Disseminated Cutaneous Rhinosporidiosis: Diagnosis by Fine Needle Aspiration Cytology

To the Editors:

Rhinosporidiosis is a chronic granulomatous disease of the nasal cavity caused by *Rhinosporidium seeberi*,¹⁻⁴ which is an aquatic protozoan formerly considered to be a fungus.⁵ The disease, first described by Seeber in Argentina and O’Kinealy in India,¹ is endemic to southern India and Sri Lanka.¹⁻⁴ However, sporadic cases have been reported from other parts of the world including the United States, Brazil, Argentina, South Africa and Italy. Other rare sites infected with *R. seeberi* include the bronchi, larynx, pharynx, conjunctivae and epithelia of the genitalia.¹ Isolated cases of *Rhinosporidoma* of bone and cutaneous rhinosporidiosis without disease elsewhere are also known.⁵,⁶,⁷

The histology in rhinosporidiosis is simple and consists of many sporangia at various stages of maturation, surrounded by a double layer of chitin and cellulose and filled with a large number of spores.¹ As for the cytologic diagnosis, there have been rare case reports, diagnosed using nasal scrapes, smears and irrigation fluids.³,⁸ Kavishwar et al reported a case of disseminated cutaneous rhinosporidiosis diagnosed on fine needle aspiration cytology (FNAC).⁹ Below, we document a similar case, emphasizing the importance of fine needle aspiration (FNA) in the preoperative diagnosis of rare cases of disseminated rhinosporidiosis.

A 51-year-old male presented with multiple, large (5×5–8×8-cm) sessile firm, subcutaneous nodules on both the thighs and right sole (Figure 1) that had been present for 2 years. The swelling on the sole was ulcerated. FNA of the swellings was performed using a 23-gauge needle. May-Grünwald-Giemsa– and Papanicolaou-stained smears showed moderate cellularity with a large number of globular sporangia at various stages of maturation and measuring 10–200 μm (Figure 2). Sporangia contained numerous endospores. The hemorrhagic background showed several singly scattered endospores with a granulomatous reaction. Eosinophils were conspicuously absent. Detailed history revealed removal of a nasal mass 6 years earlier, reported as rhinosporidiosis. Histopathologic examination of the cutaneous nodules confirmed the cytologic diagnosis. Mucicarmine and periodic acid–Schiff (PAS) stain highlighted the capsule of spores.

Skin lesions in rhinosporidiosis are rare and usually present as papillomas with or without nasal involvement.⁴ As for disseminated cutaneous rhinosporidiosis, only 3 cases have been documented.¹⁰ Dissemination from a primary nasal or conjunctival lesion occurs either due to autoinoculation or hematogenous spread.⁵,¹¹ Visceral involvement, particularly of the liver, lungs and brain, has been reported in rare, fatal cases of dissemination.¹²

To our knowledge, this is the second case of disseminated rhinosporidiosis diagnosed on FNAC. The characteristic cytomorphology with distinctive sporangia and spores at various stages of maturation permits a definitive diagnosis of rhinosporidiosis. In immunocompromised patients, cytologic differentiation from *Coccidioidomycosis immitis* can be performed with PAS staining.³,¹¹
Letters to the Editors

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Fungal Fruiting Bodies in a Pap Smear: Contamination or Infection?

To the Editors:

Although conceived by Papanicolaou and Traut1 as a tool for detecting precancerous and cancerous lesions, the Pap cervicovaginal smear also facilitates identification of some nonneoplastic abnormalities of the lower genital tract, including routine infections, often prompting clinical intervention. However, potential slide contamination plagues Pap smear acquisition, transmission and laboratory preparation. Both organic and inorganic material may confound interpretation, requiring a careful search for clues to confirm a suspected contaminant’s nature. While inorganic contaminants may fail to cause consternation, organisms and organic structures provoke concern and the need to determine their nature, particularly if they may require treatment.2 Pollen, insects and fungal organisms arising from laboratory solutions or tap water or through aerosolization bedevil slide preparation. Although careful laboratory techniques minimize such events, controlling similar factors within the clinician’s environment proves difficult. A recent Pap smear in our laboratory exemplified the need to remain vigilant for contaminants.

