

原文題目(出處)：	Infectious pseudotumors: Red herrings in head and neck pathology. Head and Neck Pathol 2012;6:58-63
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內文：

[Abstract]

- Infectious pseudotumors are tumor-like growths caused by specific microbial organisms.
- Specific and nonspecific immunohistochemical staining profiles may lead to the consideration of a wide range of benign and malignant neoplastic processes.
- In both cases, microbial virulence factors affecting phagocytosis prolonged their intracellular survival and resulted in active histiocytic proliferation.
- Accurately identifying these lesions and the specific causative agent is of particular significance since they can be successfully treated with antibiotics.

[Introduction]

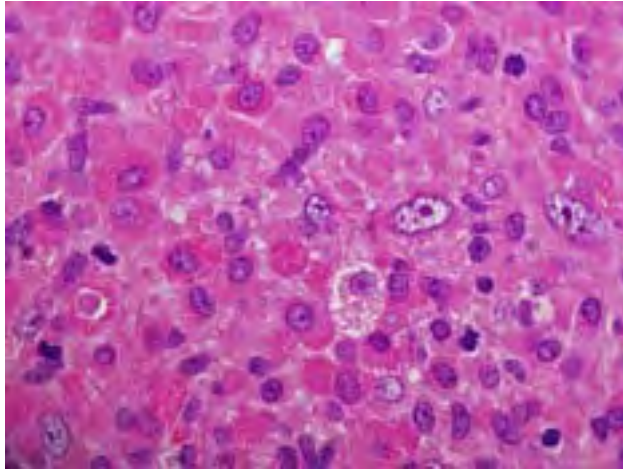
- Infectious pseudotumors of the head and neck are nonneoplastic tumorous lesions resulting from unusual histiocytic proliferation caused by specific microbial infections.
- Varied Immunohistochemical profiles with specific and nonspecific staining results can be misleading and suggest the consideration of a wide differential diagnosis including carcinomas, sarcomas, and lymphomas.
- Two such cases are reported here, one presenting as an obstructive upper tracheal mass caused by Rhodococcus equi, and the other a tumorous nasal lesion caused by Klebsiella rhinoscleromatis infection.

[Case 1]

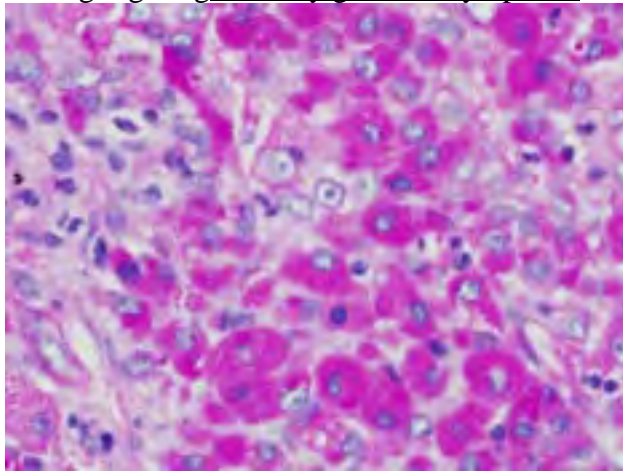
- A 47-year-old man presented to the emergency room with stridor and respiratory obstruction.
- Radiographic imaging showed an exophytic mass near the tracheo-laryngeal junction that almost completely occluded the airway.
- The lesion recurred shortly after the initial excision and another debulking was performed.
- The patient was later found to be positive for HIV with a viral load of 475 copies/mL and a CD4+T-cell count of 32 cells/mm.
- the excised material was sent for bacterial culture and the sample grew R. equi.

