Case 1
44-year-old female with a mass in the dorsal right wrist.
PLEOMORPHIC HYALINIZING ANGIEECTATIC TUMOR (PHAT)
PLEOMOPHIC HYALINIZING ANGIECTATIC TUMOR (PHAT)

- Rare tumor of intermediate malignancy.
- Slowly enlarging subcutaneous mass.
- Usually in adults.
- Site: Lower extremity, thigh, perineum, buttock, chest wall, arm, axilla, back, and hand.
- Size: 1 cm – 20 cm.
PLEOMOPHIC HYALINIZING ANGIECTATIC TUMOR (PHAT)

• Grossly may resemble a hematoma
• Microscopically:
  - Clusters of thin walled ectatic vessels with hemosiderin
  - thick rim of amorphous eosinophilic material
  - Plump spindled / rounded pleomorphic cells
  - Intranuclear inclusions
  - Lipoblast-like cells
  - Not encapsulated
  - Mitoses < 1 / 50 HPF
  - CD34 + (75%) , S100 –
  - Ki 67 (< 3.0%)
PLEOMOPHIC HYALINIZING ANGIEECTATIC TUMOR (PHAT)

• Differential Diagnosis:
  - Schwannoma
  - Psammomatous Melanocytic Schwannoma
  - Pleomorphic Sarcoma
  - Hemosiderotic Fibrohistiocytic Lipomatous Lesion (HFLL)

  - Superficial, well circumscribed fatty lesion
  - Usually around the ankle / foot, F > M
  - Plump slightly pleomorphic spindled cells
  - Inflammatory cells & iron pigment
  - Associated with venous stasis & trauma

Relationship Between Pleomorphic Hyalinizing Angiectatic Tumor and Hemosiderotic Fibrohistiocytic Lipomatous Lesion

Michal Michal, MD and Dimtry Kasakov, MD

Am J Surg Pathol • Volume 29, Number 9, September 2005
Pleomorphic Hyalinizing Angiectatic Tumor

Analysis of 41 Cases Supporting Evolution From a Distinctive Precursor Lesion

Andrew L. Folpe, MD and Sharon W. Weiss, MD


In summary, we have identified a distinctive myxoid lesion which represents the earliest stage of PHAT, a conclusion supported by the extensive histologic overlap between early and typical PHAT, the presence of foci of early PHAT at the periphery of otherwise typical PHAT, and the frequent admixture of both patterns within a single lesion. The histologic features of early PHAT are essentially identical to those of so-called hemosiderotic fibrohistiocytic lipomatous lesion, strongly suggesting that such lesions represent early PHAT, rather than a reactive process. PHAT should be considered mesenchymal tumors of intermediate malignancy, rather than benign tumors.
HFLL lesions arise in the subcutaneous tissue around the ankle most commonly in females.

Venous insufficiency $\Rightarrow$ Impaired blood circulation $\Rightarrow$ Venous Stasis changes involve the deeper tissue, mainly fat.

“...the HFLL pattern in PHAT may be the consequence not the cause or precursor,...
...and...might represent the ‘late PHAT’...”

HFLL-like areas around PHAT have similar pathogenesis. Damaged vessels in PHAT – persistent impaired blood circulation.
Clinicopathologic features of pleomorphic hyalinizing angiectatic tumor of soft parts

KE Qi, Erbolat, ZHANG Hong-ying, BU Hong, LI Sheng, SHI Dan-ni, YANG Guang-hua, CHEN Hui-jiao and WEI Bing

In our opinion, HFLL-like lesion in PHAT is a kind of atypical PHAT and is neoplastic rather than reactive, and probably represents a precursor of typical PHAT. 19,20
In conclusion, HFLL and early PHAT have an undoubtedly similar, if not identical histological appearance. Nevertheless, the pathogenetic relationship between these two lesions remains to be determined. Although both lesions may have invasive local growth and frequently recur following incomplete resection, metastases have not been described so far. Until more data become available on the biological potential of HFLL/early PHAT (e.g. reactive process or a tumor), radical surgical excision and follow up of the patient remain the best treatment option.
PLEOMOPHIC HYALINIZING ANGIECTATIC TUMOR (PHAT)

- Histologic appearance may vary depending on timing:
  - EARLY
  - INTERMEDIATE
  - LATE
Early PHAT
Early PHAT
Early PHAT
Intermediate PHAT
Intermediate PHAT
PLEOMOPHIC HYALINIZING ANGIECTATIC TUMOR (PHAT)

• Clinical Behavior:
  - Recurrence in 50% (6 mo to 25 yrs).
  - No evidence of metastasis.
  - One report of progression to myxofibrosarcoma.
Case 2
Case Presentation
March 2008

Stephen Kirschbaum, M.D.
Kaiser Permanente
Bellflower, California
Clinical History

- 60 year old female presenting with abdominal pain.

