CT of Central Nervous System Infections in Immunocompromised Patients

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*AJNR Am J Neuroradiol* 1980, 1 (3) 239-243

http://www.ajnr.org/content/1/3/239

This information is current as of October 22, 2023.
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The computed tomographic (CT) scan appearance of parenchymal central nervous system (CNS) infection in 12 immunosuppressed patients was unlike that of the usual bacterial abscess in immunologically intact hosts. The lesions were poorly circumscribed and of low density. Contrast enhancement was minimal and did not assume a "ring" configuration. These CT scan findings heralded a poor prognosis. Compared to the neuropathologic findings, the CT scan generally underestimated the extent of involvement. Three other compromised patients were better able to localize the infection. This successful defense was manifested on their CT scans as the more typical "ring" pattern of contrast enhancement. Patients with this CT scan appearance of their CNS infection had a better prognosis.

CT scanning has facilitated the diagnosis of brain abscess; this combined with accurate localization has altered the prognosis [1–10]. Despite advances in diagnostic techniques and widespread use of antibiotics, the incidence of brain abscess is not decreasing [11, 12]. However, the spectrum of central nervous system (CNS) infections is changing because of an important and relatively new clinical problem—that of CNS infection in the immunosuppressed host [13–22]. With continued advances in cancer therapy and organ transplantation, the frequency of brain abscesses caused by opportunistic organisms in compromised hosts can be expected to increase. The organisms responsible for producing brain abscesses in compromised hosts differ from those that usually cause brain abscess. These more unusual, opportunistic organisms, which are normally of low virulence and pathogenicity in man, include fungi, protozoa, bacteria, and viruses. Because of host immunosuppression, these infections are usually not well localized, and they may not evolve to an encapsulated abscess. Thus, their CT scan appearance can be quite different from the more usual bacterial brain abscess [1–6].

Subjects and Methods

Cranial CT, performed on EMI Mark I and 1005 scanners (160 × 160 matrix), yielded 34 scans in 15 patients (aged 20–62) who were immunocompromised because of their primary disease, drug treatment, or both (table 1). Many disease entities were represented, but most patients were immunosuppressed allograft recipients: cardiac (seven patients) and renal (one) [23]. Three patients had leukemia: two were receiving chronic corticosteroid therapy, one had polycythemia vera (chlorambucil therapy), and one was debilitated by alcohol abuse and renal failure (table 1).
TABLE 1: Summary of Clinical Data

<table>
<thead>
<tr>
<th>Organism/Case No.</th>
<th>Underlying Disorder</th>
<th>CT Findings</th>
<th>Clinical Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Klebsiella pneumonia/1</td>
<td>Cardiac transplant</td>
<td>Ring contrast enhancement</td>
<td>Death *</td>
</tr>
<tr>
<td>Nocardia asteroides/2</td>
<td>Chronic lymphocytic leukemia</td>
<td>Multiple ring lesions</td>
<td>Living</td>
</tr>
<tr>
<td>Toxoplasma gondii:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Cardiac transplant</td>
<td>Ring contrast enhancement</td>
<td>Living</td>
</tr>
<tr>
<td>4</td>
<td>Renal transplant</td>
<td>Nonspecific lucency, minimal contrast enhancement</td>
<td>Death</td>
</tr>
<tr>
<td>5</td>
<td>Polycythemia vera, diabetes, cirrhosis (chlorambucil)</td>
<td>Nonspecific lucency, no contrast enhancement</td>
<td>Death</td>
</tr>
<tr>
<td>Aspergillus fumigatus:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Cardiac transplant</td>
<td>Nonspecific lucency, no contrast enhancement, punctate hemorrhage</td>
<td>Death</td>
</tr>
<tr>
<td>7</td>
<td>Cardiac transplant</td>
<td>Nonspecific lucency, no contrast enhancement</td>
<td>Death</td>
</tr>
<tr>
<td>8</td>
<td>Cardiac transplant</td>
<td>Nonspecific lucency, marked contrast enhancement</td>
<td>Death</td>
</tr>
<tr>
<td>9</td>
<td>Cardiac transplant</td>
<td>Nonspecific lucency, minimal contrast enhancement, punctate hemorrhage</td>
<td>Death</td>
</tr>
<tr>
<td>10</td>
<td>Acute myelogenous leukemia</td>
<td>Nonspecific lucency, minimal contrast enhancement</td>
<td>Death</td>
</tr>
<tr>
<td>11</td>
<td>Acute lymphocytic leukemia</td>
<td>Multifocal, nonspecific, lucent lesions with faint contrast enhancement</td>
<td>Death</td>
</tr>
<tr>
<td>12</td>
<td>Cardiomyopathy (corticosteroid)</td>
<td>Nonspecific lucency, no contrast enhancement</td>
<td>Death</td>
</tr>
<tr>
<td>13</td>
<td>Acute renal failure, alcoholism</td>
<td>False negative</td>
<td>Death</td>
</tr>
<tr>
<td>Candida albicans/14</td>
<td>Chronic asthma (corticosteroid)</td>
<td>Nonspecific lucency, no contrast enhancement</td>
<td>Death</td>
</tr>
<tr>
<td>Herpes zoster/15</td>
<td>Acute renal failure, alcoholism</td>
<td>False negative</td>
<td>Death</td>
</tr>
</tbody>
</table>