[Microscopic Examination]

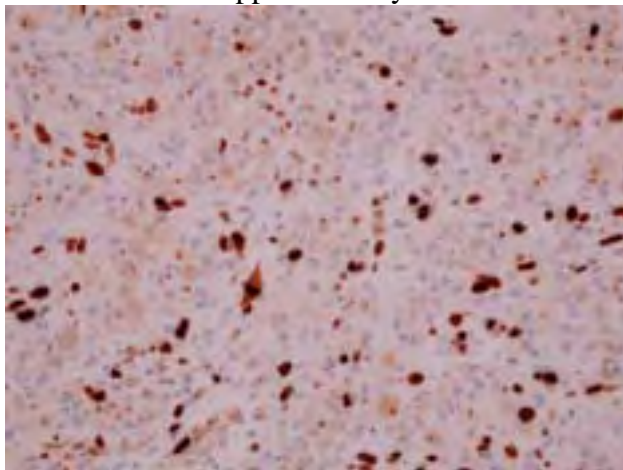
- initial biopsy specimen showed sheets of large epithelioid cells with large nuclei and prominent nucleoli. The cells were distinguished by abundant, deeply eosinophilic coarsely granular cytoplasm. Occasional mitotic figures and apoptotic cells were identified



- The epithelioid cells were positive for PAS stain after diastase digestion (PAS/D) highlighting coarsely granular cytoplasm



Ki-67 score was approximately 20%



Ki-67 immunostain showing positive nuclear reactivity in more than 20% of the cells, in some parts of the R. equi pseudotumor

(-):

- . Special stains for acid fast bacilli (Ziehl-Neelsen) and atypical mycobacteria (Fite)
- . Warthin-Starry and Gomory methenamine silver (GMS) stains
- . phosphotungstic acid hematoxylin (PTAH) stain
- . cytokeratins AE1/AE3, CAM 5.2, CK7, and CK20.
- . epithelial membrane antigen (EMA) and the muscle markers, Desmin, muscle specific

actin (MSA), and myoglobin.

. Melan A, TTF-1 and thyroglobulin

(+):

. a tissue Gram stain highlighted Gram positive intracytoplasmic coccobacilli

. vimentin, S100 protein, CEA, CD31, CD45, and CD68.

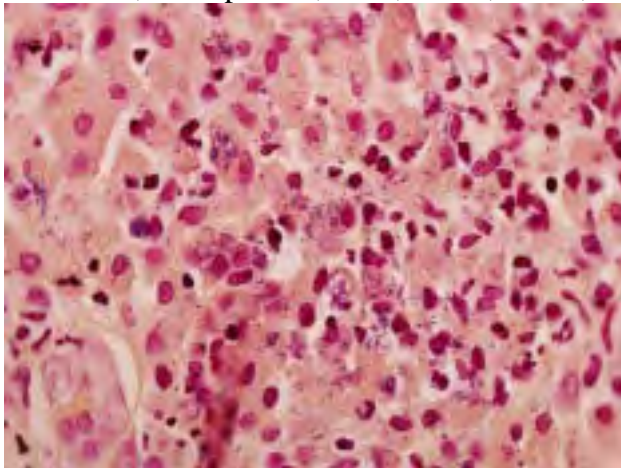


Fig. 4 Tissue Gram stain highlighting intracellular Gram-positive coccobacilli of *R. equi*

- a diagnosis of *R. equi* infectious pseudotumor was rendered.

[Discussion]

- The differential diagnosis of a lesion included oncocytic carcinoma, Hurthle cell carcinoma, and pleomorphic rhabdomyosarcoma.

Oncocytic carcinoma

- a rare malignant salivary gland neoplasm that affects predominantly the major glands
- have large nuclei and prominent nucleoli.
- eosinophilic cytoplasm is finely granular as a result of accumulation of excessive number of mitochondria
- Phosphotungstic acid-hematoxylin (PTAH) stain→(+)

Hurthle cell carcinoma

- an oncocytic variant of follicular carcinoma of the thyroid, rarely show extra-thyroidal extension into the trachea
- have large nuclei, prominent nucleoli and deeply eosinophilic granular cytoplasm
- positively for thyroglobulin, TTF-1 and may or may not be positive for keratin
- caused by excessive accumulation of mitochondria and is, therefore, PTAH positive

