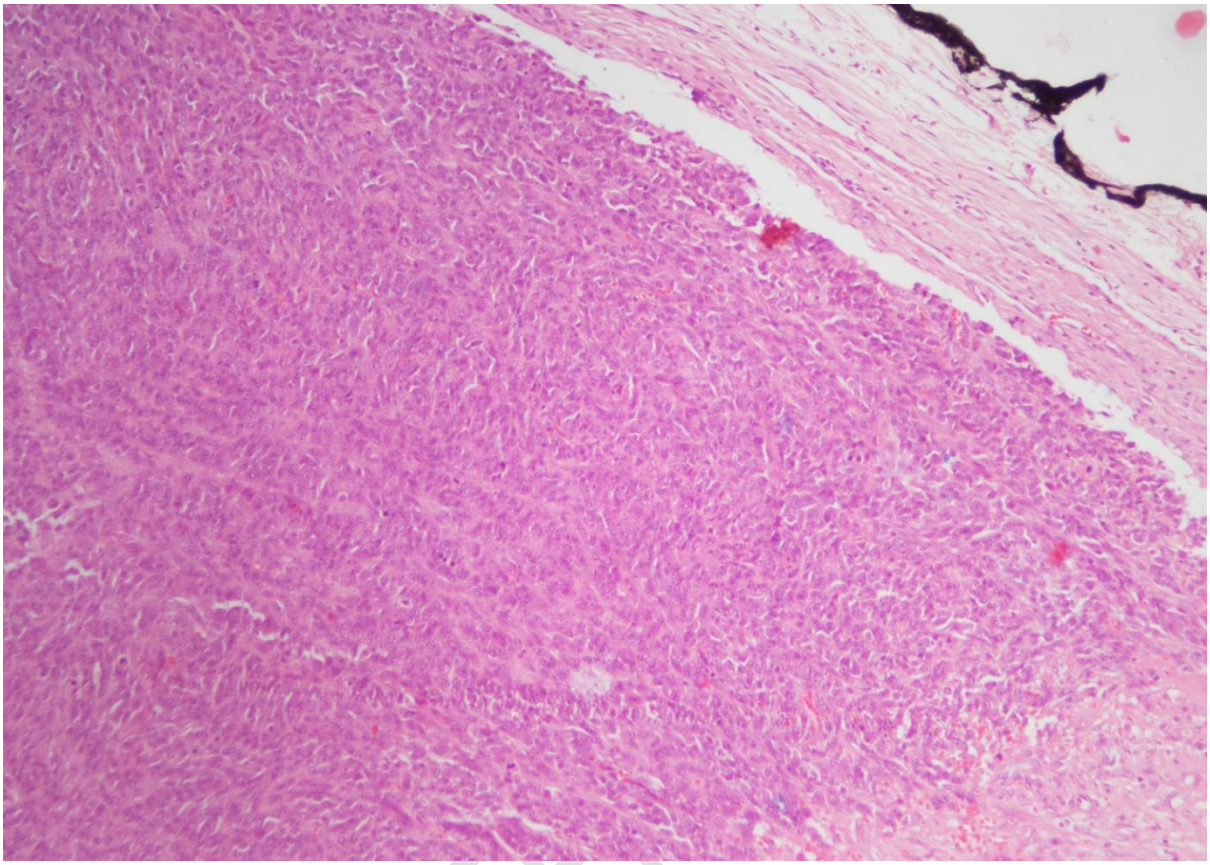


Image 6. X10 capsule

Atypical mitosis