CUTANEOUS INFECTIONS AND INFESTATIONS

Hoang, Duncan, Mihm, Murphy & Tahan

© Knowledge Books and Software
Contents

Introduction iii
About the Authors v
Contributors ix

Case 1  Ecthyma gangrenosum 1
Julie Y. Tse and Mai P. Hoang

Case 2  Epidermodysplasia verruciformis 7
Katy R. Linskey, Nicole F. Velez and Mai P. Hoang

Case 3  Cutaneous zygomycosis 15
Devon C. Gimbel and Rosalynn M. Nazarian

Case 4  Cutaneous leishmaniasis 23
Gabrielle Baker and Mai P. Hoang

Case 5  South American blastomycosis (paracoccidioidomycosis) 31
Kirsten S. W. Bellucci

Case 6  Hand foot and mouth disease 41
Johanna L. Baran, Devon C. Gimbel and Lyn M. Duncan

Case 7  Kaposi's varicelliform eruption 49
Stefan Kraft, Sarah N. Cee, Nicole F. Velez, Susan Burgin and Alireza Sepehr

Case 8  Tungiasis 57
John P. Dekker and Mai P. Hoang

Case 9  Histoplasmosis 63
Michael G. Osofsky and Vincent Liu

Case 10  Microsporidiosis 67
M. Angelica Selim

Case 11  Chromoblastomycosis 73
Anna Harris and Mary Jane Zimarowski

Case 12  Secondary syphilis 81
Sara Shalin and Mary Jane Zimarowski

Case 13  Cutaneous cytomegalovirus infection 89
Alice Z. C. Lobo and Mai P. Hoang

Case 14  Subcutaneous pheohyphomycosis 93
Anna B. Gray and Mai P. Hoang
<table>
<thead>
<tr>
<th>Case</th>
<th>Diagnosis</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>Coccidioidomycosis</td>
<td>101</td>
</tr>
<tr>
<td></td>
<td><em>Jessica Z. Sugianto and Mai P. Hoang</em></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Leprosy</td>
<td>109</td>
</tr>
<tr>
<td></td>
<td><em>Anna Harris, Johanna L. Baran, Peter Chien and Beverly Faulkner Jones</em></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Spirometra infestation</td>
<td>121</td>
</tr>
<tr>
<td></td>
<td><em>Sanam Loghavi and Steven R. Tahan</em></td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Disseminated acanthamebiasis</td>
<td>125</td>
</tr>
<tr>
<td></td>
<td><em>Ashley Ward and Steven R. Tahan</em></td>
<td></td>
</tr>
<tr>
<td>19</td>
<td><em>Mycobacterium chelonae</em></td>
<td>133</td>
</tr>
<tr>
<td></td>
<td><em>Gretchen W. Frieling and Alireza Sepehr</em></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Disseminated sporotrichosis</td>
<td>145</td>
</tr>
<tr>
<td></td>
<td><em>Gretchen W. Frieling and Steven R. Tahan</em></td>
<td></td>
</tr>
</tbody>
</table>
Introduction

The twenty cases of this seventh book in the series *Cases in Dermatopathology* illustrate the diverse types of infection and infestation that can be seen in the skin. This book is possible due to the enthusiasm and commitment of the Dermatopathology faculty and residents of the Harvard-affiliated hospitals in Boston including the Beth Israel Deaconess Hospital, the Brigham and Women’s Hospital and the Massachusetts General Hospital. We would like to also acknowledge the input of the current and former fellows of the Harvard Dermatopathology Training Program. Selected cases from this volume are presented during the Slide Seminar on Cutaneous Infections and Infestations at the Harvard Dermatopathology Update CME course held in Boston on September 15-17, 2011.

Many thanks are owed to Rob Watts, Dallas Girdler and Dean Maynard of Knowledge Books and Software on the Gold Coast, Australia for producing an exceptional product and for continuing this collaborative educational effort with the Harvard Dermatopathology Update CME course.

We hope that you will find the cases in this volume to be both educational and enlightening.

