A Case of Extramammary Paget Disease: Determining Primary or Secondary Origin

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Abstract:
Extramammary Paget Disease (EMPD) is a malignant and destructive skin lesion often seen in concurrence with an underlying malignancy (such as in the more common mammary type), but can also arise de novo⁴. These primary lesions are commonly found in areas rich in apocrine sweat glands such as the vulva, perianal region, axilla, mons pubis, glans penis and eyelid⁴ (listed in order of occurrence). There are multiple hypotheses for this presentation. Two common understandings are that it appears as an epidermotropic metastasis from a visceral carcinoma, commonly uterine or rectal, or within the skin arising from apocrine derivation. It is important to determine the derivation of an extramammary case in order to rule out an undiagnosed underlying visceral carcinoma.

Background:
Paget Disease Background⁴:
The most widely recognized treatment is wide local excision1,9 (2 cm margins).

10 year survival rate: 67%, local recurrence rate is 34-40%
Case Study Patient Background:
80 year old female with history of TAH/BSO, atrial fibrillation, as well as several cardiac medications. The patient was found to have a gray-white to red-brown area, extending grossly up to the vulvar and anal skin margins, and within less than 1.0 cm to the lateral skin margins. The soft tissue is inked black. All lateral margins are taken visible margins.

Methodology:
After discovery of the skin lesion, an initial biopsy was used to establish a diagnosis. A series of immunohistochemistry and special stains were then used to determine the origin of the lesion (primary or secondary). The biopsies were followed by a CT scan and wide local excision, with 2 cm visualized margins where possible.

Discussion:
Differential Diagnosis*: Table 1. Differential Diagnosis determination using immunohistochemical and special stains

<table>
<thead>
<tr>
<th></th>
<th>Primary EMPD</th>
<th>Secondary EMPD</th>
<th>Bowen Disease</th>
<th>Superficial spreading melanoma</th>
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</thead>
<tbody>
<tr>
<td>Mucicarmine</td>
<td>+</td>
<td>-</td>
<td></td>
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<tr>
<td>CK-7</td>
<td>+</td>
<td>+</td>
<td>-</td>
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<tr>
<td>CK-20</td>
<td>Usually -</td>
<td>Usually +</td>
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<tr>
<td>CEA</td>
<td>+</td>
<td>-</td>
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<tr>
<td>GCDFP-15</td>
<td>+</td>
<td>-</td>
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<tr>
<td>PAS</td>
<td>+</td>
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Results:

Gross Description:
Received fresh lesion, “perianal skin” is a 21.5 cm x 13.5 cm x 3 cm ellipse of perianal skin including anal and vulvar skin margins. There is a 15.0 cm x 12.0 cm rubbery, firm, granular, nodular, gray-white to red-brown area, extending grossly up to the vulvar and anal skin margins, and within less than 1.0 cm to the lateral skin margins. The soft tissue is inked black. All lateral margins are taken visible margins. Perpendicular margins of vulva and anus are taken, and representative sections of nodules. Submitted in 32 cassettes.

Figure 1. Gross photographs taken of fresh specimen. Yellow arrow shows anal margin, Blue arrow points to the vulvar skin margin. Note the polyoid erythematous lesions extending less than 2 cm from all visible margins.

Figure 2. A and B: H and E slides showing signet cells and an infiltrate of malignant cells demonstrating intracytoplasmic mucin. C: positive mucicarmine. D: positive PAS.

Microscopic Description:
Epidermis shows hyper and parakeratosis or ulceration. See infiltration by scattered or clustered large cells with abundant clear and sometimes eosinophilic cytoplasm, containing prominent vesicular nuclei. Mitotic figures are rare. Cells can be found throughout the layers of the epidermis. Occasionally, glandular or acinar differentiation is seen and signet ring cells with intracytoplasmic mucin may be identified.

References:
A Pathologists’ Assistant’s Gross Description Expedites the Diagnosis of an Uncommon Benign Multicystic Tumor in the Adult Kidney: A Case Report and Review of the Literature

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Abstract:
The Pathologists’ Assistant’s (PA’s) gross descriptions are essential to the pathologist for the differential diagnoses of both benign and malignant tumors. For example, concise, gross descriptions are extremely important in multicystic renal tumors in adults. When the PA recognizes and describes specific tumor features in these cases, the pathologist can diagnose both intraoperative and final reports more efficiently.

Descriptive names for encapsulated multicystic renal tumors arise from a spectrum of histologic findings and numerous theories of pathogenesis. The Multicystic Nephroma or Multilocular Cystic Nephroma described in this case report is one such uncommon, but specific benign tumor that can present at any age and is recognized by gross appearances. Histologic examination of this Multicystic Nephroma was identical to the microscopic features cited in the literature reviewed.

This benign tumor was expressed as the gross description suggested and followed microscopic verification from the sections selected by the PA.

Background:
The pathologists’ assistant (PA) is an intensively trained allied health professional who provides anatomic pathology services under the direct supervision of a pathologist (1). Valuable experience occurs on a daily basis both on the surgical pathology bench and in the autopsy room. Gross examination and feed-back of the final diagnoses between the PA and attending pathologist create a valuable partnership of gross recognition and microscopic verifications. When gross descriptive communication and microscopic verification are utilized, time-consuming dictations and voluminous sections can be avoided. The utilization of pathologists’ assistants in histopathology has been shown to expedite diagnoses and ultimately enhance patient care (2).

