



Rapidly Progressive Malignant Pelvic Perivascular Epithelioid Cell Neoplasm (PEComa) Associated with *Eggerthella lenta* Bloodstream Infection

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Perivascular epithelioid cell tumors (PEComa) are rare mesenchymal neoplasms composed of cells that express melanocytic and myogenic markers and grow around small blood vessels. PEComa often show benign behaviors but can also be highly aggressive. In frail and more complex patients, many conditions can overlap, compounding the diagnostic and therapeutic difficulties inherent in rare diseases. Moreover, the complexity of modern patients introduces new and significant players in host-microbe interactions, and emerging pathogens represent a relevant challenge to modern healthcare. Among these pathogens is *Eggerthella lenta*, an anaerobic gram-positive bacterium of the normal gut microbiota associated with life-threatening infections. Here, we present a case of malignant pelvic PEComa with rapid metastatic progression in a 73-year-old man who presented with an *E. lenta* bloodstream infection. Approaching differential diagnosis with open-mindedness may assist in better imaging interpretation, surgery scheduling, and proper treatment planning. Despite progress in diagnostic techniques for a more accurate pathogen diagnosis and characterization, a good dose of wisdom is vital to avoid overlooking potentially harmful pathogens, particularly in frail individuals.

Key Words: Perivascular epithelioid cell neoplasms, *Eggerthella lenta*, Infections, Abdominal abscess, Sepsis, Microbiota, Frailty, Emerging pathogens, Bloodstream infection

INTRODUCTION

Perivascular epithelioid cell tumors (PEComa) are rare mesenchymal neoplasms composed of cells that express melanocytic and myogenic markers and grow around small blood vessels. While PEComa usually exhibit benign behavior, highly aggressive forms also exist.¹⁾ In frail and more complex patients, many conditions responsible for disability, hospitalization, institutionalization, and mortality can overlap with the diagnostic and therapeutic difficul-

ties inherent in dealing with rare diseases. The complexity of modern patients introduces new and significant players in host-microbe interactions, and emerging pathogens represent a relevant challenge in modern healthcare.²⁾ Among these pathogens is *Eggerthella lenta*, an anaerobic gram-positive bacterium of the normal gut microbiota associated with life-threatening infections.^{3,4)}

We present a case of malignant pelvic PEComa with rapid metastatic progression in a 73-year-old man who presented with *E. lenta* bloodstream infection. Written informed consent was obtained for

the publication of this case report.

CASE REPORT

A 73-year-old man was admitted to our hospital with a fever and abdominal pain. He had a history of hypertension, chronic kidney disease (CKD), benign prostatic hyperplasia (BPH) treated with partial prostatic resection 14 years earlier, and bilateral internal carotid artery stenosis. He was independent in activities of daily living (ADL) and instrumental activities of daily living (IADL) before admission.

He reported chronic stypsis and weight loss during the last 4 months. Two months before, he had undergone an endoscopic closure procedure for linear fissuration of the sigmoid colon. He also reported a fever 1 week before admission, for which he had started taking ciprofloxacin without clinical benefit. On his general practitioner's advice, he presented to the emergency room (ER) of our hospital. Computed tomography-urography (CTU) performed elsewhere revealed right hydronephrosis (30 mm) associated with a large pelvic mass (10 cm × 10 cm × 11 cm) characterized by multiple hypodense formations with a multiloculated appearance of possible abscess origin. He reported a last total prostate-specific antigen (tPSA) value of 1.7 ng/mL.

Bedside ultrasound performed in the ER showed bladder enlargement, with > 500 mL residual urine. Urinary catheterization was performed because the mass was initially described as an enlarged prostate. Instead, suprapubic cystostomy and a right nephrostomy were performed. The following day, he was transferred to our Geriatric Internal Medicine ward for further evaluation.

Upon arrival, the patient was feverish (39.0°C), awake, and partially oriented in space and time. Physical examination showed that the abdomen was aching and tender in the hypogastric region, with pain radiating to all abdominal regions. The exacerbating factors were deep breathing and postural change. Physical examination of the heart, lungs, and skin revealed no abnormalities. Blood cultures collected upon arrival were positive for *E. lenta*. He began antibiotic therapy with meropenem for 5 days, and shifted to piperacillin-tazobactam for 7 more days based on the antibiogram results, with improvement in his clinical conditions and blood inflammation markers.

