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Case Presentation

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Case Report of Rare Occurrence of Perirectal Soft Tissue NFATC2-Rearranged Fusion Sarcoma

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Abstract

Background: The patient with soft tissue solid tumor presented with increasing rectal pain and fullness, and this lesion was identified by digital examination as well as confirmed with MRI of the pelvis. This lesion was surgically excised and found to be NFATC2-rearranged fusion sarcoma. NFATC2-rearragned sarcoma has not been previously reported in the Perirectal tissues, even though it has been reported retroperitoneally as well as the pelvic area. It is a very rare sarcoma occurring in the soft tissue. For that reason, this is being presented for publication and review of the literature of round cell sarcoma, and NFATC2- rearranged fusion sarcoma was performed.

Purpose: The purpose of the paper is to increase awareness of the possibility of occurrence of rare NFATC2-rearragned fusion sarcoma in patients. These tumors are very rare and, unfortunately, have a statistical probability of recurrence as well as metastatic disease. It does not respond to the chemotherapy or radiation treatment as other soft tissue sarcomas do.

Method: We are reporting a case of NFATC2-rearranged fusion sarcoma of the perirectal area without any involvement of the rectum or sphincters or the gluteus muscle presenting itself in the ischiorectal pad of fat close to the ischiorectal tuberosity, but without any