Mai P. Hoang
Case History

A 52-year-old woman presented with multiple superficial ulcerations with erythematous, hemorrhagic margins on her lower extremities. She had a history of chronic lymphocytic leukemia, status-post stem cell transplant complicated by Graft-versus-Host disease, now on immunosuppressive therapy. Her recent past medical history was significant for an episode of Pseudomonal sepsis and multiple cutaneous squamous cell carcinomas status-post resection with healing by second intention. She was admitted for septic shock secondary to her cutaneous lesions. Multiple superficial ulcerations with dark crusting, minimal oozing, and erythematous, hemorrhagic margins were noted on the lower extremities. She underwent punch biopsies of the lesions (Figures 1-4).

Figure 1: Histologic section of the biopsy shows epidermal ulceration and underlying marked dermal necrosis (40X).

Figure 2: Extensive dermal necrosis is noted in the deep aspect of the biopsy (100X).
Cutaneous Infections and Infestations

**Figure 3:** Fibrin thrombus is noted within a medium-sized vessel with minimal surrounding inflammatory infiltrate, consistent with a pauci-inflammatory vasculopathy (600X).

**Figure 4:** Tissue Gram stain demonstrates numerous Gram negative rods (inset) in the media of a medium-sized vessel (600X).

**Diagnosis**
Ecthyma gangrenosum secondary to *Pseudomonas aeruginosa* bacteremia

**Comment**
*Pseudomonas aeruginosa* is a Gram negative rod bacteria. Most *Pseudomonal* infections are nosocomially-acquired, with community-acquired infections being a rare cause of infection in previously healthy children.¹ Patients at risk for *P. aeruginosa* bacteremia usually have primary immunodeficiencies, such as those with chronic disease, burns, malignancies, and preterm newborns; however, healthy children can also be afflicted.²

**Clinical Features**
Cutaneous manifestation of *Pseudomonal* sepsis can vary from ecthyma gangrenosum to subcutaneous nodules, gangrenous cellulitis, hemorrhagic vesicles and bullae, papules, macules, petechia, and purpura.³ Ecthyma gangrenosum lesions present as painful, erythematous nodules, which progress to nodular, bullous, or pustular lesions with an indurated base, to ulcers covered by a gray-black eschar and surrounded by an erythematous rim.² Lesions most commonly affect the gluteal and perineal regions (57%) and the extremities (30%), but can also involve the trunk and face (12%).⁴

Cutaneous infection occurs by hematogenous seeding of the bacteria or by direct inoculation.² Sources of infection include gastroenteritis, pneumonia, otitis media, urinary tract infection, prosthetic valve endocarditis, and appendiceal abscess.⁵ Of note, many previously healthy children with *P. aeruginosa* sepsis are neutropenic at time of presentation, secondary to a toxin produced by the bacteria which inhibits neutrophil migration into infected areas and the circulation.⁶ Early antibiotic therapy is essential to the successful treatment of ecthyma gangrenosum. Antibiotic therapy can be guided by sensitivity-testing; in general aminoglycoside and/or an anti-*Pseudomonas* beta-lactam antibiotic are used.²

**Histopathology**
Histologic sections often demonstrate ulceration and necrosis of the epidermis and upper dermis, with underlying necrotizing vasculitis
Figure 9: Pseudoepitheliomatous hyperplasia, microabscess formation, and blastomycosis organisms in a microabscess (100X) and inset: broad based budding of yeast (600X).

Figure 10: “Sulfur granules” of actinomycosis (200X) and inset: composed of Gram positive, thin filamentous branching hyphae (Gram stain, 600X).

Table 1: Histologic features of micro-organisms in the differential diagnosis.