The case is a 64 year old caucasian male who was hospitalized for lower extremity claudication. His past medical history was generalized arteriosclerotic heart disease and peripheral vascular disease. A 12 cm. solitary cystic mass on an abdominal CT scan was found following 10% buffered formalin fixation. Gross examination and feed-back of the final diagnoses between the PA and attending pathologist create a valuable partnership of gross recognition and microscopic verifications. When gross descriptive communication and microscopic verification are utilized, time-consuming dictations and voluminous sections can be avoided. The utilization of pathologists’ assistants in histopathology has been shown to expedite diagnoses and ultimately enhance patient care (2).

Rationale and Hypothesis:
The pathologists’ assistant is a highly skilled professional responsible for the gross examination and dissection of histopathologic specimens: This includes measurements, time-consuming dictations and voluminous sections can be avoided. The utilization of pathologists’ assistants in histopathology has been shown to expedite diagnoses and ultimately enhance patient care (2).

The gross appearance of the solitary and multicystic cystic mass was unlike that of a multicellular renal cell carcinoma or a partially cystic dysplastic kidney. The diagnosis was a Multicystic Nephroma, a benign cystic tumor of the left kidney. There was no additional tumor treatment required following the nephrectomy.

Methodology:
The gross examination of the left nephrectomy utilized a routine and established procedure similar to any specimen received by the PA under the supervision of the pathologist. i.e. margins inked, specimen oriented and measured, photographed, weighed and examined both fresh and following 10% buffered formalin fixation.

Results:
Gross Description: “labeled left kidney is an 18 cm. in maximum dimension portion of fat (perinephric) and a dilated pelvis. The remaining kidney is unremarkable with smooth cortices and slightly distention of the pelvis suggestive of hydronephrosis. The loculations are smooth with clear colorless fluid to gelatinous material contents. The remaining kidney is unremarkable with smooth cortices and slightly blunted papillary tips. The corticomedullary junctions are well delineated. The ureter is thick-walled. The pelvoureteral junction is patent with a 4 mm. in diameter probe. There are no mass lesions or excrescences in the pelvis or ureter. The vascular margins are unremarkable.”

Microscopic log:
A2.4. Selected multicellular area.
A5. Normal, preserved kidney.

Microscopic Description and Summary: H & E stains show that the masses is a multicystic lesion. The cysts are lined by cuboidal epithelium which in some areas is somewhat hobnail. There are no areas of malignancy or atypia. The stroma between the cysts are fibrous. Sections away from the mass show normal renal parenchyma. The diagnosis is a Multicystic Nephroma. Malignancy is not identified.

Discussion:
The gross description of the left nephrectomy by the PA noted a well delineated multicellular cystic mass and preserved normal parenchyma. The CT scan reported by the radiologist described an extensively septated cystic renal mass suspicious for a multicellular cystic renal cell carcinoma or a partially cystic dysplastic kidney.

Figure 1. Photomicrographs of the left kidney. (L/R) A. Perinephric fat margins with multifocal localizations and a dilated pelvis. B. The cut surface of the kidney demonstrating a solitary (13 cm) multicystic cystic mass. Note the normal, preserved parenchyma in the lower lateral portions including the lower pole (white arrows) and the dilated pelvis (red arrows).

Figure 2. Abdominal CT scan demonstrating a cystic abnormality of the left kidney (arrows).

Figure 3. Photomicrographs (L to R) A. H&E 10X of localizations with fibrous stroma. B. H&E 40X of junction with normal kidney. C. H&E 40X of preserved tubule within a fibrous septa. D. H&E 100X lining of a ureter with cuboidal epithelium hobnail appearance.

Radiologic Differential on Abdominal CT Scan

Benign

Malignant

Multicystic Nephroma

Cystic Partially Nephromas

Cystic Dysplastic Nephroblastoma

Multilocular Cystic Nephroma

CPDN

Mortality is related only to single function kidney

Common ages: males< 4 yrs. , Females > 30 yrs.

Histologically distinct (Septae without embryonal elements)  Histologically distinct (Septae with blastemal & embryonal elements)  ? Biologically different?

Conclusion:
Multicystic renal tumors in adults are one example where concise, gross descriptions by the Pathologists’ Assistant (PA) are extremely important and have shown to expedite the diagnosis when specific gross tumor features are recognized by the PA and conveyed to the pathologist. The benign solitary tumor termed “Multicystic Nephroma” or “Multicellular Cystic Nephroma” is uncommon at any age and may have more aggressive behavior if blastema or embryonal elements are seen microscopically in the fibrous septate of the locules/cyst. Ultrasonography is the preferred non-invasive study for diagnosis and when combined with CT or MRI scans offer more detailed evaluation of the cystic lesion and stromal tissue.

Histologic examination of this Multicystic Nephroma in a 64 year-old male was identical to the microscopic features cited in the literature reviewed.

References: