DOI: 10.4274/tjh.galenos.2023.2023.0050
Turk J Hematol 2023;40:125-127

Invasive Aspergillosis and Candidiasis in a Patient with Plasma Cell Myeloma

Plazma Hücreli Myelom Hastasında İnvaziv Aspergilloz ve Kandidiazis

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Infections may entail life-threatening complications in patients with plasma cell myeloma (PCM) receiving steroid therapy. High doses of dexamethasone, bortezomib, lenalidomide, and autologous/allogeneic hematopoietic stem cell transplantation (HSCT) lead to cumulative immunosuppression affecting various components of the immune system with the emergence of infections such as cytomegalovirus, varicella zoster virus, *Aspergillus* spp., and *Fusarium* spp. Evidence of invasive fungal infections (IFIs) in PCM is limited and co-infections have seldom been described [1,2]. In the largest relevant autopsy series to date including 623 patients, only 3.5% had proven or probable IFIs [3]. *Candida* species constituted the majority, followed by *Aspergillus.* Dual infection by *Candida* and *Aspergillus* has not been previously reported in these patients.

A 65-year-old woman diagnosed with PCM 3 years ago presented with fever, headache, and altered sensorium of 5 days in duration. She had been receiving cyclophosphamide, bortezomib, and dexamethasone for a year. One month prior to the current admission, she experienced relapse. Investigations revealed pancytopenia with bilateral heterogenous opacities in the lungs on X-ray and focal hypodensities in the cerebral cortex on contrast-enhanced computed tomography. She died of her illness within 5 days of admission to the hospital.

In the autopsy, the kidneys were granular and scarred secondary to extensive atherosclerotic narrowing of the left renal artery (Figure 1A). Microscopically, there was evidence of light chain deposition disease (kappa-restricted) with cast nephropathy, confirmed by immunofluorescence (Figures 1B-1E). There was no amyloidosis, infiltration by plasma cells, or crystal deposition. Additionally, there were *Candida* abscesses with infection-associated localized thrombotic microangiopathy (Figures 1F and 1G). Interestingly, there was extensive invasive pulmonary aspergillosis (Figures 2A and 2B) with angioinvasion and dissemination to the brain and spleen. The gastrointestinal tract was carpeted with *Candida* spores and hyphae with dissemination to the lungs, kidneys, and heart (Figures 2C and 2D). There was evidence of influenza B pneumonia in the lungs as proven by RT-PCR, but testing for SARS-CoV-2 was negative.

While deposition diseases and cast nephropathy overshadow the pathological spectrum encountered in cases of PCM, IFIs constitute a minor subset amongst them [4]. Light chain disease, anemia, hypoalbuminemia, and HSCT are documented independent predictors of IFIs in PCM [3], all of which were present in our case except the last factor. The occurrence of IFIs increases the risk of early mortality in these patients. Our case underscores the importance of keeping a high index of suspicion for IFIs in patients with PCM receiving immunosuppressive therapy.

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Received/Geliş tarihi: February 2, 2023
Accepted/Kabul tarihi: March 8, 2023

