

The Emergency Department as the Gateway: When Infection is Not the Answer in the Older Adult

O Serviço de Urgência como Porta de Entrada: Quando a Infecção Não é a Resposta no Adulto Idoso

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Abstract:

Symptoms suggestive of infection, such as fever, cough, or dysuria, are frequent reasons for presentation to the Emergency Department (ED), and infection is often assumed during the initial assessment of older adults. However, not all suspected infections are ultimately confirmed. We describe a 70-year-old male adult with a one-month history of headache, myalgias and fatigue. Dry cough, tachypnoea, and low-grade fever (38.1°C) were noted in the emergency room. Despite initial suspicion of infection, the infectious workup was negative. Anti-myeloperoxidase antineutrophil cytoplasmic antibodies serology (MPO-ANCA) and renal biopsy established the diagnosis of small-vessel vasculitis with crescentic pauci-immune glomerulonephritis, treated with corticosteroids and rituximab. This case highlights that not all acute presentations resembling infection in older adults have infectious origins and underscores the importance of maintaining a broad differential diagnosis to ensure timely and appropriate management.

Keywords: Aged; Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis Fever of Unknown Origin.

Resumo:

Sintomas sugestivos de infecção – como febre, tosse ou disúria – são motivos frequentes de apresentação no Serviço de Urgência (SU), sendo a infecção um diagnóstico frequentemente assumido na avaliação inicial do doente idoso. No entanto, nem todas as infecções suspeitas se confirmam. Descrevemos o caso de um homem de 70 anos com um mês de evolução de cefaleias, mialgias e fadiga. Na admissão, apresentava tosse seca, taquipneia e febre (38,1°C). Apesar da suspeita inicial de infecção, a investigação infecciosa foi negativa. A serologia dos anticorpos anticitoplasma de neutrófilos

dirigidos contra a mieloperoxidase (MPO-ANCA) e a biópsia renal permitiram estabelecer o diagnóstico de vasculite de pequenos vasos com glomerulonefrite crescêntica paucimune, tratada com corticoterapia e rituximab. Este caso evidencia que nem todas as apresentações agudas semelhantes a infecção em adultos idosos têm origem infecciosa e sublinha a importância de manter um diagnóstico diferencial amplo para garantir uma abordagem atempada e adequada.

Palavras-chave: Febre de Origem Indeterminada; Idoso; Vasculite Associada a Anticorpo Anticitoplasma de Neutrófilos.

Introduction

Infection is among the most frequent diagnoses for presentation to the Emergency Department (ED) in older adults and is often considered the default diagnosis when nonspecific symptoms such as fatigue, confusion or functional decline occur. However, this age group frequently exhibits atypical clinical and laboratory features, and the absence of fever or localizing signs can render the diagnostic process challenging.¹

Beyond infections, several non-infectious conditions may present with similar complaints, including neoplastic, thromboembolic and autoimmune diseases. These entities can mimic infection both clinically and biochemically, leading to empirical antimicrobial therapy and delayed recognition of alternative diagnoses.^{2,3}

A careful diagnostic approach that considers the patient's comorbidities, medication profile, and overall clinical context is crucial to distinguish infectious from non-infectious causes of acute illness. In emergency settings, where decisions must often be made rapidly and with limited information, maintaining a broad differential diagnosis is essential to avoid delays or misdirection in management.

Case Report

Male, 70 years of age, with a Clinical Frailty Scale score of 2 and an ECOG performance status of 1, with a past medical history of arterial hypertension, dyslipidemia, type 2 diabetes mellitus, ischemic heart disease, and a former smoker. He presented with a one-month history of intense

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frontal headache, myalgias, progressive dyspnea, fatigue, dry cough, anorexia, and unintentional weight loss of 7 kg (10% of initial body weight). He reported feeling feverish in the preceding days, although no temperature measurements had been taken at home. In the ED (Emergency Department) evaluation, he was febrile (38.1°C), with tachypnea, and minimal changes on pulmonary auscultation and a systolic aortic murmur.

