

Pulse Granulomas Detected in Gallbladder, Fallopian Tube, and Skin

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● **Context.**—Foreign material typically elicits reactions dominated by multinucleated giant cells. Pulse granulomas are peculiar reactions to particles of food that are characterized by clusters of small to medium-sized hyaline rings. Pulse granulomas are rare and have occupied only the lungs, in association with aspiration, and the alimentary canal, in association with oral pathology, colonic diverticula, and a rectal mass.

Objective.—To report pulse granulomas that occupied previously unrecognized sites and to alert pathologists to the diagnostic pitfall of mistaking pulse granulomas for other entities.

Design.—We retrospectively reviewed 3 recently encountered cases that involved pulse granulomas in the gallbladder, fallopian tube, and skin.

Results.—In all cases, pulse granulomas were associated with fistulae involving the gastrointestinal tract. One fistula was clinically occult. Microscopy showed barium-lad-

en histiocytes admixed with hyaline rings, with or without vegetable matter, confirming fistulae involving the gastrointestinal tract. Absence of other features of chronicity, including sarcoid-type granulomas and Langhans-type giant cells, helped to essentially exclude Crohn disease. In 1 case, hyaline rings of pulse granulomas closely resembled hyaline vasculopathy of amyloidosis, diabetes, or hypertension. Surprisingly, polariscopy failed to detect any vegetable matter. In 1 case, negative polariscopy contributed to the difficulty in finding rare vegetable matter.

Conclusions.—We demonstrated that pulse granulomas can occur outside the lungs and alimentary canal, and can be associated with fistulae involving the gastrointestinal tract. Awareness of this finding is necessary to avoid confusion with Crohn disease and hyaline vasculopathy. Polariscopy may fail to detect vegetable matter.

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Pulse granulomas are rare entities characterized by aggregates of thin, faintly eosinophilic hyaline rings often admixed with acute and chronic inflammation and multinucleated giant cells. The rings vary in size and shape, and are usually associated with demonstrable particulate vegetable matter.¹ Therefore, pulse granulomas are widely regarded as unusual reactions to vegetable matter.^{1,2} Most pulse granulomas affect the oral cavity, in association with oral pathology or dental procedures,³ or the lungs after aspirating vegetable matter.⁴ Pulse granulomas were recently shown to occupy the colorectum in association with colonic diverticula² and a rectal mass.¹ To the best of our knowledge, we report the first demonstration of pulse granulomas to involve the gallbladder, fallopian tube, and skin.

MATERIALS AND METHODS

All cases were obtained from the in-house files of the Department of Pathology and Laboratory Medicine at the University of California Irvine Medical Center, Orange. The cases were accessioned between September 3, 2004, and May 13, 2005. For each

case, 4 μm -thick hematoxylin-eosin-stained sections were prepared from routinely processed, formalin-fixed, paraffin-embedded material.

RESULTS

Case Histories

The Table summarizes the clinicopathologic findings of all cases.

Case 1.—A 65-year-old woman with a history of multiple surgeries for enterocolonic diverticula presented for operative management. Fistulogram and small bowel follow-through with barium showed 2 abdominal midline enterocutaneous fistulae. At laparotomy, 4 fistulae (2 jejuno-cutaneous, 2 ileocutaneous) were found. Extensive enterectomy and fistulectomy were performed. Her postoperative course was complicated by sepsis caused by methicillin-resistant *Staphylococcus aureus*.

The pathologic specimens consisted of large fusiform pieces of skin attached to enteric segments. The aggregate length of the enteric segments was 140 cm. Extensive enteroenteric adhesions markedly distorted the specimens. Opening the bowel revealed fecal impaction by abundant yellow and bilious vegetable matter.

