Case study

CEREBELLAR BLASTOMYCOSIS IN AN IMMUNOCOMPETENT PATIENT: A CASE REPORT

Abstract

Introduction

Blastomycosis dermatitidis is a fungal infection that mostly involves the skin and lung with only a 5-10% incidence of Central nervous system involvement.[1] It is endemic to the Midwestern United States, Manitoba and Ontario provinces of Canada and equally affects both immunocompetent and immunocomprimised individual with the likelihood of being more aggressive in the latter.[1]

Case Presentation

We present a 51 year old hypertensive factory machine operator from a blastomyces non-endemic area with no immunosuppressive condition who presented with worsening protracted headaches and cerebellar signs. Brain Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) appearance of a heterogeneously enhancing left cerebellar lesion posed an initial diagnostic dilemma which led to worsening of the patient's clinical condition from hydrocephalus as a result of increased perilesional oedema and compression of the fourth ventricle. Eventual biopsy, histomicrobiological tests and culture after craniectomy yielded a diagnosis of primary cerebellar blastomycosis with necessitated a 6 week intravenous treatment with amphotericin B followed by oral itraconazole for 12 months leading to complete radiological resolution of the cerebellar lesion and clinical resolution of the headaches and ataxia.

Discussion

Our index patient is an immunocompetent patient from a non-endemic area without any travel history who initially presented with headaches and clinical features referable to the cerebellum without any other organ or system involvement. Our patient's scenario on the background of a history of hypertension lowered the clinicians' suspicion indices toward an infective cause and less so a fungal cause. The use of other MRI modalities like Diffusion

Weighted Imaging (DWI) and Magnetic Resonance Spectroscopy (MRS) and early biopsy followed by histopathological and microbiological tests would have resolved the initial diagnostic dilemma irrespective of the patient's non-specific history and clinical features and the complication of hydrocephalus might have been prevented.

Conclusion

Blastomyces brain abscess like other atypical brain abscesses usually present non-specifically and imaging findings are non-specific making early biopsy/excision and histomicrobiological confirmation very important in making prompt diagnoses.

Keywords: blastomycosis, immunocomprimised, immunocompetent, blastomyces dermatitis, atypical brain abscess.

Introduction

Blastomycosis dermatitidis is a fungal infection that mostly involves the skin and lung only rarely involving the CNS with an incidence of 5-10%.[1]Central nervous system (CNS) blastomycosis without evidence of lung or other organ involvement is very rare. [1]Leers et al reported cerebellar Blastomycosis in 1972 as a primary infection with no meningitis as was the situation with our index case.[2] The most common primary CNS manifestation is basilar leptomeningitis followed by solitary or multiple brain parenchymal masses then epidural abscess. It is endemic to the Midwestern United States, Manitoba and Ontario provinces of Canada.[1] The optimal habitat for blastomyces is wetland enriched with animal droppings and decaying veetation. The most common route of infection is by inhalation of conidia released from disruption of soil containing the fungus. It can also be acquired by direct skin inoculation.[1] Transmission from dog bite has also been reported in literature.[3] Clinical presentation may vary from subclinical infection to a rapidly progressive dissemination and death. Symptoms may include weight loss, malaise and fatigue as well as features referable to the CNS.[1] . Bariola et al reported in his multicenter review of 22 patients that headache was the most common symptom (86%)[4,5] The likelihood of infection is equal amongst immunocompetent and immunosuppressed individuals but may be more aggressive in the latter.[1] CSF findings typically include pleocytosis with lymphocytic predominance and elevated protein but staining and fungal culture from CSF is mostly negative and cross reactions give a diagnostic dilemma with the use of Blastomyces antigen detection[1,4] Biopsy or resection thus provides the best diagnostic yield and such cultures yield growth