Blood tests revealed new-onset anemia (Hb 9.6 g/dL), folate and vitamin B12 deficiency, leucocytosis (11 000/μL, 84% neutrophils), C-reactive protein 6 mg/dL, negative procalcitonin, and an erythrocyte sedimentation rate (ERS) of 61 mm, positive D-dimers, and arterial blood gases with hypocapnia and hypoxemia (Table 1). An initial working diagnosis of atypical pneumonia and possible pulmonary embolism (PE) was assumed, empirical antibiotics and anticoagulation were started.

During hospitalization, under treatment with azithromycin, he remained febrile daily, fine inspiratory crackles were heard on auscultation, and ESR rose to 120 mm without other inflammatory marker progression. Serial blood cultures and cardiac evaluation were negative.

Chest computed tomography (CT) angiography revealed bronchiolitis and bilateral interstitial pulmonary edema, without PE. Extended screening for respiratory viruses and atypical pathogens was negative, except for a low-titer positive IgA for *Chlamydia pneumoniae*, not confirmed by nucleic acid amplification tests (NAATS). Two interferon-gamma release assay (IGRA) tests were indeterminate, and an enzyme-linked immunospot (ELISPOT) interferon-gamma release assay for *Mycobacterium tuberculosis* was negative.

He developed progressive renal impairment, with creatinine rising from 1.44 to 1.96 mg/dL, associated with microscopic hematuria with dysmorphic erythrocytes and non-nephrotic proteinuria (albumin/creat ratio 1806.4 mg/g creat, prot/creat ratio 2817.1 mg/g creat, albuminuria 1468.6 mg/L, total protein 2510 mg/L).

Serum protein electrophoresis, immunofixation, serum free light-chain (FLC) assay, and 24-hour urine electrophoresis revealed no monoclonal component.

Autoimmune testing revealed positive MPO-ANCA (253.7 IU/mL), leading to a diagnosis of small-vessel vasculitis and initiation of corticosteroids (prednisolone 1 mg/kg).

Renal biopsy confirmed crescentic pauci-immune glomerulonephritis pattern (Fig. 1), and treatment with rituximab was initiated. Clinical context and laboratory findings are suggestive of microscopic polyangiitis (MPA).

Discussion

This case highlights the diagnostic challenge of acute presentations in older adults whose symptoms may initially suggest an infectious etiology upon admission to the ED. In the described situation, the initial clinical impression could

point towards a possible infection, as it is frequent in this age group and clinical setting. However, a more extensive diagnostic workup ultimately ruled out an infectious origin.

The case reported fever remained unexplained after broad infectious screening, with persistent inflammatory markers and progressive renal impairment. Subsequent detection of MPO-ANCA antibodies and confirmatory renal biopsy established the diagnosis of microscopic polyangiitis (MPA), a small-vessel vasculitis with crescentic pauci-immune glomerulonephritis. This case highlights the need to expand the differential diagnosis of febrile syndromes in older adults to include autoimmune diseases, particularly when systemic inflammation or organ dysfunction emerges.

MPA is a rare systemic ANCA-associated vasculitis characterized by necrotizing inflammation of small vessels with few or no immune deposits. It typically manifests with necrotizing glomerulonephritis and may also involve pulmonary capillaritis.^{4,5} Common presenting symptoms include fever, fatigue, malaise, weight loss, myalgias, arthralgias, rhinosinusitis, cough, hemoptysis, hematuria, and proteinuria.⁶ In older adults, diagnostic delay is frequent, and the disease often presents with more advanced renal involvement.^{7,8} In our patient, the initial manifestation included fever, fatigue, weight loss, and cough, with erythrocyturia (++) on urine sediment and nonspecific thoracic CT findings, illustrating the diagnostic complexity of early-stage vasculitis in this age group.

