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Central nervous system aspergillosis confused with secondary localisation of a chronic lymphocytic leukemia (CLL)

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Abstract

Systemic aspergillosis may be a disease increased in immunocompromise terrain as HIV, chronic immunosuppressant/steroid use. We report the case of a 39-year-old female patient who had an antecedent of chronic leukemia treated. The patient developped focal neurologic deficits, mental status changes, headache. CT scan of the top shows an outsized left frontal hypodense, nonenhancing lesion with mass effect. Intra-operative cytopathology show perivascular lymphocyts. On microscopic study, we diagnosed true hyphae with septations Grocott + , vasculitis resulting in necrosis. On some areas, their was an abondant inflammation composed with small lymphocyts and plasmocyts. An immunostain with antibodies anti- CD20, anti-CD3, anti-CD5, anti-CD23, anti-IgD and anti- Kappa and Lamda was realize in hospital of Paris. Their was no argument for secondary localisation of CLL. Cerebral aspergillosis is never seen. His diagnosis is multidisciplinar. The pathologist got to exchange with clinicians and radiologists. Ibrutinib, an irreversible Bruton's tyrosine kinase (Btk) inhibitor, has dramatically improved progression-free and overall survival in patients with a spread of lymphoid malignancies within the midst of its therapeutic success, however, several cases of invasive fungal infections (IFI) in patients receiving ibrutinib have emerged We present a case of central systema nervosum (CNS) aspergillosis during a patient with chronic leukemia (CLL) on ibrutinib who had not received any previous or concurrent corticosteroid, chemo- or immunotherapy and was successfully managed with this life-threatening CNS infection. When nearing the top of the antibiotic therapy, the patient began to possess intermittent fevers and progressive word finding difficulty (day +34). His symptoms progressed to confusion and profound motor aphasia (day +36). He was subsequently admitted to the hospital on day +36 for work-up. Upon arrival to Duke University center , the patient was poorly cooperative with the exam and was confused. He was unable to state his name, location or the date. His cranial nerves were intact, and his strength symmetric throughout. However, the patient exhibited an unsteady gait, moderate dysarthria and significant word finding difficulties. He had difficulty reading words but recognized pictures. A non-contrast head computerized tomography (CT) demonstrated an outsized 3.2 cm (cm) hyperdense mass within the left hemisphere with surrounding vasogenic edema, a mass effect on the left ventricle and little hyperdense masses within the right hemisphere . The patient was started on dexamethasone and levetiracetam. Laboratory analysis was remarkable for a light leukopenia (WBC 3.2 × 10^9/L) Noninvasive infectious markers were unrevealing A resonance imaging (MRI) of the brain with and without contrast demonstrated three enhancing mass lesions with surrounding vasogenic edema. Specifically, there was a 3.2 cm round heterogeneous mass noted within the left parieto-temporal region, a 12 mm (mm) mass within the right lobe and an oval shaped 8 mm mass within the right lobe The patient subsequently underwent brain biopsy (day +41), and therefore the pathology revealed necrosis, acute inflammation and granulation according to an abscess and a Gomori methenamine-silver (GMS) stain highlighting septate hyphae Cultures from the biopsy grew Aspergillus fumigatus species complex (identification supported morphologic criteria) on day +43. Notably, a chest CT was also obtained and demonstrated a replacement spiculated lung nodule within the proper lower lobe measuring 1.5 × 1.7 cm with surrounding ground glass opacity.

The patient was treated with 1 year of voriconazole therapy (300mg by mouth every 12 hours) with brief combination echinocandin (micafungin 100mg intravenously every 24 hours) upfront for 2 weeks. Ibrutinib was discontinued upon presentation of symptoms and was held for the entire duration of aspergillosis treatment. Voriconazole dosing was adjusted based on trough levels which were obtained every 7–14 days throughout his treatment. Overall his voriconazole troughs were within the desired target range.

Serial CT and MRI imaging of the chest and brain, respectively, demonstrated an excellent response to antifungal therapy with imaging at the close of 1 year of therapy with no suggestion of residual infection. Fortunately, the patient's underlying CLL remained stable during this period, and he did not necessitate additional therapy with the exception of infrequent doses of granulocyte colony stimulating factor for intermittent mild neutropenia. However, he experienced multiple toxicities on voriconazole therapy including gastrointestinal disturbances, significant photosensitivity and nail changes. The patient also had a history of non-melanoma skin cancers; hence, the decision was made to transition to isavuconazole for secondary fungal prophylaxis after completion of 1 year of voriconazole therapy. The transition to isavuconazole also occurred alongside impending plans by the oncology team to initiate venetoclax as his next line of CLL therapy.

We present a case of CNS aspergillosis in a 62-year-old man with CLL who had initiated ibrutinib less than one month prior to the diagnosis. To our knowledge, we present the first case of CNS aspergillosis in a patient on

ibrutinib monotherapy who had not received prior corticosteroid, chemo- or biologic therapy for a chronic lymphoid malignancy.

Since the introduction of ibrutinib to treat hematologic malignancies, multiple reports of IFIs emerged prompting larger studies to investigate the incidence of IFI with ibrutinib in the hematologic malignancy population. The prevalence reported in these studies ranged from 2.4% [6] to 4.2% [7], and the majority of these IFIs were due to *Aspergillus* with a trend towards CNS involvement.

Biography

Ouattara Souleymane currently working at Ouagadougou, Burkina Faso and he completed his studies Université de Ouagadougou, Burkina Faso Science • Ouagadouga, Kadiogo, Burkina Faso. He published many research works in many journals. His research interested is Digital Pathology.

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