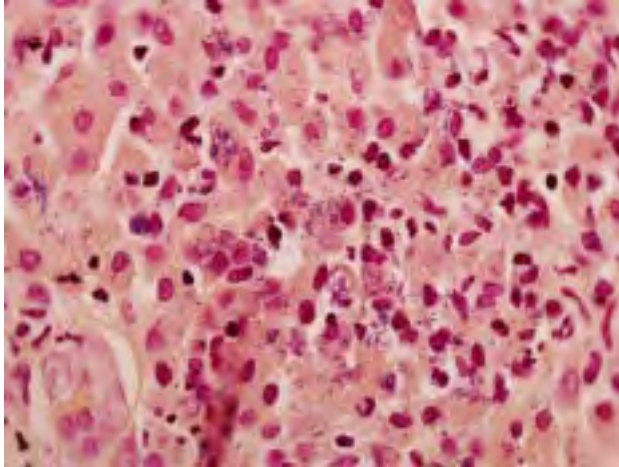
Pleomorphic rhabdomyosarcoma

- a rare neoplasm affecting adults, more commonly male patients, usually in the muscles of the extremities but may rarely occur in the head and neck
- desmin, muscle specific actin (MSA) and myoglobin are generally positive

Acinic cell carcinoma

- PAS-positive diastase-resistant cytoplasmic granules were identified in the lesion.
- PAS-positive diastase-resistant material identifies zymogen granules in acinic cell carcinoma.
- the cytoplasmic granules in acinic cell carcinoma are basophilic.
- the vimentin and S100 immunoreactivity may suggest malignant melanoma, the deeply eosinophilic granular cytoplasm seen in this lesion makes it unlikely, moreover, a Melan-A immunostain was negative

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- Immunoreactivity for CD45 and CD68 identified the cells as histiocytes/macrophages
 - Special stains for acid fast bacilli (Ziehl-Neelsen) and atypical mycobacteria (Fite) were negative
 - Warthin-Starry stain was negative for spirochetes
 - GMS stain was negative for fungi but highlighted bacterial organisms.

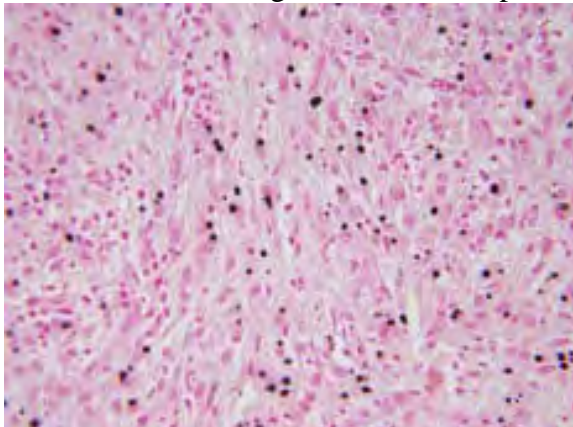


A tissue Gram stain highlighted gram positive intracytoplasmic coccobacilli

- The patient was started on HAART therapy in addition to an antibiotic regimen including vancomycin, meropenem, and azithromycin, based on known susceptibility of *R. equi*

R. equi

- a Gram positive coccobacillus soil organism that has long been known as a pulmonary pathogen that causes pneumonia in foals, and more recently, in AIDS patients
- arresting the normal pathway of phagosome maturation and normal phagocytosis
- can survive the phagolysosomal microenvironment in macrophages by suppressing acidification of the phagolysosomes
- Virulent *Rhodococcus* strains carry extrachromosomal plasmids expressing a variety of virulent genes in the Vap family (VapA-G). Vap A protein has been shown to stabilize the phagosomal membrane, thus suppressing its acidification by lysosomes
- able to survive and proliferate within an almost neutral phagolysosomal environment
- Some cases of *R. equi* pseudotumors show Michaelis-Gutmann bodies analogous to those that are diagnostic of malakoplakia