We received a conventional cervicovaginal smear from a 28-year-old, African American woman, gravida 3, para 3, with a past medical history of a Pap smear diagnosis of atypical squamous cells of undetermined significance (ASC-US). She presented for colposcopy and repeat Pap smear. Low magnification revealed a collection of intermeshed fungal hyphae (Figure 1). Review on high magnification confirmed the presence of fruiting bodies (Figure 2). The hyphae were approximately 6–8 μm and broad and stained strongly with hematoxylin, with distinctly parallel borders and true septations. The fruiting bodies consisted of branching phialides with tapered ends. Conidia were attached and adjacent to phialids, suggesting a hyalo-

Figure 1 Hyphae overlying squamous cells (Papanicolaou stain, ×40). Inset: hyphae (Papanicolaou stain, ×200).
The hyphae lay above the plane of the cervical cells, suggesting that the fungi were not deposited on the slide at the same time as the cervical cells. The conventional smear’s background possessed only a scanty number of inflammatory cells. Had the fungal organism been pathogenic, a more severe inflammatory response would have been expected. We contacted the colposcopy clinic and confirmed that spatulas were kept in sterile packages prior to usage. The patient did not suffer from itching or erythema of the vagina, and no other cases of *Paecilomyces* spp were identified in subsequent weeks.

The identification of unusual organisms in routine cervicovaginal smears should prompt a careful investigation of clinical symptoms and findings, and the slides should be carefully examined for clues favoring infection or contamination. An analysis of physician and laboratory workflow and processes may be necessary. Because infection of the vagina by *Paecilomyces* spp, an emerging infection in immunocompetent hosts, has been reported, identification of *Paecilomyces* hyphae and fruiting bodies on cervicovaginal smears warrants careful investigation.

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Are All Subcutaneous Parasitic Cysts Cysticercosis?

To the Editor:

We read with interest the letter “Cysticercosis Diagnosed by Fine Needle Aspiration Cytology” by Agrawal et al.1 The authors stated that “Cysticercus cellulosae diagnosed by fine needle aspiration is very unusual” and that “the case is reported because of its unusual presentation and rarity.” A quick review of the literature2-5 suggests the reverse. The cytomorphology of cysticercosis has been described in minute detail, covering the entire range, from viable cysts through necrotic and calcified lesions.2

Agrawal et al1 saw “classic scolices.” However, each Cysticercus has only 1 scolex.6 Multiple scolices characterize other cestode larvae found in humans, notably the larva (hydatid cyst) of Echinococcus granulosus, which bears more than a passing resemblance to Cysticercus. Both possess a bladder wall: a thin, membranous bladder wall in Cysticercus and a thicker, acellular, lamellated membrane surrounding the germinal layer in a hydatid cyst. Protoscolices grow from this germinal layer, differentiating into broods and forming daughter cysts. A hydatid cyst that develops from a single egg may therefore contain thousands of scolices.6

While it is unusual, but not unknown, for hydatid cysts to occur in subcutaneous tissues, this is a common location for cysticercosis. Both cysts may yield clear, watery fluid on aspiration. The findings vary with the stage of evolution.

Humans are accidental intermediate hosts of both parasites. Over months, the larva of Cysticercus dies,

Figure 1  Relative sizes of scolices and hooklets of Cysticercus and Echinococcus. (A) Single hooklet of Cysticercus cellulosae (May-Grünwald-Giemsa stain, × 400). (B) Entire scolex (rostellum and 4 suckers) of Cysticercus cellulosae (May-Grünwald-Giemsa stain, × 400). (C) Three scolices of Echinococcus granulosus (May-Grünwald-Giemsa stain, × 400). (D) Single hooklet of Echinococcus granulosus (May-Grünwald-Giemsa stain, × 400).
proving the characteristic inflammatory response culminating in disintegration of the parasite. The viable cyst and the necrotic and calcified lesion all have distinctive cytomorphic patterns. The most common finding in the clear fluid aspirated from viable cysts are delicate fragments of bladder wall with tiny, parasitic nuclei in a clear, acellular background. Aspirates of necrotic lesions may contain fragments of bladder wall, the invaginated portion, including calcareous corpuscles and detached, single hooklets. The inflammatory background ranges from acute inflammation with prominent eosinophils, through granulomatous inflammation with necrosis, to acellular necrosis without significant residual inflammation. Occasionally an entire scolex can be found in an inflammatory background. Single, detached hooklets and calcareous corpuscles may be the only recognizable remnants in aspirates of calcified cysts.

