

## Beyond the Knife: A new approach with targeted therapy

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Resident Symposium  
June 10, 2011



## Financial Disclosures

- None



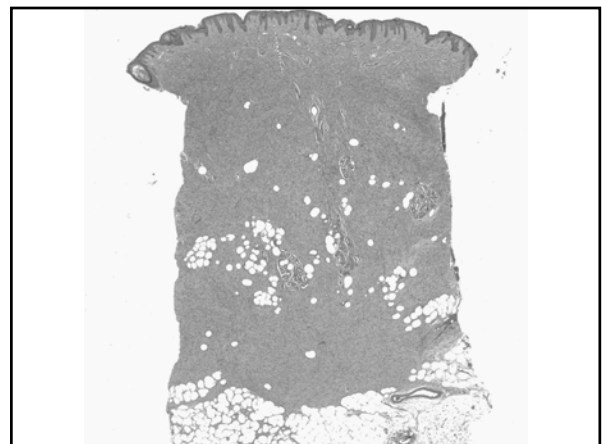
## Case

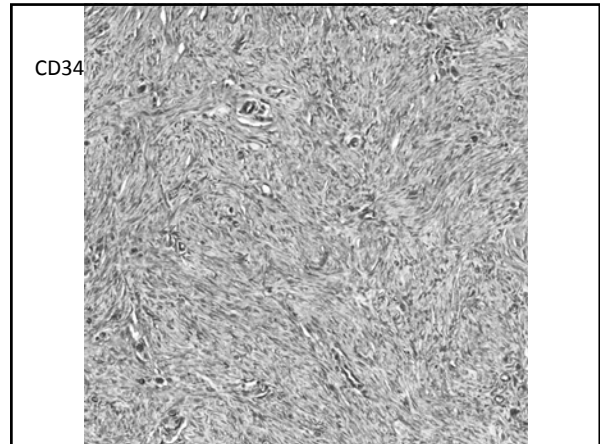
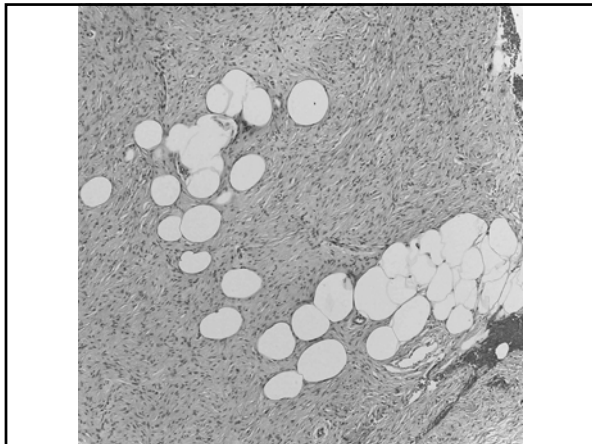
- 48 year old AA M
- Enlarging growth on back x few months
- Tingling sensation
- PMH/Medications: none
- ROS: negative



## Clinical Differential Diagnosis


- Dermatofibrosarcoma protuberans
- Dermatofibroma
- Keloid
- Granular cell tumor
- Melanoma
- Metastatic neoplasms





## Diagnosis


Dermatofibrosarcoma Protuberans  
(DFSP)



## Dermatofibrosarcoma Protuberans (DFSP)


- Low grade soft tissue neoplasm
- 1% of all soft tissue sarcomas
- Locally invasive, low metastatic potential
- AA > whites, M=F
- Common on trunk and extremities

Johnson-Jahangir, H and Ratner, D. Advances in Management of Dermatofibrosarcoma Protuberans. *Dermatol Clin.* 2011;29(2):191-200.



## Pathogenesis

- Chromosome 17 and 22 fuse via
  - Supernumerary ring
  - Translocation
- Activates PDGFβ receptor - always turned on




- Chromosome 17: type 1 alpha 1 collagen gene (COL1A1)
- Chromosome 22: beta chain of platelet derived growth factor gene (PDGFβ)
- Activates PDGFβ receptor

**A**

**B**

**C**

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## Treatment

- Surgery
- Radiation
- Targeted molecular inhibition



## Surgery

- Local Recurrence rates (f/u ~ 3 years)
  - 39.7% - conservative margins
  - 8.8% - wide surgical margins
  - 1.5% - Mohs micrographic surgery



## Radiation

- DFSP are radiosensitive
- Use:
  - Primary or locally recurrent DFSP
  - Preoperative or postoperative adjuvant therapy
- Has been shown to improve local control rate compared to surgery alone



## Imatinib mesylate

- Selective tyrosine kinase inhibitor
  - BCR-ABL (CML)
  - KIT (GI stromal tumors)
  - PDGFR alpha and beta
  - ARG (ABL related gene)
  - FMS (receptor for Colony Stimulating Factor 1)



## How Imatinib works in DFSP

- Blocks PDGF $\beta$ -PDGRT $\beta$  signaling pathway
- Works only in patients with the COL1A1-PDGFB fusion product
  - Detected by RT-PCR (via t(17;22)) or FISH (via COL1A1-PDGFB)



## Imatinib in DFSP Trials

- In 2006, FDA approved Imatinib as single agent or adjuvant treatment for patients with unresectable, recurrent or metastatic DFSP
- Preoperatively to reduce tumor size
- Postoperatively if positive margins remain
- Helpful to screen patients for translocation of fusion product



### Imatinib in DFSP

- Pooled case reports suggest time to response is 3 months
- Doses of 400 or 800 mg/day



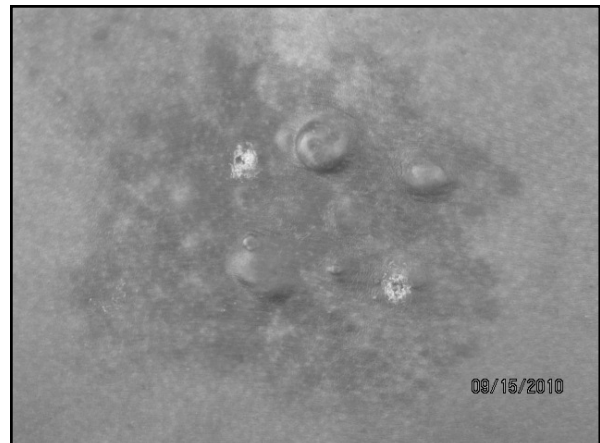
### AE of Imatinib

- Usually well-tolerated
- Most common adverse events:
  - Diarrhea, CHF
  - Edema, anemia, fatigue, nausea, skin toxicity (bullae), emesis
  - Neutropenia, thrombocytopenia, elevated LFTS and bilirubin



### Our Patient's Course

- Due to size of DFSP, referred to oncology for consideration of imatinib
- CT scans: wnl
- Labs: CBC and CMP wnl
- Plan:
  - Imatinib 400 mg po daily x at least 3-4 months
  - Surgery after shrinkage of tumor



### Summary

- DFSP –uncommon but often difficult to treat
- Based on analyses of mutations in DFSP, rationale exists for using targeted therapy for this neoplasm
- Imatinib is a well tolerated oral agent that can be useful in select patients with DFSP, either alone or as adjuvant therapy



## References

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