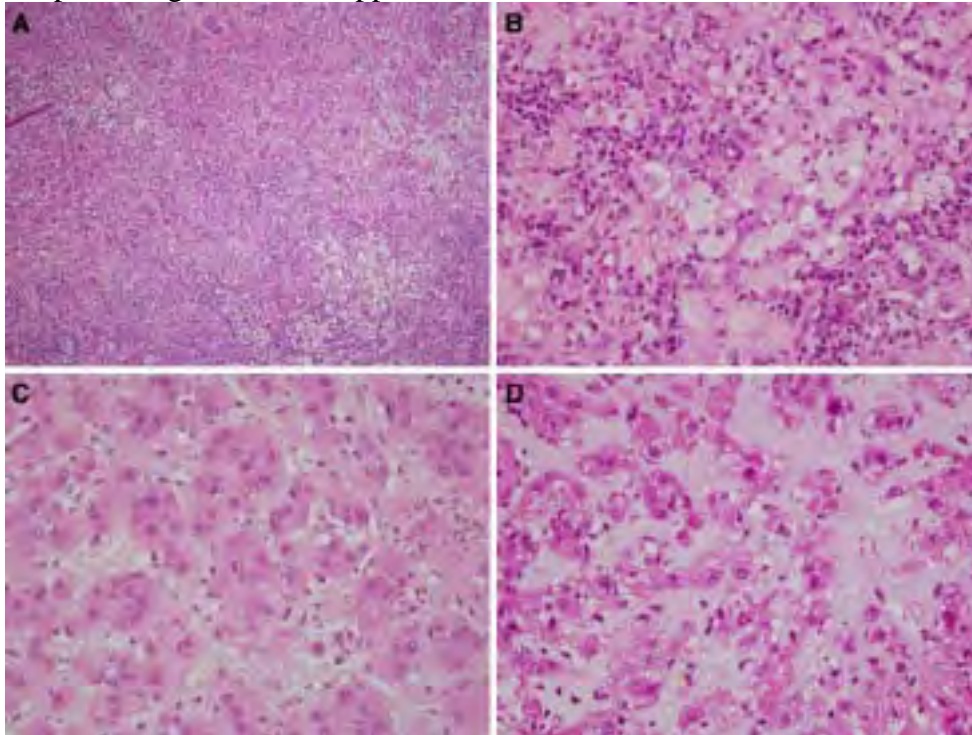
- the lysosomal abnormality is believed to be an inherent rather than acquired one
- The abnormality has been shown to be due to an intra-cellular cyclic-GMP deficiency, which is correctable by cholinergic agonists

[Case 2]

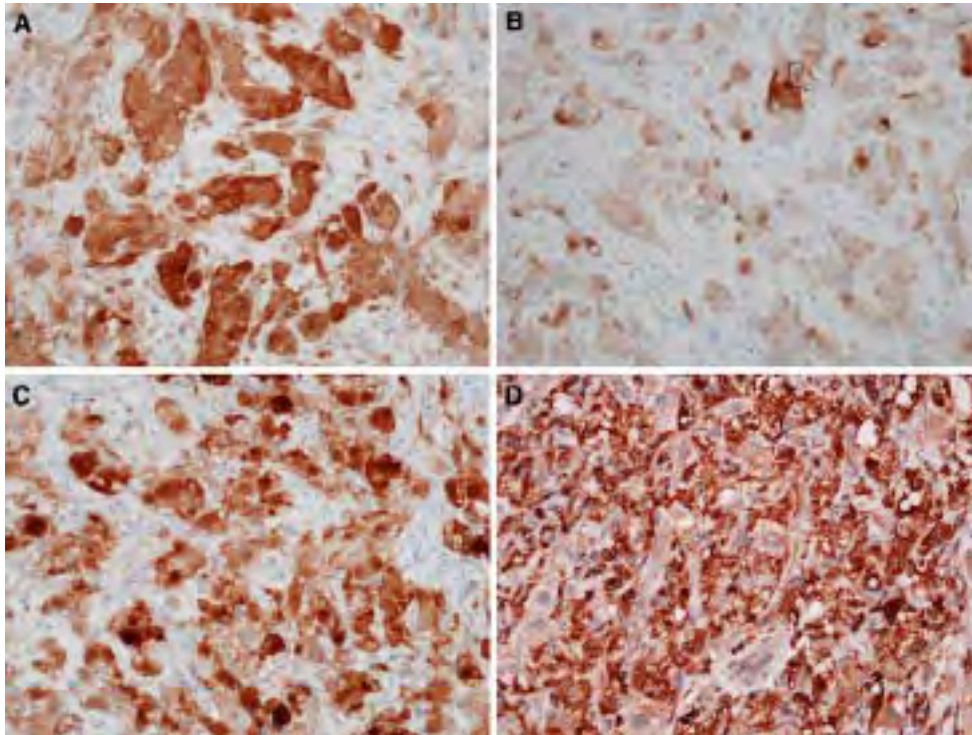
- A 44-year-old male patient had a polypoid lesion of the nasal cavity.
- The lesion was biopsied and the frozen section diagnosis was carcinoma.
- the case was received as a consult with a differential diagnosis including paraganglioma and chordoma.