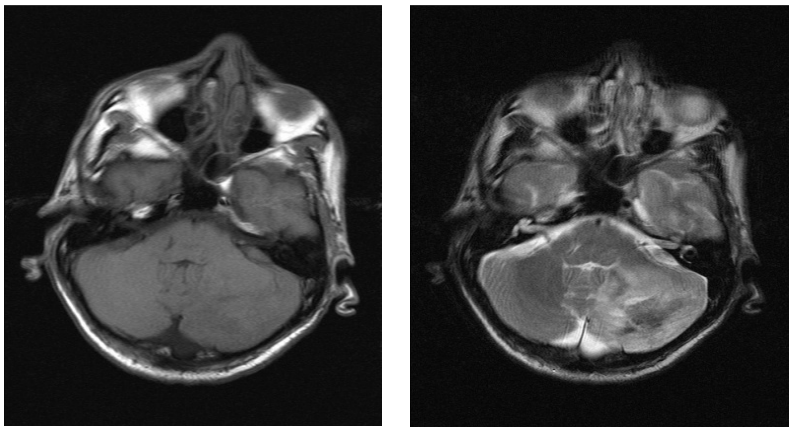
with microscopic features necrotizing granulomatous inflammation with yeast forming fungi.[1,6] Histopathologic findings include polymorphonuclear leukocytes clustered granulomas usually non-caseating, budding yeast cells with capsules, stains positive with Grocott-methenamine silver (GMS) and weakly Acid Fast positive.[1,6] The biopsy specimen culture yields the pathogen in 71% of histology confirmed cases having studied 16 cases with proven or probable CNS Blastomycosis.[7] The imaging characteristic is difficult to differentiate from other fungal entities especially Histoplasma capsulatum and Coccidiodes immitis[1] MRI consistently demonstrates an abnormality in all cases compared to 58% of CT scans.[7] Magnetic Resonance Spectroscopy (MRS) may show diminished N-acetyl aspartate (NAA) to creatine ratio (1.10), normal choline to NAA ratio (0.82), normal choline to creatine ratio (0.9) and a diminished myoinositol to creatine ration (0.39). There may be peaks between 3.6 and 3.8 ppm over the enhancing area thought to represent a trehalose peak.[8] Amphotericin B is the treatment of choice for immunocoprimised patients, those with life threatening or CNS disease or those for whom azole treatment has failed. Amphotericin B is the only drug approved for treating Blastomycosis in pregnant women. The azoles are worthy and less toxic alternatives to amphotericin B for treating immunocompetent patients with mild to moderate pulmonary and extra-pulmonary disease including the CNS. [9] The combination of surgical resection with antifungal therapy (amphotericin B and/or voriconazole/itraconazole) is considered the optimal management of solitary fungal brain abscesses.[1,8]. The disturbing side effects of amphotericin B including hepatic and renal insufficiencies and electrolyte imbalances should however be well noted for prompt action.[1]

We describe the clinical course and management of an immunocompetent patient treated for cerebellar blastomyces abscess treated in the Department of Neurosurgery of a South African Hospital.

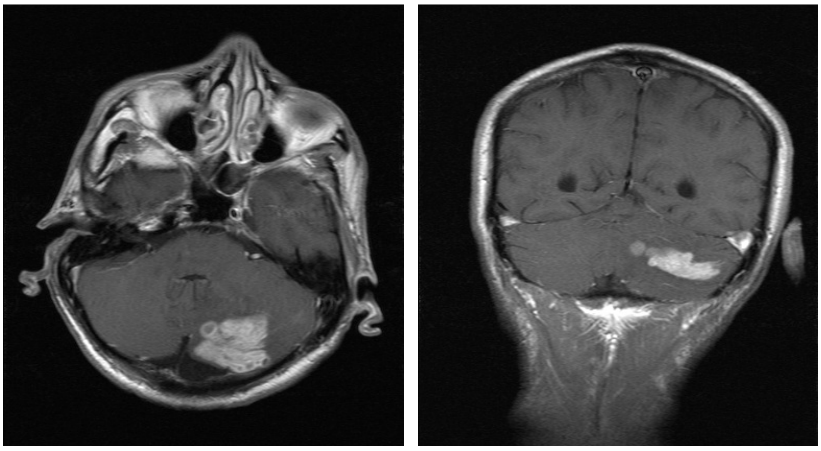
Case presentation and Management

A 51 year old male, known hypertensive, HIV negative and a non-diabetic factory machine operator presented to a teaching hospital in South Africa with a 7 month history of gradually increasing headaches. The headaches were aggravated by almost any form of straining including coughing and passing stools. They became more localized to the occipital area and more difficult to control with common analgesics over time. He also had a 2 months history of worsening ataxia and a 3 weeks history of intermittent vomiting, especially after meals. He

had no fever and no chest symptoms. A CT scan of the head done at this stage showed a heterogeneously enhancing left cerebellar mass lesion with some compression of the fourth ventricle, attenuation of the basal cisterns and mild enlargement of the third ventricle and both lateral ventricles. Differential diagnoses of metastasis and infective lesion or a resolving hematoma were made. He was thus investigated for a possible primary neoplasm which included chest x-rays and abdomino-pelvic ultrasonography. The serum levels of various tumour markers like alpha fetoprotein, prostatic specific antigen and carcinoembryonic antigen were also measured. None of the tumour markers were raised and no primary neoplastic lesion was found. Brain MRI scan done at this stage showed a left cerebellar lesion which demonstrated heterogeneity on T2 and a heterogeneous post gadolinium enhancement showing several cystic areas with thick enhancing walls. The patient however remarkably improved clinically on steroids and analgesics.