CTU (Fig. 1) and pelvic magnetic resonance imaging (MRI) (Fig. 2) showed a coarse expansive neoplastic lesion in the central portion of the pelvis, approximately 10 cm × 10 cm × 11 cm in size, with a non-homogeneous structure that was partly solid and partly colliquated. The mass determined the dislocation of the pelvic structures without a neat cleaving surface with the bladder and sigmoid colon. The case was discussed with the consultant sur-

geon and laparotomic surgery with a subumbilical midline incision was performed. A voluminous neoformation occupying the entire pelvic cavity was found, with extended inflammation involving the greater omentum, exceeding the sigmoid colon (dolichocolon) and dome of the bladder. The top of the neoformation appeared partially colliquated, and approximately 300 mL of corpuscular material, partly necrotic and partly abscessed, was drained. Microbiological examination showed positivity for *Escherichia coli* and *Bacteroides vulgatus*, both of which were susceptible to piperacil-



Fig. 1. Computed tomography-urography showed a coarse expansive neoplastic lesion in the central portion of the pelvis, approximately 10 cm × 10 cm × 11 cm in size, with a non-homogeneous structure that was partly solid and partly colliquated.

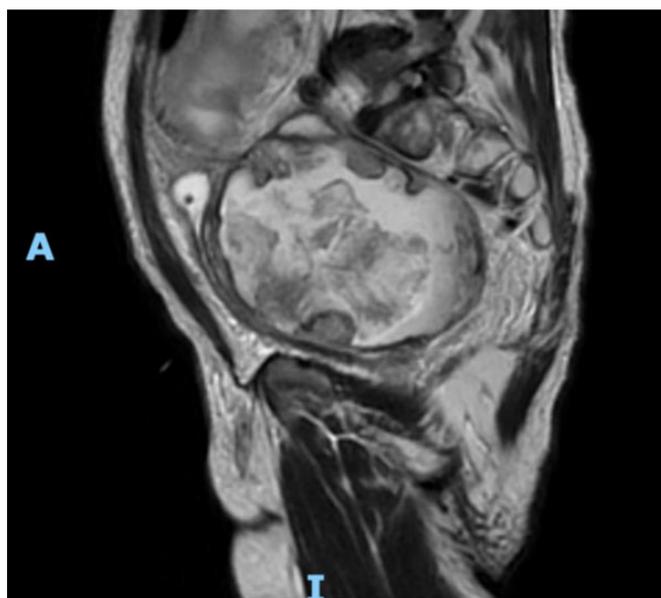


Fig. 2. Pelvic magnetic resonance imaging showed a coarse expansive neoplastic lesion in the central portion of the pelvis, approximately 10 cm × 10 cm × 11 cm in size, with a non-homogeneous structure that was partly solid and partly colliquated.

lin-tazobactam. Debulking of the neoplasm confirmed infiltration of the bladder and the left iliac axis. During the procedure, 3/4 of the mass was removed. An omental flap was placed between the bladder and rectum in the residual tumor bed. Morphological examination of the intraoperative sample showed neoplastic mesenchymal proliferation characterized by epithelioid cells with variable cytoplasm (from clear to eosinophilic), severe cytological atypia, neoplastic necrosis, and a high mitotic index. Immunohistochemical investigations showed positivity for cathepsin K, SMA, INI1, and focal expression of Melan-A, HMB45, and H-caldesmon. The cells were negative for a large panel of cytokeratin (CK AE1/AE3, Cam5.2, EMA), desmin, myoglobin, myogenin, MyoD1, S100, MDM2, CDK4, CD34, calretinin, chromogranin, synaptophysin, and inhibin (Fig. 3). These findings were consistent with the diagnosis of PEComa with malignant behavior according to the current classification criteria.⁵⁾

Two weeks later, because of a new temperature elevation and worsening of the patient's clinical condition, antibiotic therapy with piperacillin-tazobactam was reinstated. A new contrast-enhanced CT scan of the abdomen showed an abscess (14 cm × 6 cm × 12 cm) on the right side of the neoplasm. The infected collection was drained using an ultrasound-guided percutaneous procedure. Staging CT did not reveal any metastasis. At discharge, the antibiotic therapy was shifted to oral amoxicillin-clavulanate and trimethoprim-sulfamethoxazole.

