International Journal of Infectious Diseases 50 (2016) 18–20

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Medical Imagery

Oral Cryptococcosis in a Patient with Chronic Lymphocytic Leukemia

ARTICLE INFO

Article history:
Received 30 April 2016
Received in revised form 6 July 2016
Accepted 7 July 2016

Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Cryptococcus
chronic lymphocytic leukemia
rituximab
mucicarmine

1. BODY

A 68 year-old male with chronic lymphocytic leukemia (CLL) presented with a new mass along the left lower gum line that had enlarged over 3 weeks (Figure 1**A**). He retired from carpentry work after being diagnosed with CLL four years prior to presentation. He had received rituximab for the previous 18 months. He was evaluated in a dental clinic and biopsy was performed. The preliminary pathology report indicated histoplasmosis and he was admitted to the hospital for further evaluation. His review of systems was significant for a 50-pound weight loss over the past year, night sweats for several months, and fatigue. Both he and his family members denied that he had headaches, memory loss, personality changes, worsening cough or increased use of inhalers prescribed for his long-standing chronic obstructive pulmonary disease. Examination revealed a catechetic male with diffuse non-tender lymphadenopathy but was otherwise unremarkable. Specifically he did not have any meningeal signs, increased oxygen requirements or skin changes. His white count was 7.0×10^9 cells (normal range $3.6–11.0 \times 10^9$ cells) with 81% lymphocytes (normal range 21-51%). Images obtained using computed tomography (CT) scanning showed extensive axillary, inguinal, thoracic, abdominal and pelvic lymphadenopathy, which was described as near confluent. CT images did not report pulmonary nodules, cavitations or effusions. Compared to imaging done 10 months prior, the lymphadenopathy had substantially increased and, in conjunction with his weight loss and night sweats, was felt to represent progression of his CLL. His oncologist recommended hospice and the patient was started on itraconazole.

After his discharge, negative tests for urinary histoplasma antigen prompted review of the histopathological slides used to make the presumptive diagnosis of histoplasmosis. The histopathology demonstrated a submucosal lymphocytic infiltrate of small hyperchromatic homogenous lymphocytes characteristic of CLL (Figure 1**B**). The submucosa immediately below the squamous epithelium appeared expanded with round areas that appear "punched out" using hematoxylin and eosin stains. Additionally, the Gomori's methenamine silver stain revealed dark grey yeast forms of varying size and morphology, typical of *Cryptococcus* spp. (Figure 1**C**). Finally, the mucicarmine stain confirmed *Cryptococcus* spp. by rendering the yeast capsules bright pink (Figure 1**D**).[1] When these findings were discussed with the patient and his family, he had undergone significant decline and was in hospice care. They decided to continue with the itraconazole.[2] He died 2 weeks later.

Oral mucocutaneous manifestations of cryptococcosis are rare. To our knowledge, only one previous report describes oral cryptococcal disease in a non-HIV patient.[3] As the diagnosis of Cryptococcus occurred after the patient left the hospital, we were unable to complete the diagnostic studies to fully stage our patient's disease. Cryptococcus grows in bird guano and decaying wood so our a patient, a carpenter, may have experienced occupational exposure to Cryptococcus.[1,4] This case highlights the importance of histopathological studies in the diagnosis of