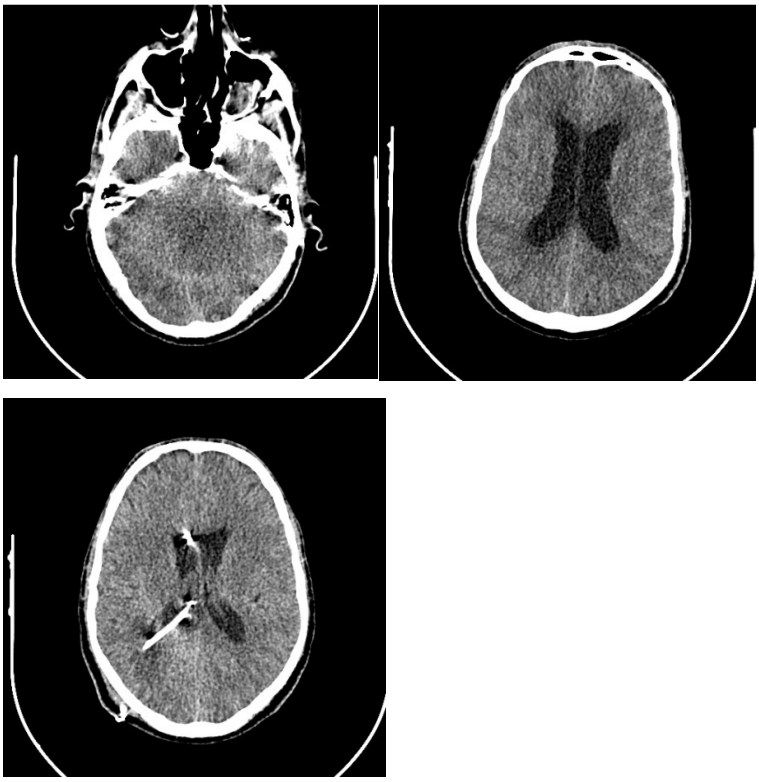
Axial T1 (left) and Axial T2 (right) MRI Brain scans showing a heterogeneous left cerebellar hemispheric lesion



Axial T1 post gadolinium contrast (left) and Coronal T1 post gadolinium contrast (right) MRI Brain scans showing a heterogeneous contrast enhancing lesion with areas of thick ring enhancement in the left cerebellar hemisphere.

In consultation with the Neuro-radiologist, a diagnosis of a resolving cerebellar bleed was made and the patient discharged to be followed up with an MRI in one month time including a gradient echo with or without an MRA.

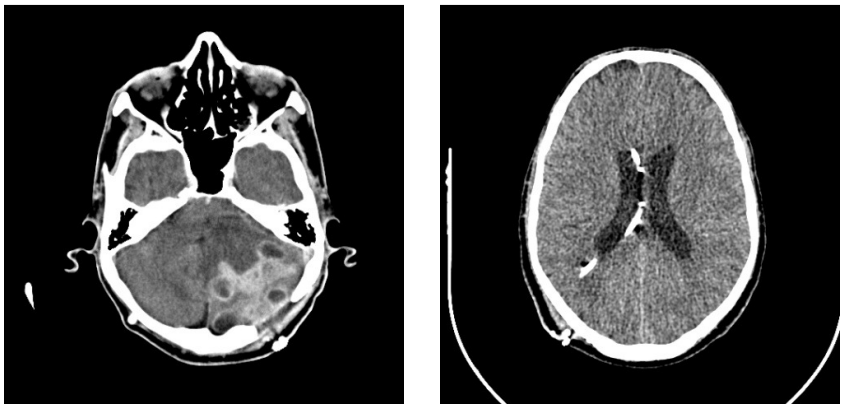
The patient however presented 3 days after discharge with a sudden onset of a very severe intractable headache with vomiting and confusion. An urgent CT Brain revealed the same left cerebellar heterogeneous lesion but now with some surrounding vasogenic edema, marked compression of the fourth ventricle and severe acute hydrocephalus.



Non-contrast Brain CT scans just before (right and middle images) and after a ventriculoperitoneal shunt placement(image on the left).