<table>
<thead>
<tr>
<th>Micro-organism</th>
<th>Size</th>
<th>Morphology</th>
<th>Angioinvasion</th>
<th>Tissue Reaction Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zygomycosis</td>
<td>6-16µm, wide</td>
<td>Aseptate hyphae, 90 degree branching, can appear folded or ribbon-like</td>
<td>present</td>
<td>Vessel thrombosis, tissue infarction and necrosis</td>
</tr>
<tr>
<td>Aspergillosis</td>
<td>2-3µm, thin</td>
<td>Uniform, septate hyphae, 45 degree dichotomous branching</td>
<td>present</td>
<td>Dermal abscess with granulomas with fungi in necrotic centers</td>
</tr>
<tr>
<td>Candidiasis</td>
<td>2-3µm, thin</td>
<td>Yeast and pseudohyphae</td>
<td>may be present</td>
<td>Acanthosis, spongiosis, fungi in stratum corneum, prominent mixed mononuclear infiltrate and neutrophilic microabscesses</td>
</tr>
<tr>
<td>Histoplasmosis</td>
<td>2-4µm</td>
<td>Oval yeast forms with clear halo</td>
<td>absent</td>
<td>Granulomatous inflammation with clusters of intracellular yeast forms in macrophages and giant cells</td>
</tr>
<tr>
<td>Cryptococcus</td>
<td>2-20µm</td>
<td>Round-oval yeast with thick mucoid capsule that stains positive for mucicarmine</td>
<td>absent</td>
<td>Paucicellular gelatinous reaction or granulomatous with dense lymphohistio-cytic inflammation, variable necrosis</td>
</tr>
<tr>
<td>Blastomycosis (North American Blastomycosis)</td>
<td>8-15µm</td>
<td>Broad-based budding yeast</td>
<td>absent</td>
<td>Dermal mixed inflammatory infiltrate including neutrophils and multinucleated giant cells; yeast in center of abscesses and in giant cells; prominent overlying pseudoepitheliomatous hyperplasia</td>
</tr>
<tr>
<td>Actinomycosis</td>
<td>Granules average 300µm in diameter</td>
<td>Filamentous branching hyphae (Gram positive, acid-fast negative)</td>
<td>absent</td>
<td>Chronic abscesses, granulation tissue and sulfur granules composed of slender filaments</td>
</tr>
</tbody>
</table>
References

Case History

An 83 year-old female presented to the emergency department with a three-month history of a widespread, pruritic, superficial exfoliative eruption. She had been treated for a presumed fungal infection without improvement. The patient was admitted to the hospital for further evaluation. On examination, there were erythematous, exfoliative plaques with adherent scale on her face, trunk, and extremities. Several plaques under the pannus were macerated and covered with malodorous yellow and green discharge. A punch biopsy was performed (Figures 1 and 2).

Figure 1:
(A) A medium power view shows subcorneal clefting with intraepidermal vesicle formation and underlying superficial dermal inflammatory infiltrate (hematoxylin & eosin; 100X). (B) A high power view demonstrates acantholysis of rounded keratinocytes with eosinophilic cytoplasm within the upper epidermis, and neutrophils and rare eosinophils within the epidermal cleft (hematoxylin & eosin; 400X).
Figure 2: Direct immunofluorescence studies (DIF) show strong intercellular deposition of IgG in the subcorneal layer, predominantly at the upper half of the stratum spinosum (DIF; 400X). Labeling with C3 antibodies shows similar findings (not shown). Immunofluorescence antibodies against IgA, IgM, and fibrinogen showed non-specific reactivity (not shown).

Diagnosis 1

Pemphigus foliaceus (PF)

Therapy with systemic prednisone (60mg/day) was initiated. The patient improved over the following days and was discharged one week later. One week after discharge, the patient returned to clinic reporting a progression of the rash with pain, fever, and malaise. Cutaneous examination was notable for discrete circular ulcers coalescing into larger, ulcerative plaques with hemorrhagic crusting, most prominent on the face, neck, lower pannus and inner thighs. Clinical concern for a herpetic infection was high and the patient was started empirically on intravenous acyclovir. She was readmitted and a biopsy from the edge of an ulcer was obtained (Figures 3 and 4).
Case History

The patient is a 32-year-old African American female who presented with a 2-year history of multiple, recurrent, ulcerated, tender skin nodules with purulent drainage on her upper back. Her past medical history was significant for traumatic implantation of wood splinters in her back during a tornado at the age of 10, as well as a diagnosis of systemic lupus erythematosus at age 27. She first noticed the back mass soon after the diagnosis of lupus and beginning of treatment with prednisone. At age 31 the mass began to ulcerate and become painful. Biopsies showed a fungal infection, for which she was treated with itraconazole and fluconazole with no significant response.