attachment to the bone. The patient underwent successful excision of this lesion. The tumor measured approximately 7 cm x 5 cm x 3.8 cm. The pathological confirmation of this tumor was performed at an institute specializing in soft tissue sarcoma. At this time, the patient has received radiation treatment and, so far, has no clinical or radiological evidence of recurring disease at approximately four months post treatment.

Results: At four months post-treatment, having received radiation following the surgical treatment with full healing of the wound, with dedicated frequent follow ups clinically, and with radiological evaluation at 10 weeks postoperatively, the patient has not had any evidence clinically or radiologically of recurring disease.

Conclusion: A vast review of the medical literature indicated that most NFATC2-rearragned fusion sarcomas occur in the skeletal tissue. Only four cases have occurred in the soft tissues. It has occurred in the abdominal, pelvis and retroperitoneum, but there has not been a report of a case of NFATC2-rearragned fusion sarcoma in the ischiorectal fossa in the Perirectal pad of fat.

Keywords: Small round cell sarcoma; Sarcoma of soft tissues; NFATC2-rearranged fusion sarcoma of the soft tissues; Perirectal tumor; Ischiorectal tumor

Material and Methods

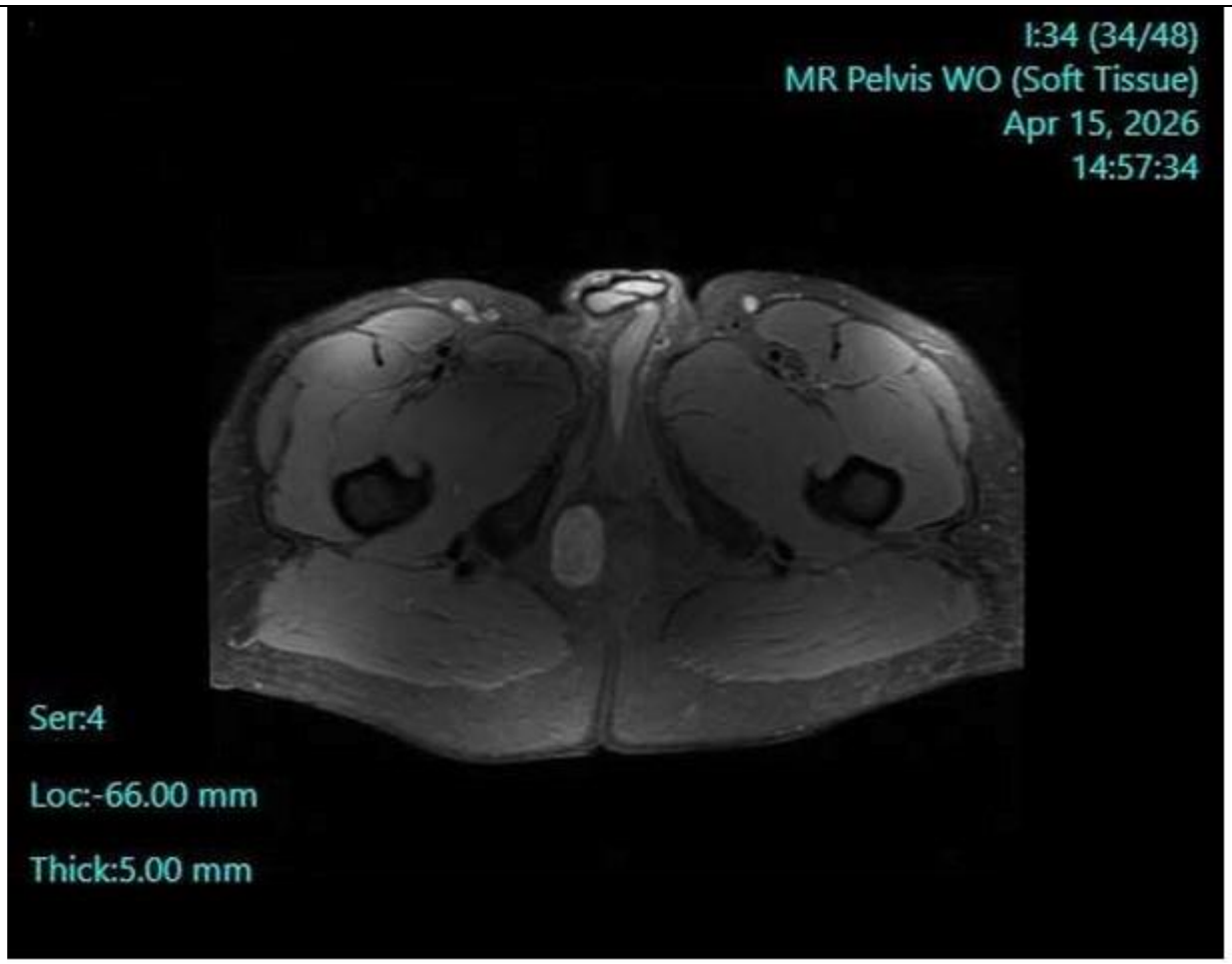
This case report was given site approval by our institutional human research review committee, Tri-City Colo-Rectal Surgery Institute. The authors have also obtained a full informed consent from the patient described in this case report.