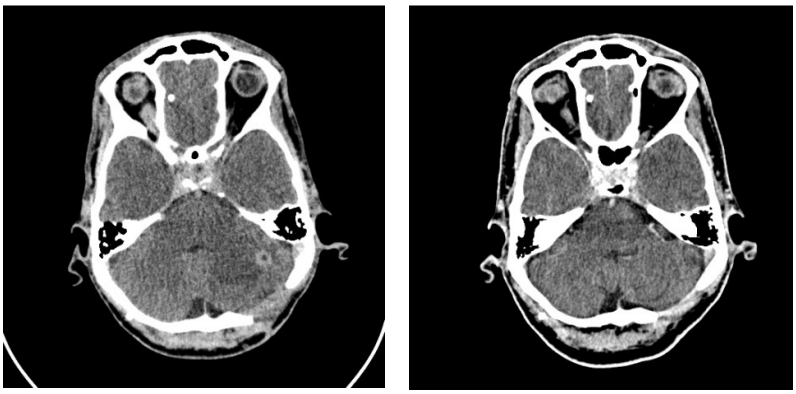
A ventriculoperitoneal shunt was immediately placed, following which the patient improved clinically. A left occipital craniectomy was then done and an open biopsy of the cerebellar lesion was performed and sent for histopathology as well as microbiological analysis. The histopathology report came as fragments of gliotic brain tissue with multinucleated giant cells

and broad based budding yeasts with double contour refractile walls and areas of pseudo hyphae formation. Ziehl-Neelsen (ZN) staining was negative. Microbiology cultures yielded a fungus which was subsequently confirmed to be a Blastomyces dermatitidis. Treatment with intravenous amphotericin B was then commenced at this stage and continued for 6 weeks. In addition, replacement of magnesium, potassium, calcium and iron was commenced to correct the concurrent derangements in serum levels over the treatment period.



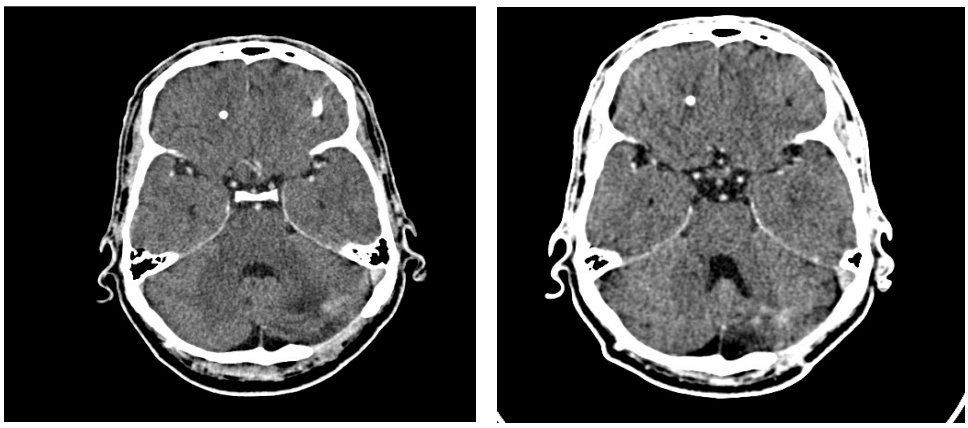
Post contrast CT Brain scan after 6 weeks of treatment with intravenous Amphotericin B showing the area of the sub-occipital craniectomy with the residual heterogeneous ring enhancing left cerebellar hemispheric lesion after open biopsy.

Serial CT Brain scans done revealed gradual decrease in size of the cerebellar lesion and the mass effect. The 6 weeks course of intravenous Amphotericin B was then followed with a 6 months course of oral Itraconazole. Itraconazole was used instead of the recommended Voriconazole because of unavailability (Voriconazole was out of stock at the pharmacy). The patient was then monitored clinically with weekly follow up visits for one month, 2 weekly visits for 2 months then monthly visits for the last 3 months of treatment. CT Brain scans done during these follow up visits showed progressive decrease in the size of the lesion with corresponding improvements in the patient's clinical condition over the treatment period.



Post contrast CT Brain scans after 3months (left) and 5 months(right) of oral Itraconazole treatment

A Brain CT scan at the end of the treatment period showed complete resolution of the left cerebellar hemisphere lesion with an open fourth ventricle and patent basal cisterns with complete resolution of the patient's symptoms including the ataxia and the headaches. The patient has since returned to his formal work as a factory machine operator without any residual neurological deficit.