One month later, the patient was treated with everolimus (Afinitor). Everolimus was discontinued and replaced with pazopanib (Votrient) after 2 months because of disease progression. Two weeks later, the patient was re-admitted to our hospital for intestinal occlusion, for which colostomy placement surgery was performed. Contrast-enhanced CT of the abdomen revealed two hepatic metastases localized in segment VI. A colostomy placement

was scheduled. To date, the patient continues to have infectious disease and oncological and radiotherapy follow-ups.

DISCUSSION

PEComa is a rare mesenchymal tumor comprising perivascular epithelioid cells (PEC). PEComa is characterized by a clear to granular cytoplasm and a central round to oval nucleus without prominent nucleoli that grow in a distinctive perivascular pattern. PEComa express both melanocytic markers, including HMB-45, Melan A/Mart 1, and MITF, as well as myogenic markers, including actin, myosin, and calponin. To date, the "normal" counterpart of PECs is not known. It shows a strong genetic association with tuberous sclerosis complex (TSC) genes *TSC1* (9q34) and *TSC2* (16p13.3).^{1,6)} PEComa mainly affects young women (73%, median age at diagnosis 43 years). It is often unifocal and has benign behavior, although multiple lesions have also been reported, especially in malignant variants. The most common locations in adults are the uterus, retroperitoneal space, pelvis, and kidney.⁷⁾ The symptoms of PEComa are non-specific. Symptomatic forms are usually locally advanced and manifest as pelvic or abdominal pain and discomfort, weight loss, or vaginal bleeding (in uterine PEComa). Malignant forms often spread to the lungs (up to 90% for pelvic PEComa), liver (up to 77.8% of tumors located in the kidneys and mesentery), and bones. PEComa is often an incidental finding (20% of cases). While imaging features may help identify neoplasms,⁸⁾ the diagnosis is based on histopathological characteristics. The differential diagnoses include gastrointestinal stromal tumor, melanoma, chromophobic renal cell carcinoma, clear cell sarcoma, alveolar soft part sarcoma, and epithelioid leiomyosarcoma.¹⁾ Radical surgery is the only effective treatment for pelvic PEComa. Radiotherapy can be administered to unresectable tumors

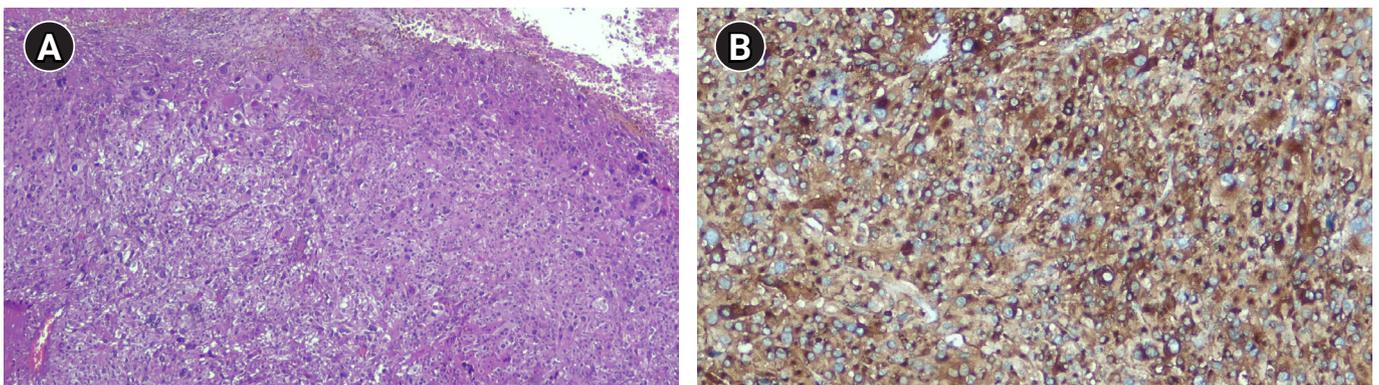


Fig. 3. (A) Histopathological evaluation showed a lesion composed of high-grade epithelioid cells with clear to eosinophilic and granular cytoplasm (original magnification x10); necrosis and brisk mitotic activity were reported. (B) The cells were positive for cathepsin-K (original magnification x20), melanocytic and smooth muscle markers.