Hydatid cysts live for many years and usually continue to grow unless the contents of the cyst die, presumably due to trauma or therapy, resulting in inflammation and disintegration of the parasite parts; those events are similar to those seen in cysticercosis.

To the cytopathologist, the distinction lies in the cytomorphic details. The scolex of Cysticercus is large, almost 1 mm in diameter. It has a rostellum and 4 suckers. The armed rostellum has 2 rings of alternating large and small hooklets measuring 170 (Figure 1A) and 130 μm, respectively. The scolex is visible to the unaided eye and is easily recognized at scanning magnification (×4) (Figure 1B). Finding an entire scolex in a fine needle aspirate is a rare event and, for reasons that are unclear, occurs in the inflammatory background of a partially necrotic cyst. In contrast, multiple scolices suspended in clear fluid are aspirated from viable hydatid cysts. In stark contrast to the scolex of Cysticercus, individual scolices of Echinococcus are small, albeit each with a rostellum and suckers (Figure 1C). The hooklets measure 22 and 40 μm (Figure 1D). The rostellum can be detailed only at high magnification, as illustrated by Agrawal et al.

On the basis of the evidence presented by Agrawal et al, their case is Echinococcus, not Cysticercus. The perception that a condition is rare or otherwise is closely linked to our ability to recognize what we see. At our institution we have seen cysticercosis transform from a rare to a fairly common diagnosis ever since we learned to recognize its various cytomorphologic manifestations. Our experience confirms endorsing the aphorism, “What the mind does not know, the eye does not see.”

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Intrapelvic Botryoid Wilms’ Tumor: Diagnosis with Fresh Voiding Urine Cytology

To the Editors:

Wilms’ tumor is the most common malignant neoplasm of the kidney in children. Most Wilms’ tumors present as intrarenal parenchyma tumors and may form a palpable abdominal mass. Common imaging studies, such as computed tomography (CT), ultrasonography and fine needle aspiration cytology, are useful in preoperative diagnosis. In rare cases the tumor arises from the renal pelvis, with minimal renal parenchyma invasion, and mimics the gross appearance of botryoid sarcoma.1-7 The preoperative diagnosis may be difficult due to the unusual presentation. Macroscopic hematuria is frequently observed in such case. We report a case of intrapelvic botryoid Wilms’ tumor with fresh voiding urine cytology.

A 22-month-old boy was hospitalized with gross hematuria for 1 day. The urine routine revealed hematuria (> 4 red blood cells per high-power field), proteinuria (2+) and bilirubinuria (1+). Complete

Letters to the Editors
Letters to the Editors

ACTA CYTOLOGICA
Volume 50 Number 1 January–February 2006

blood count and biochemistry, including blood urea nitrogen, creatinine and urinary vanillyl mandelic acid, were normal. Abdominal CT scan revealed tumor growth in the left renal pelvis with low attenuation. Intravenous pyelogram showed multiple, expansile, filling defects of the left collecting system with marked hydronephrosis. The initial diagnosis was transitional cell carcinoma.

Fresh voiding urine cytology with Papanicolaou stain disclosed small, round tumor cells (Figures 1 and 2), 1.5–2 times the size of small lymphocytes, with a round to oval nucleus and fine, evenly distributed, chromatin, scanty blue cytoplasm and indistinct cell border. Most of the tumor cells were singly distributed, and no organoid structure was noted. The initial differential diagnosis included lymphoma, neuroblastoma and Wilms’ tumor. Left radical nephroureterectomy was done, and a botryoid mass, 8×4×3 cm, was found in the left renal pelvis (Figure 3). The tumor mass connected to the renal pelvis with a short, thin stalk. Neither renal parenchyma invasion nor renal vein involvement was found grossly.

Microscopically, the tumor showed the typical triphasic pattern of Wilms’ tumor, with parts of diffuse blastema cells, loose stroma with smooth muscle and skeletal muscle differentiation and a few primitive tubular and glomeruloid structures. The tumor cells seen on urine cytology were identical to the blastemal component of the tumor. Minimal stromal invasion was seen in the base of the stalk (Figure 4). Most parts of the tumor were covered with uroepithelium, but some of them, especially the blastemal part, showed direct contact with the intrapelvic space and urine. No anaplastic changes were found through the whole section of the tumor bulk. There was also no evidence of renal vein invasion. At this writing the patient was undergoing postoperative chemotherapy.