Microscopy showed skin and subcutis with extensive fibrosis and patchy acute and chronic inflammation. Two prominent pulse granulomas occupied the reticular dermis, the largest measuring 9×4 mm (Figures 1 and 2). The pulse granulomas contained thin, faintly eosinophilic hyaline rings ranging from $39 \times 28 \mu\text{m}$ to $415 \times 232 \mu\text{m}$ admixed with moderately dense acute and chronic inflam-

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Summary of Clinicopathologic Findings							
Case	Age, y/ Sex	History	Fistulae	Site of Pulse Granuloma	Subsite	Other Findings	Postoperative Course
1	65/F	Diverticulitis	Enterocutaneous	Skin	Reticular der- mis	Barium-laden histiocytes	Sepsis
2	81/F	Diabetes, cholelithiasis	Cholecystogastric	Gallbladder	Muscularis	Congophobia	Hypertension, anxiety
3	76/F	Adenocarcinoma	Rectosalpingeal	Fallopian tube	Plicae	Barium-laden histiocytes	Uneventful

mation. The hyaline rings were rounded, ellipsoidal, or convoluted. Inflammatory cells, erythrocytes, fragments of faintly eosinophilic hyaline material, and calcium phosphate were in the lumina of the rings. Abundant vegetable matter was interspersed between the hyaline rings. The pulse granulomas also contained multinucleated foreign body-type giant cells, which appeared to ingest vegetable matter, as well as collections of barium-laden histiocytes (Figure 3).

Microscopy of the enteric segments revealed severe acute serositis and fibrosis.

Case 2.—An 81-year-old woman with a history of diabetes mellitus type 2 and cholelithiasis was admitted for evaluation of pain in the abdominal right upper quadrant, nausea, and vomiting. She was bacteremic with *Escherichia coli*, but hemodynamically stable without sepsis. Computed tomography showed attachment of the gallbladder to the stomach. Exploratory laparotomy was performed for presumptive acute cholecystitis and cholecystogastric fistula. At laparotomy, a small, contracted gallbladder attached by a fistula to the gastric antrum was noted. Cholecystectomy was followed by ligation of the fistulous tract and gastric repair. Postoperatively, the patient was treated for hypertension and anxiety.

The pathologic specimen was a cylindrical portion of gallbladder measuring 4.5 × 3 × 2 cm that was received opened and without choleliths. There was diffuse fibrosis with a maximal mural thickness of 0.6 cm.

Microscopy showed acute and chronic cholecystitis. There were several small pulse granulomas in the muscularis. Vegetable matter was initially difficult to find. Further review showed 1 small pulse granuloma consisting of small hyaline rings and multinucleated foreign body-type giant cells partially surrounding vegetable matter (Figure 4). The hyaline rings closely resembled hyaline vasculopathy of amyloidosis, diabetes, or hypertension. A precautionary special stain proved the hyaline rings to be Congo-phobic.

Case 3.—A 76-year-old woman with a history of rectal adenocarcinoma resected 1 year previously was admitted for evaluation of pelvic pain. Colonoscopy showed purulence at the colorectal anastomosis. Barium enema showed a sinus tract distal to the anastomosis. At laparotomy, massive adhesions, fibrosis, and purulent exudate in the pelvis were encountered. Adhesions were lysed and the anastomosis was resected. Hartmann operation and colostomy were then performed. The patient had an uneventful postoperative course and continues to be free of complications.

The pathologic specimens consisted of multiple colorectal segments, including the anastomosis, ranging from 2.4 × 2.2 cm to 9.5 × 7.8 cm. Opening the segments revealed focal rectal ulceration and a small amount of fecal mate-

rial. Gynecologic organs were difficult to appreciate grossly.

Microscopy of 1 specimen showed rectal tissue attached to an incidental portion of fallopian tube. The portion of fallopian tube had plicae expanded by pulse granulomas containing small to medium-sized hyaline rings, multinucleated foreign body-type giant cells, barium-laden histiocytes, and calcium phosphate (Figure 5). The specimens were negative for polyps, diverticula, adenocarcinoma, or vegetable matter.

