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False Parasites in Tissue Sections

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FOCUS False Parasites in Tissue Sections

J.K. Baird

An accurate histopathological diagnosis of parasitic infections may elude experienced parasitologists and pathologists. The parasitologist is often unacquainted with parasites presented in cross-section, and the pathologist is generally unfamiliar with parasitology. Thus the parasite in tissue sections is sometimes an enigma to those with diagnostic responsibilities.

The histopathological diagnosis of a parasitic infection is often a 'best fit' based on anatomic location, histopathology and geographic location. For example, *Dirofilaria repens* in a subcutaneous abscess from an African patient can be misidentified as *Onchocerca volvulus*. Specific morphological features in tissue sections that would allow an accurate diag-

nosis are not widely known and not often considered, so it is not surprising that foreign bodies bearing a resemblance to parasites cause confusion. The result is not just misidentification, but a false positive diagnosis of a parasitic infection. Certain types of misidentification occur relatively often; occasionally quite startling errors are made (Figs 1–16, centrefold).

Common Confusion

Liesegang bodies, the product of diffusion, nucleation, flocculation/precipitation and supersaturation in colloidal solutions¹, may form in living tissues in the presence of inflammation and/or necrosis and can be confused with nematodes in tissue sec-

Some cases of misidentification are obvious...

tions. Their location in the centres of necrosis creates the illusion of cause and effect.

Artefacts in Histopathological Diagnosis of Parasites

Histopathological diagnosis can be a minefield for the unwary. Misdiagnosis can take many forms. Liesegang bodies found in living tissues in the presence of inflammation and/or necrosis are often confused with nematodes in tissue sections (Figs 1 and 2). Diagnosis tends to reflect anatomic location (eg. pulmonary dirofilariasis in lung, or the giant kidney worm in renal tissue). Serial sections should reveal the spherical geometry of the bodies. Starch grains from a bean in a necrotizing lung granuloma have also been confused with nematode eggs (Fig. 3). The non-infectious fungus *Lycopodium* produces spores that appear in necrotizing granulomas on the surfaces of organs in the peritoneal cavity and may be mistaken for eggs of *Ascaris lumbricoides* (Fig. 4). Spores of the non-infectious fungus *Helicospirum* bear a striking resemblance to microfilariae (Fig. 5), seemingly displaying cephalic spaces, nerve rings, terminal nuclei and caudal spaces. They are, however, about half the size of the smallest microfilaria. A splinter of wood in an axe wound was diagnosed as a maggot (Fig. 6). Besides lacking the morphologic features of maggots the splinter but not the parasite would have stained brilliantly with PAS (periodic acid-Schiff's reagent). A seed in an inflamed appendix was mistaken for a nematode, having a 'cuticle', 'pseudocoelom' and 'intestinal tract' (Fig. 7). Serial sections reveal seed geometry. Structures thought to be eggs of *Enterobius vermicularis* (Fig. 8) in an inflamed fallopian tube led to a diagnosis of enterobiasis. The 'eggs' are too small, incorrectly shaped and lack embryos. Insect parts occasionally appear in tissue sections. For instance pathologists occasionally see the commensal mite *Demodex folliculorum* and confuse it with pathogenic organisms such as *Sarcoptes scabiei*, lice or schistosomes; anatomic location, size and appearance should allow identification (Fig. 9). What may be parts of a moth proboscis (Fig. 10) were mistaken for eggs of *Schistosoma mansoni*. Although the 'egg' is oval, of appropriate dimensions and has a lateral spine, extraneous 'spines' are not reconcilable with helminth eggs. The 'maggot' in Fig. 11 with the essential characteristics of an arthropod (cuticle, spines, striated muscle and tracheal tubules), is really a worker Pharaoh's ant, *Monomorium pharaonis*. The ant, a common hospital pest, probably wandered into the lymph node soon after excision. AIDS patients may suffer several opportunistic infections simultaneously. This can lead to confusion. The intracellular bodies in Fig. 12 were thought to be tachyzoites of *Toxoplasma gondii* and toxoplasmosis was diagnosed, but they are cytoplasmic inclusions of cytomegalovirus (CMV). The inclusions lack nuclei, and tachyzoites of *T. gondii* are usually pyriform. A cell infected with CMV (Fig. 13) is actually a cross-section of a female *Strongyloides stercoralis*. The 'nucleus' and 'cytoplasm' show characteristics of cells infected by CMV. The 'nucleus' is, however, the ovary of the worm. A lung biopsy of a patient with pulmonary cryptococcosis and intestinal strongyloidiasis revealed an 'adult *Strongyloides stercoralis*' (Fig. 14); it was really an unknown aquatic metazoan contaminant. Diatoms in the biopsy specimen gave the game away (Fig. 15). A biopsy specimen may miss the cause of histopathologic changes. Scabies mites (Fig. 16) from erythematous nodules on the scrotum of a homosexual patient were missed initially and Kaposi's sarcoma was diagnosed. Subsequent sections revealed the mites.