Fever of unknown origin (FUO) is characterized by a body temperature of 38.3°C or higher on at least three separate occasions, persisting for a minimum of three weeks, and without an established focus after one week of in-hospital investigation.⁹ It remains a demanding diagnosis due to its nonspecific manifestations. In older adults, FUO is most often attributable to non-infectious causes, with inflammatory diseases accounting for approximately one-third of cases.^{10–12} The likelihood of autoimmune etiologies increases with age, underscoring the importance of considering vasculitis and other inflammatory disorders when evaluating persistent fever in this population.²

This case demonstrates how apparently typical symptoms—low-grade fever—can mask non-infectious diseases in older adults. The clinical overlap between infection, malignancy, and autoimmune disease is well documented in the study of fever of unknown origin (FUO), where neoplastic and inflammatory etiologies account for a substantial proportion of diagnoses.² Moreover, older patients often present with muted or nonspecific symptoms—sometimes afebrile, with functional decline or delirium as the first sign of illness—further complicating the diagnostic process.^{2,13}

In the ED, clinical priorities necessarily focus on identifying rapidly treatable conditions and causes of potential early deterioration. However, recognizing when a clinical presentation may not be fully explained by infection alone is essential, as this awareness informs appropriate disposition decisions. In the

Table 1: Laboratory and Imaging Findings at Admission and Extended Investigation (MPO-ANCA Vasculitis).

Category	Test / Parameter	Result
Hematology	Hemoglobin (VR 13.0-17.5 g/dL) Leukocytes (VR 4.0-11.0x10 ⁹ /L) Platelets (VR 150-450x10 ⁹ /L)	9.6 g/dL 11 000 ×10 ⁹ /L (84% neutrophils) 352x10 ⁹ /L
Inflammatory and coagulation markers	CRP (VR< 0.5 mg/dL) ESR (VR ≤ 30 mm/h) Procalcitonin (VR <0.5 ng/mL) D-dimer (VR 0.0-0.5 µg/mL)	6 mg/dL 61 → 120 mm/h Negative Positive (2.28 µg/mL)
Renal function	Creatinine (VR 0.70-1.20 mg/dL) Urinalysis 24-hour urine / ratios Albuminuria (VR<20 mg/L) R Alb/Cr (VR <30 mg/g creat) Proteinuria/creatininuria (VR< 150 mg/g creat.) Proteinuria (VR<12 mg/dL)	1.96 mg/dL Haematuria (45.8/uL RBCs, dysmorphic); Albuminuria 1468.6 mg/L R. alb/creat ratio 1806.4 mg/g creat; Prot/creat 2817.1 mg/g creat Proteinuria 251.0 mg/dL
Serum proteins	Serum immunofixation Ig G (VR 700-1600 mg/dL) Ig A (VR 70-400 mg/dL) Ig M (VR 40-230 mg/dL) K Chains (VR 312 mg/dL) L Chains (VR 216 mg/dL) K/L (VR 1.44) β ₂ -microglobulin (VR 0.8-3.0 mg/L) Serum amyloid A (VR < 6.4 mg/L)	No monoclonal component IgG 1263 mg/dL; IgA 252 mg/dL; IgM 29 mg/dL; cadeias K 312 mg/dL; L 216 mg/dL; ratio K/L normal 5.62 mg/L (↑) 485 mg/L (↑)
Urine protein studies	Urine immunofixation (VR Ig G <5.7 mg/L) (VR K Chains <10 mg/L) (VR L Chains <7 mg/L)	Polyclonal immunoglobulins IgG 255 mg/L; K Chains 191 mg/L; L 96.2 mg/L
Autoimmunity panel	ANA / anti-dsDNA Complement (VR C3c 90-180 mg/dL) (VR C4 10-40 mg/dL) (CH50 41.0-95.0 U/mL) Anti-glomerular basement membrane Anti-citrulline antibody c-ANCA (PR3) p-ANCA (MPO)	Negative C3c 209 mg/dL C4 24 mg/dL CH 50 60.5 U/mL Negative Negative Negative Positive (253.7 IU/mL)
Infectious workup		
Bacterial/atypical agents	Brucella, Q fever, Lyme disease, Bartonella <i>Mycoplasma pneumoniae</i> , <i>Legionella pneumophila</i> <i>Chlamydomphila pneumoniae</i>	Negative Negative Low positive IgA; NAATs negative
Tuberculosis	IGRA ×2 T-SPOT.TB	Indeterminate Negative
Viral	Respiratory virus panel (rapid antigen) CMV, EBV, HBV, HCV, HIV 1/2	Negative Negative
Microbiology	Serial blood cultures (before and after antibiotics) Urine culture	Negative Negative
Cardiac imaging with trans-thoracic and transesophageal echocardiography	Mild systolic dysfunction; slightly decreased ejection fraction. Fibrocalcific mitral–aortic disease; low-flow, low-gradient aortic stenosis. No vegetations or valve thickening	