or as a neoadjuvant treatment. Support therapeutic options include mTOR inhibitors (mTOR is often upregulated in association with *TSC1/TSC2* mutations) and VEGF inhibitors (because of abundant vascularization).^{8,9)} Patients with malignant PEComa require strict follow-up as relapse can occur even within 10 years from surgery.^{10,11)}

E. lenta is an anaerobic, gram-positive bacterium of the normal gut microbiota. It is an emerging pathogen, as it has been recently associated with life-threatening infections, with a mortality rate of up to 20%.^{3,4)} The shift toward a pro-inflammatory phenotype and immune dysregulation in frailty have attracted increasing interest in recent years. In this regard, a “frailty cytokinoma,” a system of inflammatory biomarkers involved in dysregulation of the cytokine network, has been identified.¹²⁾ Systemic inflammation is closely related to changes in the microbiota that occur with aging and accumulation of frailty, among others. Almost oversimplifying such a complex topic, frailty is associated with a reduction in the diversity of the gut microbiota, with a shift toward a “inflammatory microbiome”. Dysbiosis causes local inflammation, which contributes to a looser gut barrier, allowing the systemic spread of molecules that fuel chronic systemic inflammation, and even the translocation of bacteria into the bloodstream.¹³⁾ Jackson et al.¹⁴⁾ suggested that such changes may occur many years before clinically relevant frailty develops and identified *Eubacterium dolichum* and *E. lenta* as abundant bacterial species in frail individuals. Recently, *E. lenta* has been associated with an important immunomodulatory role. Alexander et al.¹⁵⁾ speculated that this microorganism may provide antigenic stimulation through Th17 lymphocyte activation. As *E. lenta* infections are often reported in older adults with comorbidities and oncological patients with advanced cancer, Woerther et al.¹⁶⁾ defined it as a possible “witness of frailty.” The antibiograms and susceptibility of specific cases should be carefully considered, as *E. lenta* infections are associated with high costs and poor outcomes.¹⁷⁻¹⁹⁾

In conclusion, the present study described a case of an unusual type of cancer and bloodstream infection caused by an emerging pathogen.

Approaching differential diagnosis with an open mind may assist in better imaging interpretation, surgery scheduling, and proper treatment planning. While PEComa are generally benign, on some occasions, as in our case, it can be highly aggressive. Non-specific clinical presentations might delay timely diagnosis, while the absence of well-consolidated guidelines undermines appropriate disease management. In these cases, careful surveillance is crucial for better outcomes.

Emerging pathogens represent an important challenge in healthcare. Non-communicable diseases, immune dysfunction, aggres-

sive treatments such as surgery or chemotherapy, implants and medical devices such as central lines or catheters, prolonged exposure to antibiotics, and microbiome disruption play significant roles in the development of infections. Progress in diagnostic techniques, such as the implementation of MALDI-TOF (matrix-assisted laser desorption/ionization-time of flight) mass spectrometry for micro-organism identification,¹⁹⁾ help with more accurate pathogen diagnosis and characterization. This allows the most appropriate therapy to be implemented, as well as better surveillance of antibiotic resistance, infection prevention, and control measures.²⁰⁾ Nevertheless, a good dose of wisdom is vital to avoid overlooking potentially harmful pathogens, particularly in individuals with frailty.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, SC, CR, CM, DE; Data curation, DA; Investigation, SC, CR, CM, DE, VB, FM; Supervision, DF, VB, FL; Writing-original draft, SC, CR, CM, DE; Writing-review & editing, SC, CR, CM, DE, DF, DA, VB, FM.

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