Physical examination of her back showed multiple small, verrucous, ulcerated lesions without bleeding or purulent drainage. She underwent a full-thickness excision of the mass with skin grafting (Figures 1-5).
Cutaneous Infections and Infestations

Figure 1: Cut section of the excision shows multiple, pinpoint and dark lesions throughout the subcutaneous tissue (gross photograph).

Figure 2: Nodular aggregate of suppurative and granulomatous inflammation containing pigmented hyphae is seen in a fibrotic dermis and subcutaneous tissue (40X).

Figure 3: An aggregate of pigmented hyphae is noted in the center of these suppurative and granulomatous foci (100X).

Figure 4: Multinucleated giant cells with intracytoplasmic pigmented hyphae are seen; however thick-walled sclerotic bodies and foreign materials were not identified (400X).

Figure 5: On slide culture preparation, pigmented, septate, branched hyphae as well as unbranched acropetal chains of blastoconidia were present.

Diagnosis
Subcutaneous phaeohyphomycosis, see note.
Note: The fungus isolate was identified as *Cladophialophora bantiana* by the Fungus Testing Laboratory in San Antonio, Texas.

She was started on an itraconazole regimen, but discontinued it due to the cost of the medication. She returned seven months later with a recurrent lesion on her upper back requiring another surgical excision and fungal cultures once again grew *C. bantiana*.

Comment
Phaeohyphomycosis is a term used to describe a diverse group of dematiaceous fungal infections characterized by the presence of pigmented hyphae in tissue. Four clinical categories of phaeohyphomycosis are recognized: superficial (black piedra and tinea nigra), cutaneous or corneal, subcutaneous, and visceral (systemic). There is some overlap between the cutaneous and subcutaneous forms, and the most common fungi isolated in the cutaneous and subcutaneous lesions are *Exophiala jeanselmei* and *Wangiella dermatitidis*. Overall there are at least thirty-six different species that have been listed as...
Case History

A 48 year old Vietnamese man developed a 5 centimeter in diameter nodule in the anterior abdominal wall. The lesion was asymptomatic. It was clinically thought to be a cyst or lipoma and was surgically excised.

Figure 1: A pseudocystic space within the subcutaneous adipose tissue containing a Spirometra larva exhibiting folding and branching surrounded by dense granulomatous inflammation (20X).

Figure 2: This figure illustrated the multilayered parasite with an outer non-cellular tegument. The cellular subtegumental layer contains calcareous spherules and smooth muscle fibers. The adjacent tissue exhibits granulomatous inflammation (100X).

Figure 3: A few eosinophils are appreciated within the inflammatory infiltrate (200X).
**Diagnosis**

Spirometra infestation (sparganosis)

**Comment**

**Epidemiology**

Sparganosis is an uncommon parasitic infestation caused by the larva of the pseudophyllidean tapeworm Spirometra. The adult worms are found in the intestines of canine and feline hosts. The eggs, shed by the adult, pass with the feces and hatch in water, producing coracidia (ciliated larvae) that are consumed by the first intermediate host, a crustacean (genus cyclops), and develop there into procercoid (first-stage larvae). When a snake, frog, mouse, or raccoon (second intermediate host) drinks water containing the copepod with the procercoid, the larva penetrates the intestinal wall of the new host and migrates, usually to the muscles or subcutaneous tissues, to become a plerocercoid (second-stage larva) called a “sparganum.”

Humans acquire sparganosis by ingesting contaminated water or raw or undercooked fish, frog or snake meat containing the larvae and serve as secondary intermediate hosts. When the sparganum is ingested, it actively penetrates the intestinal wall to reach the peritoneal cavity and begins to migrate systemically to subcutaneous tissue, the breast, the brain, the eye or other visceral organs. In addition, a more uncommon mode of transmission is direct inoculation onto a wound from infected amphibians or reptiles, used as a poultice; a traditional self-treatment according to ritual belief.