Note.—Data on four women and 11 men aged 20–62 years.
* Not due to brain abscess.

Results

The CT features of CNS parenchymal infection in these patients can be divided into two major groups. One group of three patients (cases 1–3) was characterized by the typical ring contrast enhancement described for the more usual bacterial abscess (fig. 1). Three different organisms were represented: *Toxoplasma gondii*, *Nocardia asteroides*, and *Klebsiella pneumoniae* (table 1). These patients were able to localize and encapsulate the infection; two survived the infection. Necrotizing bronchopneumonia and sepsis (staphylococcal) was the cause of death in the other (case 1). Aspiration of the abscess in cases 2 and 3 revealed an abscess capsule in both. Neuropathologic examination demonstrated an abscess capsule in case 1. In each patient the offending organism was identified and treated with the appropriate antibiotic(s).

The second group was 12 patients (cases 4–15) with CT scans prior to contrast infusion that demonstrated poorly defined, low density lesions which were usually small, deep, and initially often solitary (fig. 2). Early in the disease course, abnormalities were subtle. Most frequently, they were located in the basal ganglia or in the centrum semiovale and resembled deep cerebral infarcts. In two patients (cases 6 and 9), both with aspergillosis, small hemorrhages were present within the low density lesion (fig. 3). Contrast enhancement was minimal, often consisting of vague, patchy enhancement at the edges of the lesion. Prominent but poorly circumscribed contrast enhancement occurred in only one patient as the infection became widespread (case 8, fig. 4). One patient (case 15, *herpes zoster* meningoencephalitis) exhibited prominent contrast enhancement of the subarachnoid space and tentorium, but no parenchymal lesions were detectable on the CT scan. One probable false-negative examination occurred with widespread CNS aspergillosis (case 13); a CT scan 10 days before death was
normal. Six patients in group 2 received amphotericin for disseminated aspergillosis; this organism was identified in the lung in five patients and by brain biopsy in the other (cases 6–10, 12). The six other patients in this group did not receive appropriate antibiotic coverage because the organism was not identified or suspected prior to death. Unlike the group with typical ‘ring’ lesions, this group of patients, with nonspecific, poorly defined lesions, had a 100% mortality rate. The type of organism could not be predicted from the CT scan, although hemorrhage suggested aspergillosis because of its propensity for vessel wall invasion. Aspergillosis was also characterized by an increase in size and number of lesions over 3–8 days, at times a very rapid increase. *Aspergillus* could be strongly implicated when such lesions appeared in patients known to have pulmonary aspergillosis.
The degree of enhancement did not increase as the infection spread except in one patient (fig. 4).