  - Imaging: Intussusception.
  - Operative Findings: Intussusception.
Intraoperative consultation: Received segmental small bowel (ileal) resection.

- On opening, there is a 4.5 x 3.5 x 2.5 cm dark tan/red-brown, oval, rubbery, polypoid, submucosally-based mass extending into the lumen and with overlying mucosal ulceration.
- Sections taken for frozen and permanent sections.
CASE PRESENTATION

- Immunohistochemistry:
  - + Vimentin (strong and diffuse)
  - + SMA (focal and weak)
  - - CD117 (mast cells), Desmin, MSA, CD34, S100, MyoD1, Pankeratin.
DIAGNOSIS???
Inflammatory Fibroid Polyp

- First described by Vanek in 1949, IFP coined by Helwig and Ranier in 1952.
- Benign pseudotumorous lesion.
- Any age but usually adults of mid-age.
- No sex preference vs. slight male preference.
- Relatively rare.
IFP

- 3% of stomach polyps (often prepyloric antrum).
- Stomach accounts for 70% of cases.
- Remaining cases: ileum > colon > jejunum > deodenum > esoph.
Inflammatory Fibroid Polyp

- **Etiology:**
  - Not known, but thought to occur secondary to a reactive/reparative process to an injurious agent i.e. a form of granulation tissue.
Inflammatory Fibroid Polyp

Clinical Presentation:

- Depends on site in GI tract.
- Small bowel: intussusception, diarrhea, obstruction, bleeding, asymptomatic
- Stomach: nausea, vomiting, abdominal pain, asymptomatic
Inflammatory Fibroid Polyp

Gross:

- Sessile or polypoid.
- Single or multiple (usually single).
- Size: Varies from 1-12 cm (average less than or equal to 3 cm).
- Submucosally based.
- Circumscribed, unencapsulated, firm, gray-tan nodule(s) with homogeneous cut surface without hemorrhage or necrosis.
- Can cause overlying mucosal ulceration, project into the small bowel lumen and even extend into and through the muscularis propria.
Inflammatory Fibroid Polyp

- Microscopic:
  - Mass of unencapsulated loose, edematous or myxoid fibrous tissue intermixed with inflammatory cells.
  - The spindle cells are fairly bland and can be arranged in a perivascular or periglandular pattern.
  - Vascularity and cellularity are quite variable (BVVs can have hyaline or onion skin-like wall).
  - Inflammation consists of lymphocytes, plasma cells, eosinophils and mast cells.
  - Occasional mitoses seen (not atypical).
  - If ulcerated, may have exuberant granulation tissue.
  - Frequently the stroma dissects the muscularis propria in small bowel lesions.
Inflammatory Fibroid Polyp

- Positive
  - Vimentin (diffuse)
  - SMA (focal)
  - CD68 (variable, focal)
  - CD34 (variable, focal)
  - CD31 (variable, focal)
  - Desmin (variable, focal)

- Negative
  - S100
  - CD117
  - Pancytokeratin
Differential Diagnosis

- **Inflammatory lesions:**
  - Eosinophilic gastroenteritis (diffuse lesion, not single mass)
  - Parasitic infection

- **Mesenchymal neoplasms:**
  - GIST (CD117 positive)
  - Leiomyoma (diffuse SMA, desmin positive)
  - SFT (BCL-2 positive)
  - Schwannoma (S100 positive)
  - Inflammatory Myofibroblastic Tumor (rare in bowel wall and spindle cell component is generally not loosely structured)
Treatment and Prognosis

- Endoscopic or surgical resection
- Very little risk of recurrence
References

- Gastrointestinal and Liver Pathology, Christine A. Iacobuzio-Donahue, Elizabeth A. Montgomery, 2005.
- Gastrointestinal Pathology, Parakrama Chandrasoma, 1999.
Case 3
Aviv Hever, M.D.
Kaiser Permanente
Los Angeles, CA
10 year old female

• March 7, 2005 - 2 months abdominal pain and vomiting (Aabd. U/S and Upper GI Series with Small Bowel FT Negative)
• October 1, 2007 - Abdominal pain and dysuria (treated for UTI and advised to f/u)
• October 10, 2007 - Abdominal pain and fever (CT scan - large pelvic mass)
• October 12, 2007 - Exploratory laparotomy with resection of left ovary, omentum, and biopsy of right ovary
Labs

