Ocular Lesions in Disseminated Candidiasis

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Abstract
Aim: To assess the prevalence and patterns of ocular involvement in disseminated candidiasis in intensive care setting.

Materials and Methods: Institutional review board approved case review of intensive care admissions. These were patients of septicemia who had undergone ocular examination as part of their initial assessment. The records of patients in whom Candida spp. was detected in two sites or had a clinical diagnosis of candidemia were analyzed.

Results: Twelve patients (nine male, three female) were diagnosed with candida-induced sepsis during this period. Their ages ranged from 26 to 97 years (mean 52.7 years). Six patients (50%) had ocular lesions. The commonest lesion was chorioretinitis, seen in seven eyes of six patients followed by Roth spots seen in one eye. There was no evidence of vitritis or endophthalmitis in any eye. Systemic immunosuppression was present in three of six (50%) patients with ocular changes. Incidental findings included two eyes with non-proliferative diabetic retinopathy.

Conclusions: Any suspicion of disseminated candidiasis should prompt an ocular evaluation which may help in the early diagnosis and in the institution of early antifungal therapy. This may reduce ocular morbidity and patient morbidity.

INTRODUCTION
Infection with various Candida species (Candida albicans, which is the commonest, C. glabrata, C. parapsilosis and C. tropicalis) is increasingly being recognized as an important cause of ocular morbidity. The use of broad-spectrum antibiotics, abdominal surgery, indwelling central venous lines, parenteral nutrition and cytotoxic chemotherapy has contributed to this increase. Candidal infections can present as a mucocutaneous/cutaneous infection, as a deep organ infection or as a disseminated form. The disseminated form is commoner in patients with complicated post-surgical courses, hematological malignancies and in recipients of solid organ transplants, where hematogenous spread of the mycoses is the cause of ocular morbidity. Diagnosis of the disseminated form is via isolation of Candida spp. from multiple sites or from blood.

Ocular involvement in systemic candidiasis was first reported in 1958 and continues to be an important cause of visual morbidity with a prevalence ranging from 0 to 78% in western literature. Reported features include either focal or multifocal chorioretinitis or chorioretinitis with accompanying vitritis suggestive of an endophthalmitis. Treatment has included systemic antifungals or vitrectomy with or without intravitreal antifungal agents. Data from India is not available as to the prevalence and patterns of ocular complications in candidemic patients.

MATERIALS AND METHODS
We reviewed the records of patients with Candidal septicemia admitted in the intensive care unit who had undergone an ophthalmic evaluation as part of their initial admission protocol. This ICU is a multidisciplinary unit with a nurse to patient ratio of 1:1 or 1:2. Detection of Candida in the cultures of at least one tissue or fluid sample (except urine) was considered as evidence of systemic candidiasis. Patients with Candida cultured from a urine sample or from the urinary catheter only were not included as candidal colonization in these situations is commonly considered to be clinically non-significant. Records were analyzed with respect to basic demographic data (age, sex), pre-existing systemic conditions, primary focus of infection, microbiological studies, systemic findings and investigations and indirect ophthalmoscopy findings.

RESULTS
Twelve patients (9 male, 3 female) were diagnosed with candida-induced sepsis. Their ages ranged from 26 to 97 years (mean 52.7 years). Candida was isolated
from the tracheal secretions, peritoneal fluid, the central line tip, urine cultures and blood cultures. Eight of 12 patients (including all those with positive urine cultures) had evidence of candidal infection in at least two sites. The remaining four were clinically diagnosed as disseminated candidiasis based on the history and systemic findings even though culture in only one site was positive. Diabetes mellitus which was a common pre-existing disease was seen in seven patients and was of the non-insulin dependent type (NIDDM). Seven patients survived and five died. All the patients studied had at least, central lines inserted, several broad spectrum antibiotics administered and had Foley’s urinary catheters inserted.

A detailed anterior segment evaluation was not possible in these patients as they were all critically ill and hence only an indirect ophthalmoscopy was done. We defined chorioretinitis as the presence of focal, white, infiltrative chorioretinal lesions without vitritis and endophthalmitis as chorioretinitis with vitritis.

Six (4 males, 2 females) patients were found to have ocular lesions (both infective/inflammatory as well as non-specific) attributable to candidemia. The commonest lesion was chorioretinitis that was seen in six patients. The lesions were unilateral in five patients and bilateral in one yielding a total of seven involved eyes. There was no evidence of endophthalmitis in any eye. The lesions were located posterior to the equator in all cases. Additionally, Roth spots were seen in one eye. The results are summarized in Table 1. Follow-up was possible in only two cases and they resolved fully on systemic fluconazole therapy (400 mg/daily). Immunosuppression was present in three of six patients with chorioretinitis, consequent to an underlying carcinoma and cytotoxic chemotherapy while diabetes mellitus was present in the remaining three. Other findings included one patient (two eyes) with bilateral non-proliferative diabetic retinopathy.