[Microscopic Examination]

- a hypercellular lesion composed of epithelioid cells intermixed with plasma cells showing numerous Russell bodies.
- The epithelioid cells formed sheets and nests in a fibromyxoid stroma
- In focal areas, the cells demonstrated prominent cytoplasmic vacuolization producing a foam cell appearance, Occasional multinucleated cells were observed.



- lesional cells were positive for vimentin, S100 protein, NSE, calretinin, and CD68
- EMA showed cytoplasmic, nonmembranous staining
- negative for AE1/AE3, CK5/6, and MSA.



- A tissue gram stain was negative and the Steiner stain showed a few bacillary organisms but was difficult to interpret because of background staining.
- A GMS stain was negative for fungi, however, it highlighted numerous bacillary organisms within the vacuolated cells, consistent with *K. rhinoscleromatis*

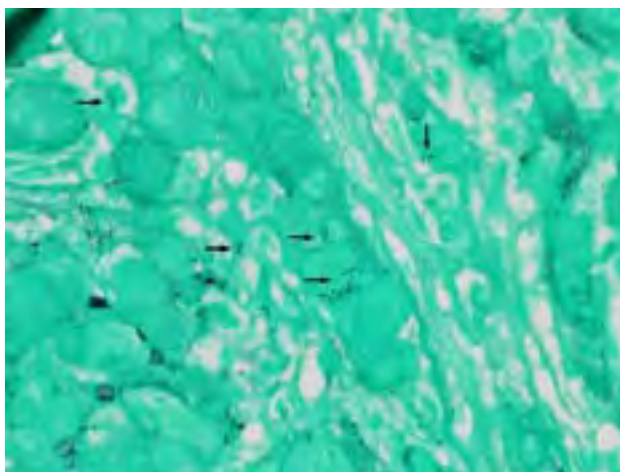


Fig. 8 Rhinoscleroma: GMS stain showing intracellular bacillary microbial organisms (arrows)

- No microbial culture was done and the patient is reportedly doing well after surgery and antibiotic treatment.

[Discussion]

paraganglioma (PGL)

- The epithelioid nesting pattern of the histiocytes in some areas and a positive reactivity to NSE and calretinin suggested the diagnosis of paraganglioma (PGL).
- two types of cells: epithelioid chief cells and spindled sustentacular cells.
- The epithelioid cells are arranged in a characteristic alveolar or Zellballen pattern and contain neurosecretory granules that stain positively for neuroendocrine markers, including NSE and calretinin.

- The sustentacular cells are devoid of neurosecretory granules and are located at the periphery of the Zellballen.
- These cells react positively with S100 protein antibodies.
- In the current lesion, the epithelioid cells were positive for S100 protein and no sustentacular cells were identified, effectively ruling out PGL as the diagnosis.
- PGLs typically arise in the carotid body, middle ear, jugular bulb, or the vagus nerve.