- AFP –
- β HCG –
- Catecholamines – high normal
- AST/ALT – normal
- Phos/Mag – low
- CA 125 – 263.4
- Calcium – 8.3 (5 days post-op)
- All other labs unremarkable
Gross Findings

- Left ovary – 331 g, 9.5 x 8.5 x 4.5 cm mass replacing the ovary.
- Right ovary – normal.
- Omentum – adherent to left ovary and involved by tumor.
D/D

- GRANULOSA CELL TUMOR (JUVENILE)
- GERM CELL TUMOR
- SMALL CELL CARCINOMA
- METASTATIC: INTRA-ABDOMINAL DESMOPLASTIC SMALL CELL TUMOR
- LYMPHOMA
Immunohistochemistry

- **Positive:**
  - Vimentin – diffuse
  - WT-1 – diffuse
  - CD10 – focal
  - SMA – patchy
  - CK – patchy
  - Syn – patchy
  - EMA – rare
  - Calretinin – focal
  - PR – rare
  - CD99 – focal
  - CK20 - rare

- **Negative:**
  - PLAP
  - OCT ¾
  - AFP
  - INHIBIN
  - CD30
  - CD43
  - CD45
  - MSA
  - DESMIN
  - MyoD1
  - Chromo
  - S100
  - HMB-45
  - MELAN-A
  - ER
  - TTF-1
  - CK7
  - HepPar-1
FINAL DIAGNOSIS

• SMALL CELL CARCINOMA, HYPERCALCEMIC TYPE
• CASE SENT TO DR. ROBERT KURMAN AT JOHNS HOPKINS WHO CONCURRED WITH THE DIAGNOSIS

“Combined staining with WT-1 and TTF-1 will distinguish SCCOH from SCCLu and SCCCx with a sensitivity of 86% and specificity of 97%. HPV is specific for tumours of cervical origin, but p16 immunohistochemistry is not useful for this purpose. The presence of diffuse WT-1 supports a Müllerian origin for SCCOH, whereas the absence of cKIT and OCT3/4 argues against a germ cell origin”

¹Histopathology. 2007 Sep;51(3):305-12
Ovarian Tumors

**ADULTS**
- 65-70% - Surface epithelial
- 15-20% - Germ cell
- 5-10% - Sex cord-stromal
- 5% - Metastasis

**CHILDREN**
- 60-70% - Germ cell (much higher % malignant than adults)
- 10-25% - Sex cord-stromal
- 15-20% - Surface epithelial
- Less than 5% - other + metastasis
SMALL CELL CARCINOMA

• HYPERCALCEMIC AND PULMONARY TYPES
• RARE
• Affects women between 10-40 years of age
• Grossly, the tumor is large, tan to gray, with areas of hemorrhage, necrosis, and cystic degeneration
• Microscopically, the tumor cells most commonly grow in a diffuse pattern. The tumor cells are small and round with scant cytoplasm, hyperchromatic nuclei, and small nucleoli.
SMALL CELL CARCINOMA

1. Hypercalcemic type:
   - By far more common
   - High grade (confused with granulosa cell tumor)
   - Young females (average age 23)
   - Nearly allows unilateral (familial bilateral)
   - 2/3 hypercalcemic, disappears after removal
   - Diploid DNA pattern
   - IHC: CK, Vimentin, EMA, Chromogranin, h-PTH
   - Poor prognosis: 33% of the patients with stage IA disease were alive and free of tumor for an average of 5.7 years postoperatively. In contrast, only 10% of patients with stage IC disease and 6.5% of patients with stages II, III, and IV disease were alive without recurrence at the last follow-up

SMALL CELL CARCINOMA

2. Pulmonary type:
   - Homonymous to lung counterpart
   - May be associated with endometrioid carcinoma
   - IHC: CK, EMA, NSA
   - EM: neurosecretory granules
   - Aneuploid DNA pattern
   - Poor prognosis
Follow - Up

- Patient recently completed round #4 of chemotherapy with cisplatin and etoposide
- CA 125 – Normal (10.4)
- Calcium – Normal (9.0)
- Cytology (Ascitic Fluid) – Negative
- CT (11/29/07) – New lesion in left pelvis measuring 2 cm
- CT (12/19/07) – Pelvic lesion significantly reduced in size
Get a life you worthless bum!