http://dx.doi.org/10.1016/j.ijid.2016.07.008

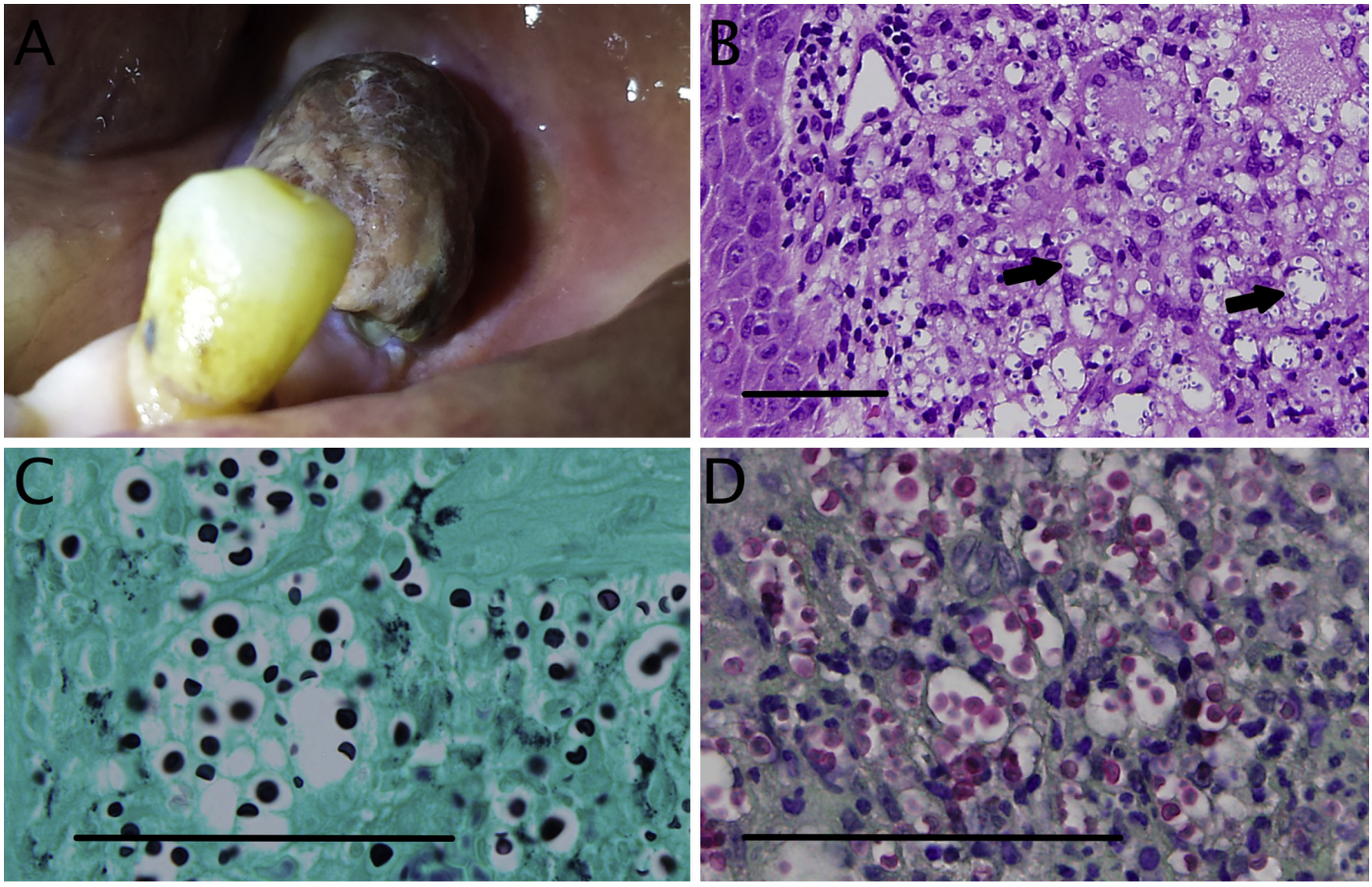

Figure 1. A. Lesion on the alveolar ridge of the left lower jaw. **B**. Hematoxylin and eosin stain shows giant cells with intracellular budding yeast forms of varying sizes (arrows) (x200 magnification). **C**. Gomori's methenamie silver (GMS) stain showing intracellular yeast forms with variable size and morphology (x1000 magnification). **D**. Mucicarmine stain showing the capsule of *Cryptococcus* spp. as bright pink (x1000 magnification). The black bar corresponds to 50 μm in all micrographs.

fungal diseases, especially when corroborated using laboratory-based tests.

Conflict of Interest

The authors report no conflicts of interest relevant to this article.

Ethics Statement

The patient's written consent was obtained and is available for review upon request.

Acknowledgements

The authors wish to thank Dr. Steven N. Emancipator for his assistance with microscopy. This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors. This material is the result of work supported with resources and the use of facilities at the Geriatric Research Education and Clinical Centers (GRECC) in Veterans Integrated Service Network (VISN)-10 (RJ) and the Louis Stokes Cleveland Veterans Affairs Medical Center (MN and RJ). The contents do not represent the views of the U.S. Department of Veterans Affairs or the United States Government. RJ gratefully acknowledges the T. Franklin Williams Scholarship with funding provided by Atlantic Philanthropies, Inc., the John A. Hartford Foundation, the Association of Specialty Professors, the Infectious Diseases Society of America and the National Foundation for Infectious Diseases.

References

1. Guarner J, Brandt ME. Histopathologic Diagnosis of Fungal Infections in the 21st Century. *Clin Microbiol Rev* 2011;**24**:247–80.
2. Perfect JR, Dismukes WE, Dromer F, et al. Clinical Practice Guidelines for the Management of Cryptococcal Disease: 2010 Update by the Infectious Diseases Society of America. *Clin Infect Dis* 2010;**50**:291–322.
3. Pagano L, Fianchi L, Caramatti C, et al. Cryptococcosis in patients with hematologic malignancies. A report from GIMEMA-infection. *Haematologica* 2004;**89**:852–6.
4. Staib F, Thielke C, Randhawa HS, Senska M, Kulins G. Colonisation of dead plants by *Cryptococcus neoformans*. *Zentralblatt Für Bakteriol Parasitenkd Infekt Hyg Erste Abt Orig Reihe Med Mikrobiol Parasitol* 1972;**222**:115–25.

Sachin Patel[a,b]
Maria Navas[c]
Courtney Batt[b]
Robin L.P. Jump[a,b,d,e,*]
[a]*Division of Infectious Diseases and HIV Medicine, Case Western Reserve University School of Medicine, Cleveland, Ohio*
[b]*Department of Medicine, Case Western Reserve University School of Medicine, Cleveland, Ohio*

[c]*Clinical Microbiology, Pathology and Laboratory Medicine Services, Louis Stokes Cleveland Veterans Affairs Medical Center (VAMC) Cleveland, Ohio*
[d]*Geriatric Research Education and Clinical Center (GRECC), Louis Stokes Cleveland VAMC, Cleveland, Ohio*
[e]*Infectious Disease Section, Medical Division, Louis Stokes Cleveland VAMC, Cleveland, Ohio*

[*]Corresponding author. GRECC 111C(W), Louis Stokes Cleveland VA Medical Center, 10701 East Blvd., Cleveland, Ohio 44106 USA; Tel.: +1 216-791-3800, ext 4788; fax: +1 216 229 2403
E-mail address: robin.jump@va.gov (R.L.P. Jump).