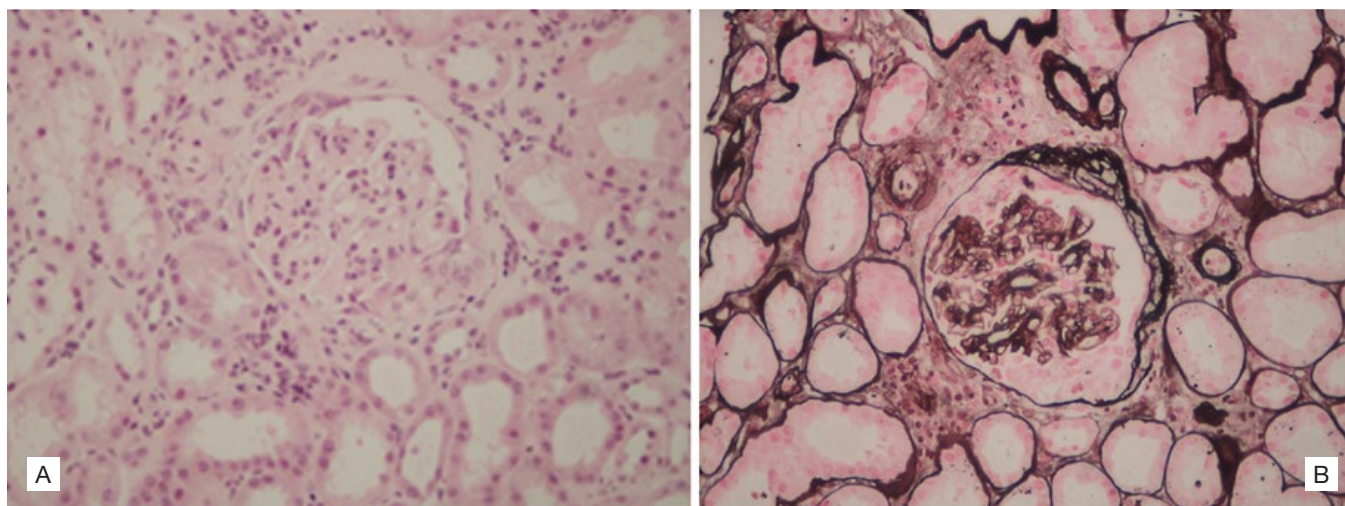


Figure 1: Glomerular crescent formation was observed in one of the biopsy specimens. [A] Hematoxylin and eosin (H&E) staining; [B] Silver staining (Marinozzi).

present case, although ANCA-associated vasculitis would not be expected to be considered at initial ED presentation, the recognition that the clinical picture might extend beyond an uncomplicated infectious process supported hospital admission for further investigation in the appropriate clinical setting. Initial treatment was therefore directed towards a presumptive respiratory infection—an appropriate working diagnosis based on the presenting symptoms and objective findings—while allowing subsequent inpatient evaluation to refine the diagnosis.

Although this particular case was managed appropriately within the existing emergency care framework and does not, in itself, demonstrate system-level shortcomings, it reflects the broader diagnostic complexity frequently encountered in older adults presenting with nonspecific symptoms. Such complexity reinforces the relevance of ongoing discussions about how emergency departments can better accommodate the needs of an aging population. ■

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NM – Data acquisition and manuscript drafting.
AMA – Manuscript drafting.
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