Chordoma

- present as an osteolytic lesion arising in the sphenoccipital region. they have rarely been reported in the sinonasal tract.
- It showed aggregates of epithelioid cells arranged in nests and sheets dispersed throughout a fibrous and myxoid stroma. Many of the cells had prominent cytoplasmic vacuoles
- “physalliferous” (bubbly or vacuolated) cells, while in rhinoscleroma they are known as Mikulicz cells.
- Positive reactivity to S100 protein and EMA in the present lesion added further support to the misdiagnosis of chordoma.
- However, the histiocytic nature of the cells was eventually confirmed by CD68 reactivity and special microbial stains, which highlighted bacillary microorganisms, many of which were intracellular and associated with Mikulicz cells

Rhinoscleroma

- Rhinoscleroma is a chronic progressive infectious disease that is endemic to areas in Africa, South East Asia, and Central and South America.
- The causative bacterium is a Gram negative bacillus known as *K. rhinoscleromatis*.
- Increased incidence among family members and household contacts has been reported and genetic predisposition has been suggested.
- has low infectivity; transmission is believed to be by airborne secretions
- affects predominantly the nasal cavity and, less commonly, the nasopharynx, larynx, nasal sinuses, and oral cavity.
- It has been suggested that the term “scleroma” is more appropriate
- Progression of the nasal disease leads to deformity and destruction of the nasal cartilage.

initial “rhinitic/catarrhal” phase

- associated with red atrophic mucosa

proliferative phase

- the characteristic microscopic features are well expressed

fibrotic or sclerotic phase

- lead to stenosis and disfigurement

- The lesion in the proliferative phase is typically composed of an inflammatory cell infiltrate with histiocytes mixed with lymphocytes and plasma cells. Mikulicz cells, which are foamy macrophages with prominent vacuolated cytoplasm, are abundant at this stage.

- *K. rhinoscleromatis* bacilli are found within the cytoplasm of these cells.
- the vacuoles contain accumulated mucopolysaccharides derived from the polysaccharide capsule of *K. rhinoscleromatis*
- Tissue Gram stain is usually negative, but silver impregnation methods often demonstrate the organism
- Tissue culture for *K. rhinoscleromatis* may be positive in only 50% of the cases

- Treatment involves surgical debridement and antibiotic therapy. Ciprofloxacin and rifampin are shown to be effective drugs

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- Other examples of microbial infections that may cause nongranulomatous histiocytic proliferation and pseudotumor formation in the upper aerodigestive tract (UADT) include histoplasmosis and lepomatous leprosy.
 - The organism also stains with GMS and PAS special stains.
 - Lepomatous leprosy may manifest in the UADT prior to the development of skin lesions. A Fite stain demonstrates the acid fast bacilli of *M leprae*.

[Summary]

- two cases are presented in which bacterial infection by *R. equi* and *K. rhinoscleromatis*, respectively, resulted in the development of tumorous masses.
- In both cases, microbial virulence factors affecting phagocytosis prolonged their intracellular survival and resulted in active histiocytic proliferation.
- In the case of *R. equi* infection, reduced acidification of phagosomes interfered with proper phagocytosis and resulted in increased pH and consequent cytoplasmic eosinophilia.
- In the second case, the polysaccharide capsule of *K. rhinoscleromatis* prevented phagocytosis.
- While infectious pseudotumors are rarely encountered in the practice of surgical pathology, it is of Importance to realize that infectious processes can closely mimic neoplastic lesions.

題號	題目
1	<i>Klebsiella rhinoscleromatis</i> 哪一個 stain 染出來為陽性反應? (A) Special stains for acid fast bacilli (Ziehl-Neelsen) and atypical mycobacteria (Fite) (B) S100 protein (C) Warthin-Starry and Gomory methenamine silver (GMS) stains (D) phosphotungstic acid hematoxylin (PTAH) stain
答案(B)	出處：Infectious pseudotumors:Red Herrings in Head and Neck Pathology
題號	題目
2	下列何者不是 Rhinoscleroma 的三個 phase 之一? (A) initial “rhinitic/catarrhal” phase (B) proliferative phase (C) Inflammation phase (D) fibrotic or sclerotic phase
答案(C)	出處：Infectious pseudotumors:Red Herrings in Head and Neck Pathology