In most cases of Wilms’ tumor, the lesion is a well-demarcated, solid mass in the renal parenchyma and invades the renal pelvis at the late stage. It frequently manifests as an abdominal mass. Preoperative chemotherapy has been advocated by the International Society of Paediatric Oncology due to the great risk of operative rupture and abdominal spillage. However, an unusual presentation of Wilms’ tumor, such as an intrapelvic botryoid mass, may complicate the diagnosis prior to an operation. About 85% of patients with intrapelvic botryoid Wilms’ tumors, including ours, present with gross hematuria, and only 37.5% have a palpable abdominal mass on the initial physical examination.
Examination. Complete blood count and biochemical tests are not helpful in the diagnosis. Macroscopic hematuria seems to be the most important symptom of botryoid Wilms’ tumor.

Some authors have suggested that the overall outcome of intrapelvic botryoid Wilms’ tumor is better than in typical cases, possibly due to minimal parenchyma invasion and rare lymph node metastasis.

Preoperative cystoscopy has been suggested to rule out ureter extension and bladder metastasis. Radical nephrectomy and total ureterectomy are recommended for Wilms’ tumor and should extend to the collecting system to prevent recurrence in the ureteral stump.

No cases of intrapelvic botryoid Wilms’ tumor with urine cytology have been reported except for 1 case in which the urine cytology was negative. The fresh voiding urine cytology in our case revealed small round tumor cells with high nuclear/cytoplasmic ratio; round to oval nucleus; scanty, blue cytoplasm; fine, evenly distributed chromat; and indistinct cell border. Neither cohesive pattern nor organoid structures were found. The presence of tumor cells in urine may result from direct contact between blastemal component of the tumor bulk and urine.

The differential diagnosis included malignant round cell tumors, such as neuroblastoma, lymphoma, rhabdomyosarcoma and clear cell sarcoma, and other pediatric renal neoplasms, mesoblastic and cystic nephroma. However, the definitive diagnosis is difficult without immunocytochemistry in cases of scanty tumor cells. In fine needle aspiration, the blastemal component is the predominant cell type of Wilms’ tumor. The cells may show peripheral palisading or rosette formation. The cytologic picture of neuroblastoma shows discrete and clustered cells in a filamentous background and occasional rosette formation. The difference between the rosette of neuroblastoma and Wilms’ tumor is that the rosettes of the former are multilayered, containing central fibrillar material, and the latter type may show a well-defined cytoplasmic border and a lumen. Neuron-specific enolase may help with the differential diagnosis. The cytologic picture of rhabdomyosarcoma shows clumps of and discrete round cells with central to eccentric, round nuclei; fibrillar cytoplasm; and pinkish intranuclear inclusions. They are usually positive for vimentin, desmin and actin. However, rhabdomyoblasts can be found in both tumors and may cause uncertainty in the diagnosis. The presence of a bimodal population of cells on cytology would favor the diagnosis of Wilms’ tumor.

As compared to aspiration cytology of typically presenting Wilms’ tumor, the urine cytology in our case was identical to that of the blastemal part of the tumor. The finding of urine cytology in botryoid Wilms’ tumor depends on the tumor part that directly contacts the urine flow and calyceal space. Unlike invasive Wilms’ tumor, in which the uroepithelium may show triple components in fresh voiding urine cytology, the tumor cells of botryoid-type Wilms’ tumor shed into urine only in the part not covered with uroepithelium. In our case, only part of the blastemal component of the tumor bulk was not covered with uroepithelium. This may explain the negative finding of urine cytology in the previously reported case. It may require more case studies and long-term follow-up to determine whether direct contact between the tumor cells and urine increases the rate of tumor seeding in the downstream uroepithelium.

In conclusion, Wilms’ tumor must be considered in children presenting with gross hematuria and an intrapelvic, botryoid mass in the kidney. Fresh voiding urine cytology may play a role in preoperative diagnosis of pediatric renal neoplasms, either botryoid-type Wilms’ tumor or other invasive malignancy in the uroepithelium.

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