Clinical Presentation

The 54-year-old African American male presented himself to the office with pain in the perirectal area, and a feeling of fullness. This has been there for a couple of months and symptoms have gradually getting more intensified. Examination indicated the presence of a lesion which is palpable on the right side in the perianal area. It was about 5 cm across and 7 cm in length. The rectal examination did not indicate any involvement of the sphincters or rectal wall. A colonoscopic evaluation did not reveal any significant abnormality of the colon or rectum. The MRI of the pelvis did indicate a well circumscribed smooth lesion measuring 65 mm x 34 mm x 32 mm demonstrating heterogeneous high T2 signal, homogenous T1 signal and containing thin septation. It was located inferior to the levator ani muscle. There was no communication or involvement of the sphincters. The lesion is located within the medial right gluteal subcutaneous fat. There is no evidence of any infiltration or subcutaneous edema. The patient was also found to have a testicular cystic lesion consistent with epididymal head cyst measuring 19 mm in size. There is no other abnormality of the other organs in the pelvis.

Relevant Medical History

The patient's past medical history included hypertension. There were no issues with cardiopulmonary problem or diabetes. There is no family history of colon cancer. His family history is positive for colon polyps occurring in father. The patient is a nonsmoker with rare social consumption of alcohol.

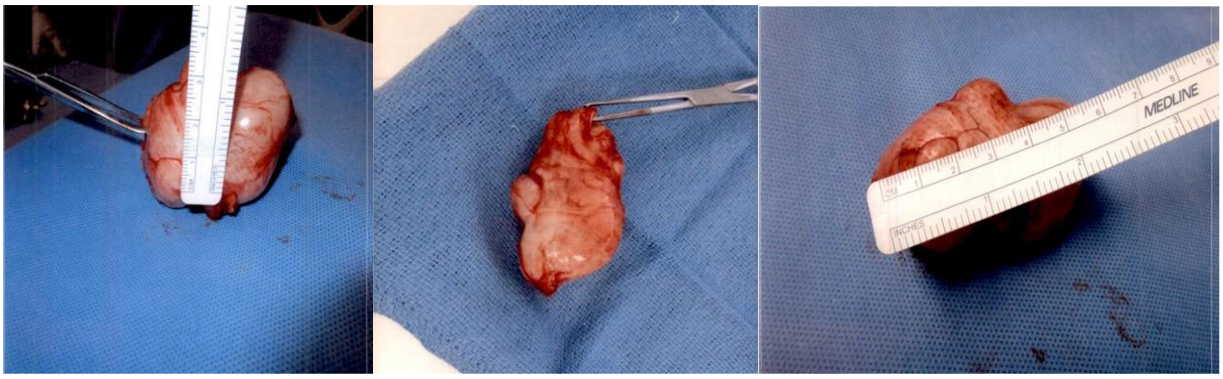


MRI of the pelvis

Surgical Treatment

The patient underwent surgical excision of this lesion after appropriate medical and laboratory evaluations. The procedure was performed under general anesthesia with the patient in prone jackknife position. At the time of surgery, the lesion could be felt. We made an incision transversely approximately 3 cm away from the anal margin, and extending the incision 4 cm upward and laterally. This lesion was identified as we proceeded to deepen the incision through the subcutaneous fat. The dissection remained lateral, superior, and inferior to the lesion as the dissection continued through the subcutaneous tissue layer. We identified the firm mass which appeared completely encapsulated. The dissection continued so that a negative margin was maintained circumferentially. When removed, the lesion appeared multi-septated and multi-lobulated. It measured closed to 7 cm x 5 cm x 3.8 cm. This confirmed the size on the MRI. Hemostasis was excellent. The surgical procedure was completed with electrocautery and sharp dissection. During the course of the surgical treatment, we were able to manually feel the rectum and sphincteric bundles with one finger inside the rectum and another finger on the outside to make sure there was no evidence of defect or involvement. After change of gloves, the wound was closed.

When examining the site where the tumor was excised, we did excise some of the fatty tissue around it, especially in the superior aspect of the incision where there was mild thickening of the fat and we were not sure if this was part of a capsule. There was no entry into the tumor. There was no capsular invasion of the tumor. At the end of the procedure, we did not identify any abnormal tissue that would raise concern for persistent tumor. The wound was closed in multiple layers so as to not leave an open space or cavity. We were able to do this without difficulty. Once the skin sutures were placed with 3-0 Vicryl, we used Dermabond to cover the area. Sterile dressing was applied. The surgical procedure was done as outpatient in a hospital setting, rather than ambulatory center, because of the size of mass and also because of our inability to predict the pathology of the mass. Apart from the fact that it resembled sarcomas, we were unable to speculate where it originated from. It was not involving the sphincters or gluteal muscles. It was closer to the ischiorectal tuberosity but not adherent to it. It was not attached to any surrounding structures.



Postoperative Course

The postoperative course has been uncomplicated, but for minimal wound disruption at the skin level that closed without significant mishap. The patient was covered with oral analgesics and antibiotics postoperatively. The patient did not show any evidence of infection or significant issues with wound healing. The patient was followed postoperatively in the office.