Recommendations for Histopathological Diagnosis of Parasitic Infections

- 1 Measure the diameter of the 'parasite' and compare it to known values.
- 2 Study multiple sections to appreciate the geometry of the object (eg., sphere or tube).
- 3 Study special stains (eg., PAS stain for plant material).
- 4 Be sceptical (eg., nematode eggs in the lungs of a patient from North America would be extraordinary).
- 5 First study a specimen without benefit of clinical history or the opinions of others—decide on the identity of an organism based on its own merits and not on potentially misleading facts.
- 6 Seek the opinions of others without revealing one's own.
- 7 Once a diagnosis is rendered, consult a text to check agreement for morphology, life cycle, clinical symptoms and geography. Compare the general appearance with known sections of the parasite.
- 8 Many parasites in tissue sections are impossible to identify for a variety of reasons—do not feel uncomfortable with this diagnosis.

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12 Section: cytomegalovirus in lung (H & E)
Errant diagnosis: tachyzoites of *Toxoplasma gondii*

13 Section: adult *Strongyloides stercoralis* (H & E)
Errant diagnosis: cytomegalovirus

14 Micrograph: metazoan contaminant in lung (H & E)
Errant diagnosis: adult *Strongyloides stercoralis*

15 Diatom from Fig. 14 (H & E)

1 Section: Liesegang body in lung (Reticulum stain)
Errant diagnosis: pulmonary dirofilariasis due to nematode

16 Histopathological change: due to *Sarcoptes scabiei* (H & E) Diagnosis: Kaposi's sarcoma

2 Section: Liesegang body in kidney (H & E)
Errant diagnosis: giant kidney worm of dog

3 Section: starch grain (H & E)
Errant diagnosis: Nematode eggs

5 Blood smear: *Helicospirum* spore (Giemsa)
Errant diagnosis: microfilaria

4 Section: *Lycopodium* spore (H & E)
Errant diagnosis: eggs of *Ascaris lumbricoides*

6 Section: wood splinter causing abscess in axe wound (H & E)
Errant diagnosis: maggot

7 Section: plant seed in appendix (H & E)
Errant diagnosis: nematode

9 Section: *Demodex folliculorum* (H & E)
Errant diagnosis: *Sarcoptes scabiei*, lice and schistosomes

8 Section: pollen grains in fallopian tube (H & E)
Errant diagnosis: eggs of *Enterobius vermicularis*

10 Section: moth proboscis(?) (H & E)
Errant diagnosis: eggs of *Schistosoma mansoni*

Non-infectious fungi produce spores that may lead to misdiagnosis. When lycopodium spores are diagnosed as *Ascaris lumbricoides* eggs, patients invariably have a history of laparotomy in the Soviet Union where the spores once occurred in the talc of surgeon's gloves. Spores of *Helicospirum* may be confused with microfilariae. Plant fibers, seeds and pollen also are a potential hazard. They may appear in almost any organ of man and present bizarre structures in tissue sections that are confused with parasites.

Insect parts occasionally appear in tissue sections. They are usually mouthparts of ticks, mosquitoes or lepidoptera, stings from hymenoptera, or commensal mites. These structures are confused with nematodes, maggots, scabies mites, maggots or helminth eggs.

Patients with acquired immune deficiency syndrome (AIDS) may suffer several opportunistic infections simultane-

ously. These are sometimes first recognized in tissue sections and misidentified, or as with the scabies mites the true cause of symptoms may be overlooked, and only discovered on subsequent re-examination².

Avoiding Errors

Although some of the examples given (such as a Pharaoh's ant stumbling into an excised lymph node) are decidedly peculiar, the problem of misidentification is more widespread. To avoid confusion, a set of guide-lines should be adhered to (see centrefold). These involve the careful analysis of the size, structure and staining pattern of the 'parasite'. Histopathological investigation should proceed without knowledge of clinical history and outside opinion, and at a later stage advice should be sought without any attempt to influence this advice. On diagnosis, texts should

be examined^{3,4} to see if they accord with the characteristics of the parasite and the patient's condition, and known reference sections^{4,5} of the parasite should be consulted. But finally, at the end of the process, it is no failure to be still unsure of the identity of the parasite.

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