Post contrast CT Brain scan after 6 months of oral Itraconazole and 6 months after completion of treatment with complete resolution of the left cerebellar hemispheric lesion and an open fourth ventricle.

Discussion

The same diagnostic dilemma was encountered in our management of this patient as repeatedly reported in literature. Our index patient is an immunocompetent patient from a non-endemic area without any travel history who initially presented with headaches and clinical features referable to the cerebellum without any other organ or system involvement. The 63 year old patient reported by Munich SA et al had a history of non-Hodgkin's lymphoma 9 years prior and was in sustained remission after treatment with chemotherapy and radiation.[5] Routine chest Xray also showed a non-specific left upper lobe opacities and

CT findings were consistent with pneumonia.[5] Our patient's scenario on the background of a history of hypertension lowered the clinicians' suspicion indices toward an infective cause and less so a fungal cause. The non-usage of other MRI modalities like Diffusion Weighted Imaging (DWI) and Magnetic Resonance Spectroscopy (MRS) in this case to further examine the cerebellar lesion might have reduced the chance of being able to make an earlier definitive diagnosis and hence a more prompt institution of the correct treatment. Again, an early biopsy followed by histopathological and microbiological tests would have resolved the initial diagnostic dilemma irrespective of the patient's non-specific history and clinical features. Had an early correct diagnosis been made in our index case the complication of hydrocephalus might have been prevented. A high index of suspicion for atypical brain abscesses is still to be maintained by clinicians irrespective of patient's travel history, location or immune status. And therefore a more exhaustive use of all available investigative tools should be employed to be able to make an early diagnosis and expedite early appropriate treatment in order to improve outcomes and prevent complications.

Conclusion

Blastomyces brain abscess like other atypical brain abscesses usually present non-specifically and particularly does not always necessarily only occur in immunocompromised individuals or individuals from endemic areas. Imaging findings are non-specific making early biopsy/excision and histomicrobiological confirmation very important in making prompt diagnoses.

References

1. Stavrakis C, Narayan A, Voronel O. Cerebral Blastomycosis: Radiologic-Pathologic Correlation of Solitary CNS Blastomycosis Mass-Like Infection. *J Clin Imaging Sci*. 2015 May 29;5:30. doi: 10.4103/2156-7514.157854. [PubMed]

2. Leers WD, Russell NA, Laroye G. Cerebellar abscess due to Blastomyces dermatitidis. *Can Med Assoc J*. 1972 Oct 7;107(7):657-60. [PubMed]

3. Gnann JW Jr, Bressler GS, Bodet CA, 3rd, Avent CK. Human blastomycosis after a dog bite. *Ann Intern Med.* 1983;98:48–9. [PubMed]

4. Bariola JR, Perry P, Pappas PG, Proia L, Shealey W, Wright PW, et al. Blastomycosis of the central nervous system: A multicenter review of diagnosis and treatment in the modern era. *Clin Infect Dis.* 2010;50:797–804

5. Munich SA, Johnson AK, Ahuja SK, Venizelos A, Byrne RW. Large cerebellar mass lesion: A rare intracranial manifestation of blastomycosis. *Surg Neurol Int.* 2013 Oct 15;4:141. doi: 10.4103/2152-7806.119882. [PubMed]

6. Saccente M. Woods GL, Clinical and laboratory update on blastomycosis. *Clin Microbiol Rev.* 2010;23:367-81. [PubMed]

7. Outcomes of persons with blastomycosis involving the central nervous system. Bush JW, Wuerz T, Embil JM, Del Bigio MR, McDonald PJ, Krawitz S. *Diagn Microbiol Infect Dis.* 2013 Jun;76(2):175-81. doi: 10.1016/j.diagmicrobio.2013.03.002.

8. Vachhani JA, Lee WC, Desanto JR, Tsung AJ. Magnetic resonance spectroscopy imaging characteristics of cerebral blastomycosis. *Surg Neurol Int.* 2014 May 28;5:80. doi: 10.4103/2152-7806.133306. [PubMed]

9. Chapman SW, Bradsher RW Jr, Campbell GD Jr, Pappas PG, Kauffman CA. Practice guidelines for the management of patients with blastomycosis. Infectious Diseases Society of America. *Clin Infect Dis.* 2000 Apr;30(4):679-83. [PubMed]

DECLARATIONS

Ethics

Not applicable

Consent for publication

Verbal consent taken from patient but patient's anonymity still maintained.

Declaration

The authors declare that this case report has not been submitted to any other journal for publication. All authors read and approved the final manuscript.