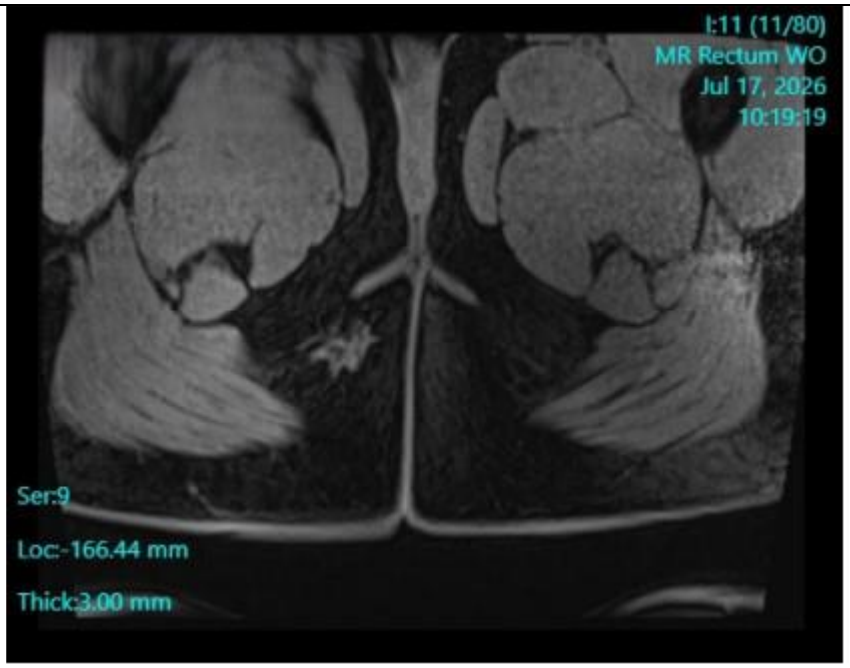
Pathological Interpretations

The original pathology report indicated myxoid spindle cell neoplasm with mild cytological atypia. Immunohistochemical studies were performed. The pathology report indicated the tumors removed completely with one focal area of extension to the capsule. They did not give us the specific site it was. Apparently, it was millimeters in size where the tumor came down to the capsular area. The fatty tissue removed superior to the tumor did not indicate the presence of any tumor involvement. The differential diagnosis provided by the pathologist included soft tissue myxoma with atypical features, myxoid neurofibromas, low grade myxoid fibrosarcoma, extra skeletal myxoid chondrosarcoma, and low grade myxoid mesenchymal neoplasms. Given the overlapping morphological features, the case was submitted to an expert in soft tissue/sarcoma for pathology consultation. The final pathology report did come back as sarcoma fusion type NFATC2-

rarranged sarcoma after immunohistochemical and molecular biological studies.

Oncological Consultation and Outcome

Oncological consultation was obtained. Once the final pathology report was complete, the patient did undergo complete evaluation with PET scan. This did not indicate the presence of any other metabolically active tumors. The repeat MRI did not indicate the presence of any residual lesion. The recommended treatment was radiation. The patient is agreeable to radiation therapy and is currently receiving treatment.



MRI post surgery

Outcome at 16 Weeks Post Surgery

At the time of this report, the patient's wound has healed well. The patient has no symptoms related to the surgical procedure. The feeling of fullness is completely gone. The patient has no issues with bowel habits, lack of control or difficulty with evacuation. The patient is undergoing radiation treatment at this time.

Discussion

After going through a vast search of prior reported soft tissue tumors belonging to the type of NFATC2-rearranged fusion sarcomas, we were able to identify only four soft tissue tumors that have previously been reported [1-3]. The majority of the tumors belonging to this rare entity occur within the skeletal system [4]. Even though it has been reported in the lower and upper extremity, soft tissues, retroperitoneum, and pelvic area, there is no report of occurrence of prior NFATC2-rearranged sarcoma occurring in the perirectal or ischiorectal fossa. The NFATC2-rearranged fusion sarcomas were recently defined in the 2020 WHO Fifth Edition. The 2020 WHO classification recognizes four categories of undifferentiated small round cell sarcoma: First is sarcoma, second is round cell sarcoma with EWSRI-9-ETS fusions, third is CIC-rearranged sarcoma, and

fourth is sarcoma with BCOR genetic alterations. These entities share morphological overlap but have distinct varying prognosis [5]. The 2025 Consensus Guidelines emphasize that the next generations sequencing (targeted RNA-based next generation sequencing RNA-NGS) should occur only in sarcoma expert institutions with multi-disciplinary review to identify these rare lesions [6]. These rare NFATC2-rearranged fusion sarcomas are identified by expert pathologists at sarcoma expert institutions. This would involve histopathology, immunochemistry and molecular biology. A brief review of these three pathological entities is as follows: [7-11]

Morphology: These round cell sarcomas are small to medium round cells with the cords, trabeculae and pseudo SNR patterns with prominent collagenous or myxoid sarcoma.

Immunochemistry:

NKX2-2: often positive

PAX7: frequently expressed (useful marker)

S100: synaptophysin typically negative

CD99: variable (often focal or patchy, not diffusely strong like Ewing sarcoma)

The key distinction from Ewing sarcoma is the underlying different morphology and staining pattern

Molecular Biology: The fusion mechanism is expressed EWSRI (or FUS) fused to NFATC2 transcription factor. This leads to the functional consequences of loss of normal NFATC2 regulation (calcineurin-dependent control removed), constitutive transcriptional activation, and oncogenic signaling activation [12-16].

These key molecular features of NFATC2-rearranged fusion sarcoma are distinct from Ewing sarcoma at genomic and epigenetic levels, enrichment of mTOR pathway activation and NFATC2 over expression is linked to tumor proliferation, immune signaling dysregulation and high tumor grade [17,18].

Conclusion

The NFATC2-rearranged fusion sarcomas are uncommon, primarily occurring in skeletal tissue with rare reported cases of these sarcomas occurring in soft tissues. We have described one case of NFATC2-rearranged fusion sarcoma occurring in the ischiorectal fossa perirectally, and review of the current literature does not indicate a prior case report of this sarcoma occurring in this location. They have distinct morphology and are potentially biologically aggressive. They are important to recognize and diagnose as they respond poorly to other sarcoma regimens. New forms of therapy may be needed. So far, our patient has done very well with no evidence of clinical or radiological recurrence. The patient has undergone radiation therapy. This patient will be followed very closely.

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