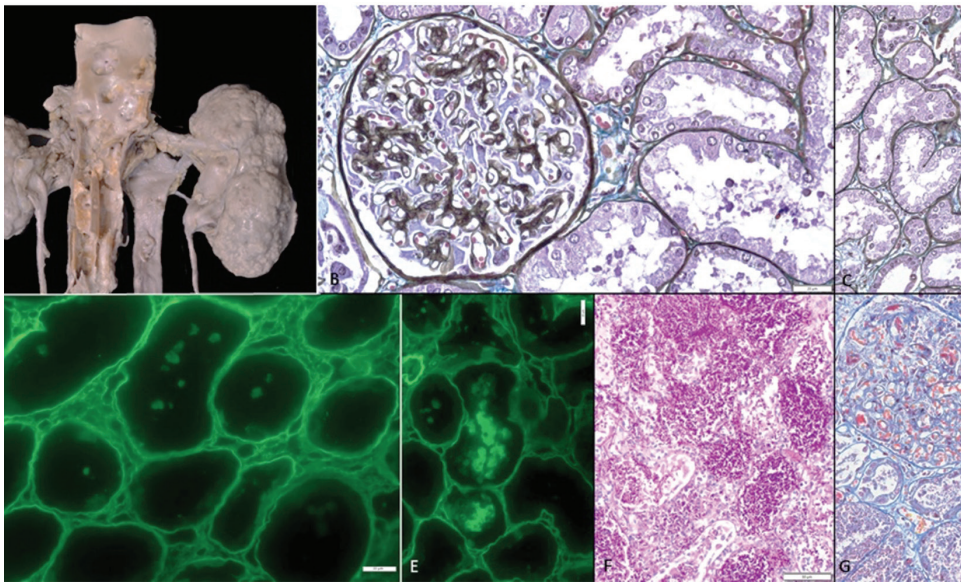

Figure 1. A) Gross appearance of both kidneys with asymmetrical sizes, scarred and granular on the outer surface. Note the extensive atherosclerosis of the abdominal aorta with calcification. Left kidney is smaller than right kidney. **B)** Mild increase in mesangial matrix with mottling upon Jones silver-Masson trichrome (JS-MT) staining (scale bar: 20 µm). **C)** Uniform thickening of tubular basement highlighted by JS-MT staining (scale bar: 20 µm). **D)** Immunofluorescence (IF) with kappa light chain revealing linear staining along tubular basement membrane (scale bar: 20 µm). **E)** Casts within the tubules highlighted with kappa light chain. IF for IgG and lambda were negative (scale bar: 20 µm). **F)** Periodic acid-Schiff staining highlights *Candida* spores and hyphae infiltrating the glomeruli and tubules, forming microabscesses (scale bar: 20 µm). **G)** Martius Scarlet Blue staining highlights fibrin thrombi within the glomerular capillaries in the vicinity of microabscesses (scale bar: 20 µm).

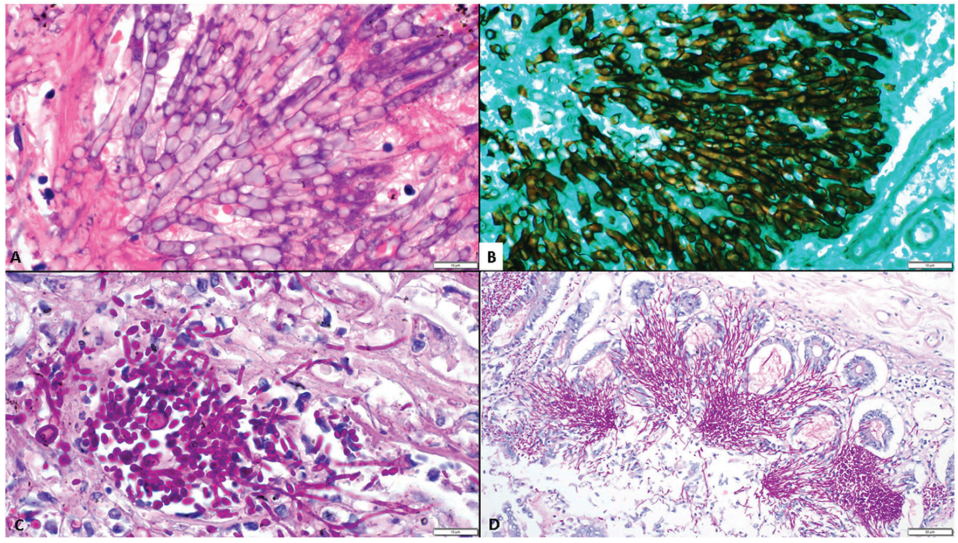

Figure 2. A) Periodic acid-Schiff (PAS) staining reveals slender, septate *Aspergillus* hyphae with dichotomous branching (scale bar: 10 µm). **B)** Grocott's methenamine silver staining further highlights *Aspergillus* hyphae (scale bar: 10 µm). **C)** Yeast form and pseudohyphae of *Candida* forming microabscesses in the lungs (PAS; scale bar: 20 µm). **D)** Pseudohyphae of *Candida* carpeting the colonic mucosa (PAS; scale bar: 50 µm).

Keywords: Multiple myeloma, Light chain deposition disease, Invasive fungal infections, Candidiasis, Aspergillosis, Autopsy

Anahtar Sözcükler: Multiple myelom, Hafif zincir birikim hastalığı, İnvasiv fungal enfeksiyon, Kandidiazis, Aspergilloz, Otopsi

Ethics

Informed Consent: Informed consent was obtained from a relative of the deceased patient.

Authorship Contributions

Concept: K.G.; Design: K.G.; Analysis or Interpretation: A.K., P.M.; Writing: K.G., A.K., P.N, N.M., M.S.

Conflict of Interest: No conflict of interests to disclose.

Financial Disclosure: The authors declared that this study received no financial support.

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