"Medical care certainly ain't what it used to be!"
Case 4

Sally T. Turla
Kaiser West Los Angeles
3.11.2008
April 2007

37 year old African American female presents for annual routine physical

DM 2, HTN, morbidly obese, 414 lbs

Lump in left groin, noticed over past 1 -2 yrs, growing; firm subcutaneous mass left groin, 5 x 2 cm

US: 6.8 cm solid mass

- Patient reportedly s/p left oophorectomy – left ovary not visualized.
- Right ovary within normal limits
CT abdomen and pelvis:

- left paraaortic lymph node (6.8 cm) with lateral displacement of left kidney
- bilateral inguinal adenopathy
paraortic mass

6.8 cm
Bilateral inguinal adenopathy
Left inguinal lymph node excision
06/01/2007
TTF-1

thyroglobulin
Diagnosis:
Lymph node, left inguinal:

**METASTATIC PAPILLARY THYROID CARCINOMA**

- Thyroglobulin: **4923.0 ng/ml**
- Thyroglobulin AB: <1.0 U/ml
- TSH: 0.47
WHERE IS THE PRIMARY?

- History of ovarian cyst removal in the late 1980’s
- Records not available on Health Connect (electronic medical record)
- Attempt made to retrieve patient’s chart from that era
Is the primary from the patient’s thyroid gland?

**US Thyroid gland:**
- Inhomogenous texture to thyroid with a 7 mm nodule seen in left lobe.
- No extrathyroidal masses.

**CT neck and thorax:**
- Negative CT neck.
- Right anterior mid chest extra-pleural soft tissue mass (2.6 cm)
- Two lymph nodes noted in epicardial space (2.4 and 2.6 cm)
- No mediastinal nor hilar adenopathy
Total thyroidectomy performed

Entire thyroid submitted

Dx: “Adenomatoid nodules. Parathyroid and lymph node tissue with no diagnostic change”
POSSIBILITIES

- Microscopic focus of tumor still present within blocks of tissue from the thyroid gland

- previous oophorectomy
  - performed 1989, pt. 20 years old
  - signed out as struma ovarii
- Thyroidectomy negative for carcinoma
- Oophorectomy: changes consistent with papillary thyroid carcinoma
CONCLUSION:

MALIGNANT STRUMA OVARI
(PAPILLARY CARCINOMA ARISING IN
STRUMA OVARI)

RECURRENCE 19 YEARS LATER
METASTASIS TO PERIAORTIC AND
INGUINAL LYMPH NODES
STRUMA OVARIII

STRUMA OVARIII:

- Mature ovarian teratoma in which greater than 50% of the total volume is composed of thyroid tissue
- Most common form of monodermal ovarian teratomas (2.7% of all ovarian teratomas)
- Histopathology: normal or hyperplastic thyroid-type tissue with patterns seen in thyroid adenoma such as microfollicular, macrofollicular, trabecular, and solid.
MALIGNANT STRUMA OVARII

- 5% to 10% of struma ovarii
- 0.1% of all ovarian tumors
- 5% - 6% of MSO demonstrated metastasis
- Pathologic diagnosis of malignancy:
  - No consensus
  - Initial criteria in 1940’s: cellular atypia, vascular invasion, and metastasis
  - Current trend: adherence to the same criteria as that used for thyroid carcinoma (*Devaney et al.)
    - Cytologically malignant; vascular/capsular invasion helpful

TREATMENT OF MALIGNANT STRUMA OVARII

Optimal treatment regimen not clearly defined secondary to limited number of cases

- Surgical treatment consisting of TAH and BSO
- Conservative surgery (unilateral oophorectomy) if preservation of fertility desired, if unilateral teratoma without evidence of capsular invasion or gross metastasis
TREATMENT OF MALIGNANT STRUMA OVARII (cont)

- Cases exhibiting gross metastasis, capsular invasion, or intraoperative frozen section demonstrating MSO should have complete staging for ovarian cancer with peritoneal washings and lymph node sampling.

- $^{131}\text{I}$ radioablation therapy:
  - Some recommend first-line treatment after surgical diagnosis and treatment
  - Others only in cases of residual malignant disease
  - In either case thyroidectomy required

- Iodine scans and thyroglobulin for follow-up
09-14-2007: CT abdomen and pelvis
  - diffuse soft tissue nodules throughout omentum and mesenteric fat, subcutaneous fat of lower abdominal wall, right lower abdominal wall mass
  - Localized area in right parotid gland, non-specific, possibly tumor
  - epicardial space, along with left periaortic mass and right inguinal node

11-27-07: I-131 whole body scan
09-14-2007: CT abdomen and pelvis
  - diffuse soft tissue nodules throughout omentum and mesenteric fat, subcutaneous fat of lower abdomen wall, right lower abdominal wall mass
  - Localized area in right parotid gland, non-specific, possibly tumor
  - epicardial space, along with left periaortic mass and right inguinal node

11-27-07: I-131 whole body scan

01-07-08: I-131 treatment (200 mCi)