In all cases, polariscopy highlighted minute shards of cytoplasmic foreign material within histiocytes (Figure 3) but failed to highlight vegetable matter. We overlooked these shards at initial examination. The shards refracted nonpolarized light at retrospective review. All patients denied using illicit drugs. In all cases, Crohn disease was considered in view of fistulae involving the gastrointestinal tract. However, Crohn disease was essentially excluded on the basis of the absence of architectural disarray, basal lymphoplasmacytosis, metaplasia, sarcoid-type granulomas, or Langhans-type giant cells.

COMMENT

Hyaline rings were initially detailed in 1969 by Knoblich,⁴ who noted these lesions in human lungs and reproduced similar lesions in various nonprimate animal lungs by injecting broth of lentils, the seeds of leguminous plants. Lentils consist of grains of starch within honeycomb-like structures, the cotyledons, and the shell-like structures that surround the cotyledons, the spermo-dermis. Knoblich showed that cotyledons, composed of cellulose, incited the hyaline rings. Until that time, such lesions were known as "lentil pulse pneumonia."

The term *pulse granuloma* was later applied to similar lesions that occupied the orofacial region.⁵ Lewars⁶ proposed that these lesions were responses to particles of food driven into mucosa by dentures. Subsequently, several orofacial and occasional pulmonary pulse granulomas have been reported. Most cases demonstrated vegetable matter, bolstering the prevailing notion that hyaline rings represent unique reactions to vegetable matter.^{1,2,7,8}

In 2001, the first gastrointestinal pulse granuloma was reported, in the context of a rectal mass.¹ Two cases involving colonic pulse granulomas associated with perforated diverticula were recently reported.² In all 3 cases, vegetable matter was identified, indicating that trauma or perforation led to deposition of vegetable matter and creation of colorectal pulse granulomas.

We demonstrated that pulse granulomas can occur outside the alimentary canal and lungs, in association with passage of gastrointestinal contents through fistulae. In all of our cases, the presence of fistulae between the gastrointestinal tract and other organs was proven by either

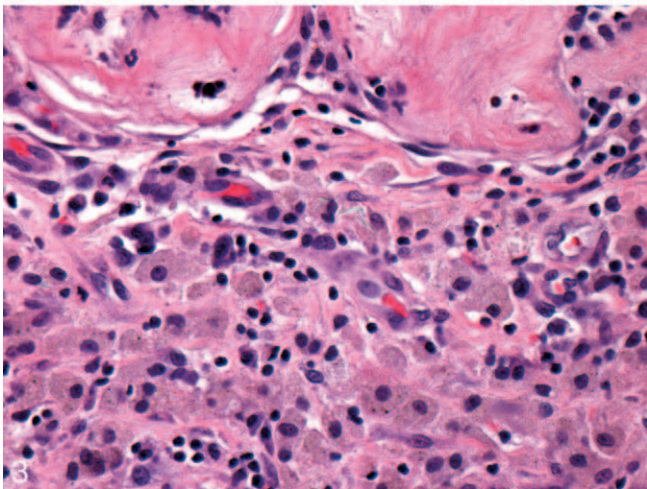
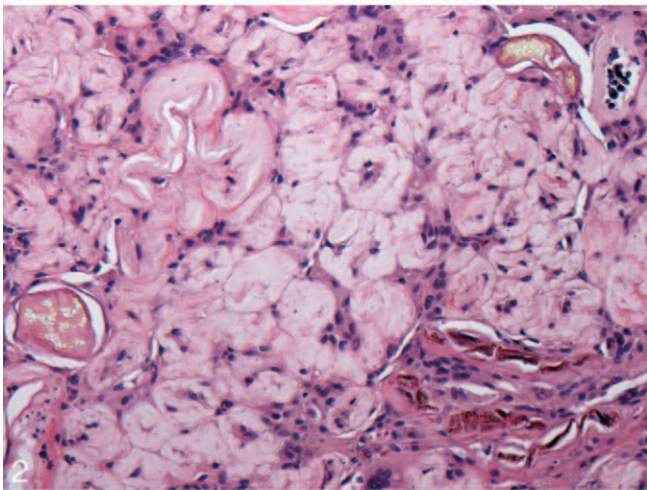
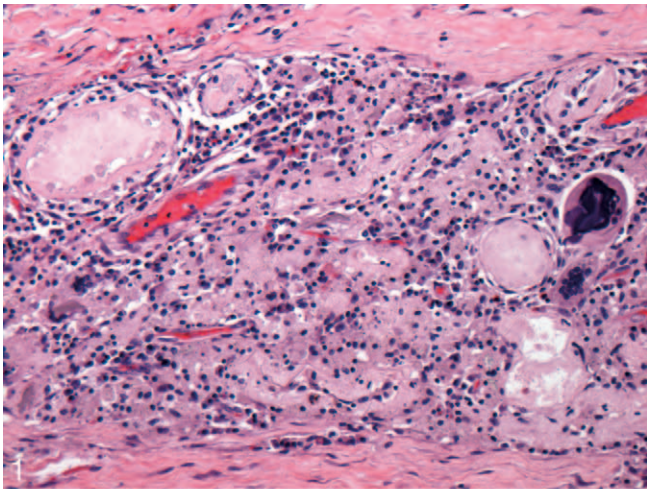