**DISCUSSION**

In recent studies worldwide, a varying prevalence of ocular involvement in candidemia has been reported. Rodriguez-Adrian et al observed lesions in 7 of 180 (3.8%) patients. These included two patients with chorioretinitis with vitritis and five without and another 10% had non-specific retinal lesions such as Roth spots, cotton wool spots or superficial hemorrhages (ascribed by the authors as either due to the candidemia or to an underlying systemic disease). Donahue et al found ocular lesions in 9% of 118 patients with non-specific lesions seen in another 20% of the patients. In an autopsy series, McDonnell found ocular lesions in only 11 of 133 patients (8.2%). There was a high prevalence of ocular infection in our series (40% of our patients).

All the patients with ocular lesions were either

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**Table 1 : Showing the demographic, clinical and ocular features of patients with disseminated candidiasis**

<table>
<thead>
<tr>
<th>No.</th>
<th>Age/Sex</th>
<th>Preexisting disease (in years)</th>
<th>Admitting diagnosis</th>
<th>Stage of sepsis</th>
<th>Ocular findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>26/M</td>
<td>ALL/Pneumonia (post-chemotherapy)</td>
<td>Sepsis</td>
<td>Roth spots (R)</td>
<td>Chorioretinitis (L)</td>
</tr>
<tr>
<td>2.</td>
<td>44/M</td>
<td>Cholangiocarcinoma (post chemotherapy)</td>
<td>Sepsis</td>
<td>Chorioretinitis (R)</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>81/M</td>
<td>DM (15) Perforation with peritonitis</td>
<td>Septic shock</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>97/M</td>
<td>DM (25) Sepsis</td>
<td>Septic shock</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>58/M</td>
<td>DM (20) Extensive cellulitis</td>
<td>Sepsis</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>52/M</td>
<td>DM (5) Bladder carcinoma (post chemotherapy)</td>
<td>Sepsis</td>
<td>Chorioretinitis (L)</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>66/M</td>
<td>DM (15) Sepsis of unknown origin</td>
<td>Septic shock</td>
<td>Chorioretinitis (R) Non-proliferative diabetic retinopathy (BE)</td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>32/M</td>
<td>Peritonitis</td>
<td>Septic shock</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>52/F</td>
<td>DM (10) Hepatitis</td>
<td>Sepsis</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>10.</td>
<td>59/M</td>
<td>Perforated duodenal ulcer</td>
<td>Septic shock</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>11.</td>
<td>50/F</td>
<td>Chronic renal failure with urosepsis</td>
<td>Septic shock</td>
<td>Chorioretinitis (L)</td>
<td></td>
</tr>
<tr>
<td>12.</td>
<td>70/F</td>
<td>Sepsis following chemotherapy for recurrent ovarian carcinoma</td>
<td>Sepsis</td>
<td>Chorioretinitis (BE)</td>
<td></td>
</tr>
</tbody>
</table>
significantly immunosuppressed as a consequence of cytotoxic chemotherapy or had long-standing diabetes. The major classes of these agents (alkylating agents, antimetabolites and antimitotic drugs) have deleterious effects on both cellular and humoral immunity. Depression of cell-mediated immunity renders these patients prone to systemic and local fungal infections. Immunosuppression coupled with severe sepsis may lead to higher fungal loads and to a greater risk of ocular involvement. Our intensive care unit functions as a tertiary care center and receives cases of sepsis from neighboring units. These cases tend to have a history of extensive instrumentation, inappropriate antibiotic use or treatment-refractive sepsis.

In our series, the only infective lesion seen was chorioretinitis and no cases of vitritis/endophthalmitis were seen. Similar patterns have been reported in recent reports. This is in contrast to older literature with high rates of endophthalmitis and visual loss. This shift in pattern may reflect prophylactic and/or earlier use of effective antifungal agents especially fluconazole. The appearance of the chorioretinitis seen is not diagnostic of candidiasis and similar appearances may be found in other fungal infections. Changes were seen in one patient of bilateral non-proliferative diabetic retinopathy and were the result of that disease.

The exclusive use of indirect ophthalmoscopy may have led us to miss a mild vitritis and by extension, an early endophthalmitis. The use of a hand-held slit-lamp to assess the vitreous may help in more accurate or earlier diagnosis in high-risk patients. Histopathological examination of enucleated globes, which we could not do, may provide data on the extent and nature of the ocular tissues involved. Rao and co-workers have noted that the primary focus of candidal infection in endogenous candidal endophthalmitis is the vitreous cavity but similar studies in patients with candidal chorioretinitis are awaited.

Immunocompromised and diabetic individuals were responsible for chorioretinitis in our study. These lesions tend to be asymptomatic, as severely ill patients may not verbalize symptoms of visual loss. The detection of chorioretinitis in patients with suspected disseminated candidiasis may help in the early diagnosis of this infection, as microbiological investigations are often time-consuming, and may allow earlier antifungal therapy with reduction of systemic mortality. Awareness of this complication coupled with prompt therapeutic measures may reduce potential ocular morbidity.

REFERENCES