01-25-08: I-131 whole body scan
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<th>T4</th>
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<td>&lt;0.01</td>
<td>2.31</td>
</tr>
</tbody>
</table>

*I-131 therapy on 01-07-08*
REFERENCES


DeSimone C, Lele S, Modesitt S. Malignant struma ovarii: a case report and analysis of cases reported in the literature with focus on survival and I-131 therapy.
REFERENCES (cont)


Case 5
26yo presented with an enlarging left testicular mass over two months

Henry Tsai
Fontana KP
Imaging studies

- Right testicle 5.9 x 3.5 x 2.8 cm
- Left testicle 8.9 x 4.4 x 3.3 cm
- Heterogenous texture, suspicious for neoplastic process
- Left adrenal nodule 1.8 x 1.4 cm
- Right adrenal nodule 1.5 x 1.1 cm
- Nodules/nodes in the left paraaortic area and mesentery
AFIP25 p23: Frozen Section

- Not routinely required
- Frozen section of a biopsy obtained by an inguinal approach, applied most frequently to epidermoid cysts
- Correct diagnosis in 81% of cases, and a second biopsy established correct diagnosis in additional 11%
- Difficult to subcategorize germ cell tumors, but subtyping of germ cell tumors does not affect management
Intraoperative consultation

- 118 gram orchiectomy specimen with a 9 x 2 cm portion of attached unremarkable spermatic cord
- The testis measures 7.5 x 4.0 x 4.0 cm and the unremarkable epididymis measures 3.0 x 1.0 x 0.3 cm
- The testis is entirely replaced by a tan-orange firm mass
Differential: Leydig cell tumor

- 1-3% of all testicular tumors
- Typically well demarcated and brown color
- Abundant eosinophilic and granular cytoplasm with variably sized round to oval nuclei with prominent nucleoli.
- Lipochrome pigments
- Reinke’s crystals can be seen in 35% of cases
- 3% are bilateral
- 10% of Leydig cell tumor are malignant and have lymph node, liver and lung metastases
Differential: Malignant Leydig cell tumors

- Adult (tumors in prepubertal children are benign)
- Malignant features include >5 cm, cytologic atypia, increased mitotic activity, necrosis, and vascular invasion
- Managed by radical orchiectomy and retroperitoneal lymphadenectomy
- Do not respond to radiation or chemotherapy
- Majority of patients developing metastases that result in death
Testicular “Tumor” of the Adrenogenital Syndrome

- Testicular adrenal rest tumor (TART)
- Uncertain histogenesis
- Histologically resembles a Leydig or interstitial cell tumor
- Even in contemporary series, cases were initially misdiagnosed as Leydig cell tumors
- May not a neoplastic in view of its dependence on ACTH
- Also been noted in Nelson’s syndrome and Addison's disease
Evidence for adrenal rest

- Embryologically, adrenal glands are adjacent to gonadal ridges
- One of the most frequent sites of accessory adrenal tissue is in the area of celiac axis
- Extratesticular nodules along the spermatic cord or adjacent to the epididymis
- 86% in hilum of testis
• Area of celiac axis 32%
• Broad ligament 23%
• Spermatic cord 3.8-9.3%
• Adnexa of testes 7.5%
• Rare sites: placenta, liver, lung, intracranial
## Immunohistochemistry

<table>
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<th>Statdxpathiq:</th>
<th>Leydig cell</th>
<th>Adrenal cortical</th>
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<td>96%</td>
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<tr>
<td>CALRETININ</td>
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Melan-A
Tumor of Congenital Adrenal Hyperplasia

- Controversial as to whether it arises from Leydig, adrenal cortical, or multipotent testicular stromal cells
- Reticulum staining pattern isolates individual and small groups of cells; in contrast to broad radial cords in entopic or heterotopic adrenal cortical hyperplasia
- Female adrenal rest tumors are very rare even in imaging studies
- Bilateral Leydig cell tumor of the ovary in a woman with congenital adrenal hyperplasia. The first reported case Presse Med. 1991 Jan 26;20(3):109-12
Summary

- 83% bilateral and 75% multifocal
- Lacks crystals of Reinke
- Nuclei can be atypical
- Surgical excision is generally considered unnecessary except for cosmetic reasons
- AFIP 3rd series: One patient with adrenogenital syndrome who developed malignant Leydig cell tumor
- 4th series: Lack of malignant behavior in cases reported to date
Additional History

• Patient was diagnosed soon after birth with 21-hydroxylase deficiency, salt-losing variant
• Off the Kaiser plan for several years
• Non-complaint with his florinef and dexamethasone
• Admitted for adrenal crisis at an outside facility
• S/p left orchiectomy
Any question?