Aspergillus Brain Abscess in a Patient with Waldenström Macroglobulinemia

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Introduction

Aspergillus species, a group of mold, ubiquitous in nature, found worldwide. Inhalation of infectious conidia is a frequent event. Despite this, tissue invasion occurs most frequently in those who are immunocompromised. While rare, prompt recognition of central nervous system (CNS) aspergillosis is crucial as this condition is known to carry a high mortality rate even with appropriate treatment.

Case Presentation

A 77-year-old male with Waldenström macroglobulinemia who presented to the emergency department with “arm weakness and twitching” which started two hours earlier while at a baseball game with his son.

Past Medical History:
- HF/EF due to ischemic cardiomyopathy
- Atrial fibrillation
- Hypertension
- Type II diabetes mellitus
- Hyperlipidemia
- Benign prostatic hypertrophy

Social History:
- Retired carpenter
- Lives with his wife, no pets
- Does not smoke cigarettes, drink alcohol or drug use
- No domestic or international travel within the last 5 years

Physical Exam:
General: Awake, in no acute distress
HEENT: No jaundice, no oral thrush
Heart: Irregularly irregular, IVI systolic murmur at LSB
Lungs: No wheeze or crackles
Abdomen: BS present, soft, no distention or tenderness
Neuro: Left facial droop. RUE +5/5, LUE +0/5, RLE +5/5, LLE +5/5
Skin: No rashes, jaundice, or petechiae

Labs and Imaging:

<table>
<thead>
<tr>
<th>Table 2: CBC</th>
<th>Table 3: BMP</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>9.33 K/uL</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>13.5 g/dL</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>38.3%</td>
</tr>
<tr>
<td>Platelets</td>
<td>118 K/uL</td>
</tr>
<tr>
<td>Na</td>
<td>131 mmol/L</td>
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<tr>
<td>K</td>
<td>4.4 mmol/L</td>
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<tr>
<td>Cl</td>
<td>92 mmol/L</td>
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<tr>
<td>HCO3</td>
<td>25 mmol/L</td>
</tr>
<tr>
<td>BUN</td>
<td>32 mg/dL</td>
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<tr>
<td>Creatinine</td>
<td>0.96 mg/dL</td>
</tr>
<tr>
<td>Glucose</td>
<td>276 mg/dL</td>
</tr>
</tbody>
</table>

Head CT scan without contrast:
10 mm acute parenchymal hematoma in the right precentral gyrus with mild surrounding vasogenic edema.

Brain MRI with and without contrast:
1.8 x 3.0 cm T2 hypointense rim-enhancing lesion at the gray-white junction with surrounding vasogenic edema.

CT Thorax:
Ill-defined multifocal tree-in-bud opacities in the lungs.

Hospital Course:
- Right frontal craniotomy revealed abscess
- Antiebacterials: cefepime, vancomycin, metronidazole
- Further workup:
  - HIV (+), Galactomannan (+), B-D-glucan (+), cryptococcal Ag (+)
  - CT Sinuses: no evidence of invasive fungal infection
  - Echocardiogram: no vegetation
  - All blood and intraoperative cultures (aerobic, anaerobic, AFB, and fungal) were negative
  - Pathology report: rare fungal hyphae, possible septation
  - Broad range PCR, tissue (+), Aspergillus fumigatus DNA
  - Liposomal amphotericin B + voriconazole

Discussion

Epidemiology of invasive Aspergillosis:
- Aspergillus spp are found in soil or decaying vegetation
- Inhalation of conidia inoculate lungs or sinuses of immunocompromised patients

Clinical Presentation of CNS Aspergillosis:
- Classic triad:
  - Headache (69%)
  - Fever (45-53%)
  - Focal neurologic deficits (50%)
- Seizures (~25%), neck stiffness, AMS, vomiting

Diagnosis of CNS Aspergillosis:
- Histology: Septate hyphae with branching on 45° angle
- Galactomannan antigen
  - Sensitivity: 30-100%; specificity: >75%
- Best detects early infection in high risk patients with hematologic malignancy
- S-D-glucan assay
  - Sensitivity: 77%; specificity: 85%
  - Not unique to Aspergillus—detects Candida spp. and Pneumocystis jirovecii
  - Best detects early infection before symptoms onset
- Broad range PCR
  - Sensitivity: 84%; specificity: 76%
  - Best detects symptomatic invasive infection

Treatment of CNS Aspergillosis:
- First line: voriconazole
- Refractory infection:
  - Liposomal amphotericin B
  - Voriconazole + an echinocandin
- If invasive fungal infection is suspected but aspergillosis is not confirmed: liposomal amphotericin B

Conclusion

CNS infection with Aspergillus is rare and requires a high degree of suspicion. This case shows the importance of Broad-Range PCR and next generation sequencing in the diagnosis and treatment of invasive aspergillosis.

References