Figure 1. Case 1, pulse granuloma with mixture of hyaline rings (upper left), inflammation, including multinucleated foreign body-type giant cell (right), and calcium phosphate (right) (hematoxylin-eosin, original magnification $\times 400$).

Figure 2. Case 1, hyaline rings, one filled with calcium phosphate (upper right) and vegetable matter (upper right, lower left, and lower right) (hematoxylin-eosin, original magnification $\times 400$).

Figure 3. Case 1, barium-laden histiocytes with rare minute refractile shards (center) (hematoxylin-eosin, original magnification $\times 600$).

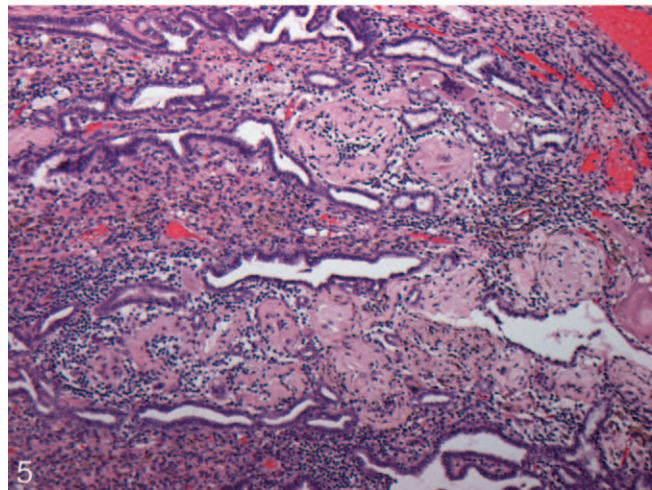
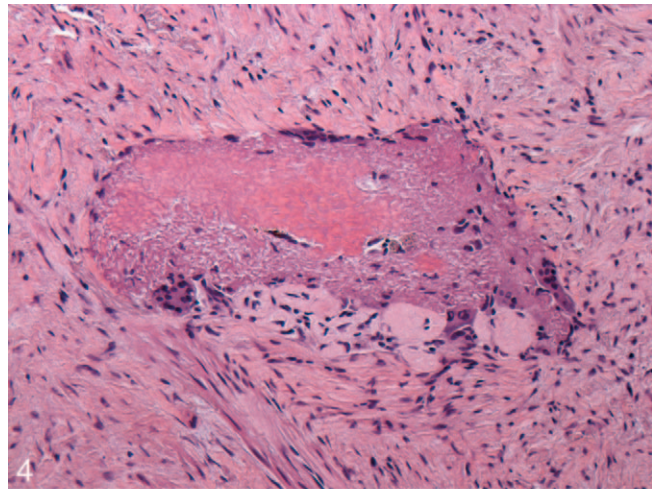


Figure 4. Case 2, small hyaline rings and multinucleated foreign body-type giant cells partially surround vegetable matter (hematoxylin-eosin, original magnification $\times 400$).