Neuropathologic findings, available for all in group 2, confirmed the patients' inability to confine or wall off the infecting organism. Patients with different fungal infections showed similar neuropathologic changes which represented a hybrid of cerebral infection and infarction. Vessel wall invasion by Aspergillus (septated, branching hyphae) was a prominent finding resulting in vessel destruction, thrombosis, hemorrhage, and cerebral infarction. Focal areas of necrosis with surrounding acute and chronic inflammatory cells were widely dispersed. However, severe and widespread Aspergillus invasion was distinguished by its relative lack of inflammatory infiltrate. Aspergillus invasion was not limited to the brain parenchyma; meningitis with vascular invasion and ventriculitis were commonly present.

In patients with toxoplasmosis, the findings included multiple necrotic foci with Toxoplasma seen both intra- and extravascularly. Blood vessels themselves were necrotic resulting in small hemorrhages. The inflammatory infiltrate was primarily perivascular. The Herpes zoster varicellous meningoencephalitis was characterized by mononuclear perivascular infiltrates, scattered areas of infarction, moderate neuronal loss, intranuclear eosinophilic inclusion bodies, and diffuse meningitis. In none of these patients was the formation of an abscess wall detected around areas of necrosis and inflammation. The extent of neuropathologic involvement in these poorly localized infections was greatly underestimated by the abnormalities detected on the CT scan.

Patients with CNS aspergillosis all had disseminated disease; the most likely origin was pulmonary, since the lungs were always involved. CNS candidiasis also occurred in the context of disseminated disease. Herpes zoster and one of the two toxoplasmosis infections were limited to the CNS; the other toxoplasmosis infection involved the CNS and the myocardium.

Discussion

Immunocompromised patients are susceptible to "opportunistic" organisms which are normally of low pathogenicity in man but are more resistant to antibiotic therapy because of their reproduction and growth pattern. The decreased host resistance in immunosuppression derives from defects in three main areas of defense: decreased phagocytosis, impaired cell mediated immune response, and altered humoral response (gamma globulin) [12]. These defects can arise from the primary disease itself and/or immunosuppressive therapy required for its treatment.

The CT scan appearance of CNS infections seems to be a function less of the specific infecting organism and more of the host's reaction to it. Therefore, the same organism can be handled differently, depending on the host's immune status. The CT scan accurately reflects this interaction of host and organism by the pattern of contrast enhancement. Despite their susceptibility to opportunistic agents, some immunocompromised patients are still able to mobilize enough of a defense to forestall rapid spread of the organism and to eventually wall off the infection (i.e., form an abscess). The CT scan appearance of this interaction is that of typical "ring" contrast enhancement. In our series of patients, this occurred with Nocardia and Toxoplasma but not with fungi. This "ring" pattern may not represent the abscess capsule itself, but indicates the infection is localized and an abscess is evolving [24]. Hence, a brain abscess caused by opportunistic organisms may have CT scan findings identical to those of the more usual bacterial agents. In our series of patients, the same organism, (Toxoplasma gondii) produced both the typical "ring" appearance in one patient and the more nonspecific findings in others. Lesions caused by Aspergillus fumigatus were consistently of the nonspecific type in this series of immunosuppressed patients; however, in normal hosts capsule formation, in abscess or granuloma formation, and "ring" contrast enhancement have been described [2, 16, 25, 28].

If a patient was unable to localize the infection, the lesions were of poorly circumscribed low density and usually exhibited little contrast enhancement. The role of corticosteroids in limiting enhancement is difficult to determine. Although corticosteroid treatment can reduce the degree of contrast enhancement, it is not likely to eliminate it [27]. These lesions resembled cerebral infarction but were often distinguished by the rapid increase in their size and number. The CT scan resemblance to infarction is understandable since in aspergillosis and mucormycosis, fungal invasion of vessel walls characteristically results in thrombosis and infarction [16, 17]. Toxoplasma gondii infects all types of cells in the brain and can cause thrombosis and cerebral infarction by disruption of endothelial cells [18, 19]. In addition, the inflammatory infiltrate in compromised hosts with fungal infections may be conspicuous by its absence, especially early in the course of the infection. When rapid spread was recognized on the CT scan, typically the extent of the disease was underestimated compared to the neuropathologic examination, especially in aspergillosis. A CT scan showing poor localization and no "ring" contrast enhancement presaged an extremely poor prognosis.

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