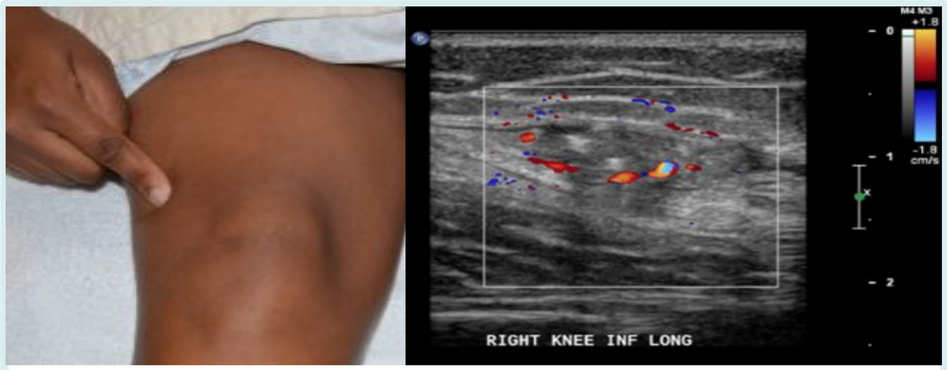
Sirolimus as Salvage Medicotherapy for Recurrent Fibroadipose Vascular Anomaly

Rebecca T. Le MD[1] (rebecca.le@rochesterregional.org), Ananya Majumdar BA[2], Craig Johnson DO[2,3]

1. Rochester General Hospital - Department of Radiology; 2. University of Central Florida School of Medicine; 2,3. Nemours Children's Hospital

FIBROADIPOSE VASCULAR ANOMALY (FAVA)

- Somatic overgrowth disorder from PIK3CA mutation where fibrofatty tissues replace physiologic muscle
- Presentation: aggregated fatty intramuscular mass + venous malformations, no cutaneous changes



Child with a painful palpable right knee lesion with no cutaneous changes. Ultrasound correlate demonstrated a hypervascular lesion with hyperechoic foci (phleboliths) within phlebectasias, characteristic of FAVA.

- Singular vs multifocal disease, with possibility for recurrence and/or concurrence with other PIK3CA malformations

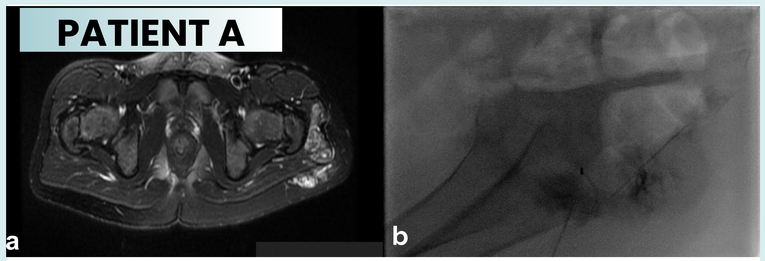
Goals for management - **pain reduction or resolution** with maximizing function (not complete lesion obliteration)

INTERVENTIONAL MANAGEMENT OPTIONS

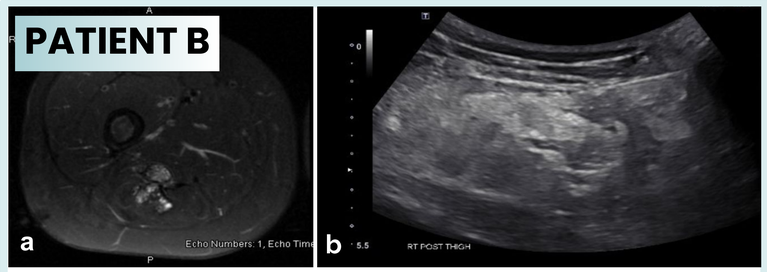
- Sclerotherapy: sclerosant promotes endothelial damage to vessels; inconsistent outcomes (only treats vascular components of malformation, risk of nontarget embolization/sclerotherapy)
- Cryoablation: emerging therapy, can offer consistent pain relief by destroying fibrofatty and vascular parts of lesion; not primary standard of care/limited provider ability
- Significance: surgery only curative option to treat FAVA, but considered last resort to spare patient from limb loss, disfigurement, and reduced mobility
  - Need to consider patient's goals of care, ability/desire for intervention and symptom relief

WHAT CAN BE DONE IF LESIONS ARE REFRACTORY TO LOCALIZED TREATMENT?

- Sirolimus: mTOR inhibitor, prevents cell growth, immunosuppression (requires strict monitoring to achieve therapeutic window)
  - Indications: prophylaxis of organ rejection in renal transplants, treatment of patients with lymphangioleiomyomatosis (LAM)[1]
  - Considered off-label use for management of FAVA, only discussed in one case report for two patients[2], but known to be more widely used given social media reports and vascular anomaly center communications



14-year-old presenting with right gluteal pain at 8-years-old. MR correlate (axial T2-fat sat) revealed a fat-containing intramuscular lesion, compatible with FAVA (a). The patient underwent sclerotherapy (b) complicated with sclerosant extravasation/nontarget embolization, resulting in extensive tissue necrosis and ulceration, requiring multiple surgical debridements. The patient did not require additional treatment for over four years, but, when the FAVA lesion and symptoms recurred, the patient opted for sirolimus, given past complications with prior interventions. The patient tolerated medical therapy, noting a reduction in the tumor burden and pain.



12-year-old presenting with poor gait secondary to a right leg mass at 9-years-old. MR correlate (axial T2-fat sat) revealed an indistinct margin intramuscular mass with fatty infiltration, compatible with FAVA (a). Initial sclerotherapy resulted in persistent pain and paradoxical increase in lesion size postprocedure. She subsequently started sirolimus, which she took intermittently over two years and controlled symptoms. She initially experienced a minor adverse reaction, a oropharynx mouth ulcer one month after treatment initiation, which resolved with supportive care.

DISCUSSION

- Need for further research in role of medicotherapy in management of vascular anomalies, including FAVA
  - retrospective with 14 patients with varied vascular anomalies (generalized lymphatic anomaly (n = 4), Gorham-Stout disease (n = 2), central conducting lymphatic anomaly (n = 1), lymphatic malformation (n = 4), tufted angioma (n = 1), kaposiform hemangioendothelioma (n = 1), and venous malformation in a patient with CLOVES syndrome (n = 1)): most serious adverse events (SAEs) observed in the first year of therapy; most common adverse event was viral pneumonia
    - Low toxicity from sirolimus when used in management of other vascular anomalies
- Importance in strict monitoring of sirolimus levels to optimize therapeutic window, minimize SAEs

REFERENCES

1. RAPAMUNE Indications and Usage. Pfizer. Accessed December 30, 2021. https://www.pfizermedicalinformation.com/en-us/rapamune/indications-usage
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