**Clinical Features**

Subcutaneous mass lesions, ocular sparganosis, deep visceral infections and CNS sparganosis are some of the most common clinical presentations. CNS infestations usually present with repeated and intractable headaches and progressive neurodeficit and are usually diagnosed on imaging or by surgery. Other rare presentations include pulmonary (cavitary mass lesions), intraosseous (osteolytic mass-like lesions) and intraperitoneal sparganosis. Systemic signs such as peripheral blood eosinophilia are less common. Ultrasound studies reveal a heterogeneous, hyperechoic mass with hypoechoic tubular lesion. Magnetic resonance imaging reveals multiple serpiginous tubular tracts and peripheral rim enhancement. Serologic studies such as indirect immunofluorescence and enzyme-linked immunosorbent assay (ELISA) have been shown to be useful adjunct tools in the diagnosis of sparganosis. The definitive diagnosis can be made by surgical removal and identification of the parasite.
Histopathology

The distinctive morphology of spargana in addition to the gross and histologic features is adequate for identification of Spirometra. The larva is characterized by a folded surface acellular tegument with multiple invaginations and branching and a subtegumental layer of cellular condensation. Within the body of the worm there are longitudinal muscle fibres, numerous excretory channels and calcareous corpuscles. The surrounding tissue usually exhibits a granulomatous and mononuclear cell inflammatory infiltrate composed of histiocytes, lymphocytes and eosinophils. Neutrophils are also appreciated in some cases. Varying degrees of fibrosis may be present.1-12

Therapy and Clinical Course

At this point in time, no effective chemotherapy is available for the treatment of sparganosis and surgical removal is the recommended mode of therapy which can lead to satisfactory results and favorable outcome.

References


Sanam Loghavi and Steven R. Tahan
Cases in Dermatopathology
Cutaneous Infections and Infestations

This publication is the result of collaboration of Dermatopathology Faculty of Harvard-Affiliated Hospitals in Boston including Beth Israel Deaconess Hospital, Brigham and Women's Hospital and Massachusetts General Hospital and current and former fellows of Harvard Combined Dermatopathology Training program. It contains 20 cases presented during the Slide Seminar on Cutaneous Infections and Infestations at the Harvard Dermatopathology Update CME course held in Boston on September 15-17, 2011.

Case 1  Ecthyma gangrenosum
       Julie Y. Tse and Mai P. Hoang
Case 2  Epidermodysplasia verruciformis
       Katy R. Linskey, Nicole F. Velez and Mai P. Hoang
Case 3  Cutaneous zygomycosis
       Devon C. Gimbel and Rosalynn M. Nazarian
Case 4  Cutaneous leishmaniasis
       Gabrielle Baker and Mai P. Hoang
Case 5  South American blastomycosis (paracoccidiomycosis)
       Kirsten S. W. Bellucci
Case 6  Hand foot and mouth disease
       Johanna L. Baran, Devon C. Gimbel and Lyn M. Duncan
Case 7  Kaposis' varicelliform eruption
       Stefan Kraft, Sarah N. Gee, Nicole F. Velez, Susan Burgin
       and Alireza Sepehr
Case 8  Tungiasis
       John P. Deiker and Mai P. Hoang
Case 9  Histoplasmosis
       Michael G. Olofsky and Vincent Liu
Case 10  Microsporidiosis
       M. Angelica Selim
Case 11  Chromoblastomycosis
       Anna Harris and Mary Jane Zimarowski
Case 12  Secondary syphilis
       Sara Shalin and Mary Jane Zimarowski
Case 13  Cutaneous cytomegalovirus infection
       Alice Z. C. Lobo and Mai P. Hoang
Case 14  Subcutaneous pneumococcosis
       Anna B. Gray and Mai P. Hoang
Case 15  Coccidioidomycosis
       Jessica Z. Sugianto and Mai P. Hoang
Case 16  Leprosy
       Anna Harris, Johanna L. Baran, Peter Chien
       and Beverly Faulkner Jones
Case 17  Spirometra infestation
       Sanam Loghavi and Steven R. Tahan
Case 18  Disseminated acanthamebiasis
       Ashley Ward and Steven R. Tahan

Case 19  Mycobacterium chelonae
       Gretchen W. Frieling and Alireza Sepehr
Case 20  Disseminated sporotrichosis
       Gretchen W. Frieling and Steven R. Tahan