Figure 5. Case 3, hyaline rings expand plicae of fallopian tube (hematoxylin-eosin, original magnification $\times 200$).

gross visualization of the fistulae or by the presence of barium-laden histiocytes or vegetable matter deep in the various organs. In case 1, multiple enterocutaneous fistulae were seen radiographically, and the presence of barium-laden histiocytes and vegetable matter deep in the dermis confirmed the escape of enteric contents through enterocutaneous fistulae into skin. In case 2, although the patient was spared procedures with barium, laparotomy demonstrated a cholecystogastric fistula and rare vegetable matter was seen deep in the gallbladder. In case 3, a fistula was clinically occult and vegetable matter was absent. However, pulse granulomas in the plicae of the fallopian tube provided indirect evidence for the presence of vegetable matter, and along with barium-laden histiocytes provided evidence for a rectosigmoid fistula.

The subsites of each organ occupied by pulse granulomas were also significant. If the pulse granulomas had been confined to the serosa of the gallbladder or fallopian tube, the pulse granulomas would have represented implants secondary to perforation. However, because pulse granulomas were deeply embedded in the muscularis or plicae, they most likely indicated fistulae rather than merely perforation. Fistulae involving the gastrointestinal tract

raised the possibility of Crohn disease; however, absence of other characteristics that define Crohn disease, such as architectural disarray, basal lymphoplasmacytosis, metaplasia, sarcoid-type granulomas, or Langhans-type giant cells with arcuate multinucleation, strongly argued against Crohn disease.

The histology and ultrastructure of pulse granulomas have been well described.^{3,4,7} Our histologic findings generally correlated well with those described by others, particularly in case 1, in which there was abundant vegetable matter and frequent hyaline rings. In case 2, however, hyaline rings were small and rare, and closely resembled hyaline vasculopathy. Staining with Congo red and a meticulous search for vegetable matter helped exclude amyloidosis, diabetes, or hypertension, as noted previously by others.²

Surprisingly, in all of our cases, polariscopy failed to highlight vegetable matter, but polarized minute shards of cytoplasmic foreign material in histiocytes that we overlooked initially. At retrospective review with nonpolarized light, these shards were translucent and refractile. Other authors described similar foreign material and presumed this foreign material to be cellulose originating from polarizable vegetable matter.⁹ However, because vegetable matter in our cases failed to polarize, these shards may represent other foreign materials, possibly talc or calcium oxalate. In case 2, negative polariscopy contributed to the difficulty in finding rare vegetable matter.

The precise composition of the hyaline rings is controversial. In our cases, vegetable matter was exclusively outside the hyaline rings, suggesting that the hyaline rings represented structures other than vegetable matter. Similar findings have been reported by others.⁷ The hyaline

rings were previously thought by some authors to represent vasculitis¹⁰; however, there remains little evidence to support this theory. Hyaline rings have shown ultrastructural features of degenerated collagen⁷ and cellulose.⁸

We discovered pulse granulomas in new sites, namely, the gallbladder, fallopian tube, and skin. Pulse granulomas and barium-laden histiocytes situated deeply in organs, with or without vegetable matter, can indicate fistulae involving the gastrointestinal tract that result from causes other than diverticula or Crohn disease. Hyaline rings of pulse granulomas may closely resemble hyaline vasculopathy. Polariscopy may fail to highlight vegetable matter.

We dedicate this article to the memory of Klaus J. Lewin, MD, FRCPath.

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