CRYPTOCOCCAL INTRACEREBRAL MASS LESIONS ASSOCIATED WITH CRYPTOCOCCAL MENINGITIS

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Abstract. 12 patients with cryptococcal intracerebral mass lesions associated with cryptococcal meningitis are reported. There were 6 males and 6 females with a mean age of 41 years. Most of them presented with symptoms and signs of meningitis initially without focal neurological signs. Computed tomography revealed single or multiple, well or poorly marginated hypodense lesions without perilesional edema, except 1 case which had marked edema, with or without ring enhancement. One case had small hyperdense, diffuse, enhanced nodules. New lesions or progression of the existing lesions occurred during medical therapy in some patients. The clinical manifestations of patients with intracranial mass lesions did not significantly differ from patients without mass lesions, but the mortality was higher (50% vs 29%).

INTRODUCTION

Cryptococcosis is caused by inhalation of airborne *Cryptococcus neoformans.* The most common form of central nervous system infection is meningitis. Cryptococcal intracerebral mass lesion is a rare form and may be seen with or without meningitis.

In this paper, we present our experience with cryptococcal intracerebral mass lesions, associated with meningitis.

MATERIALS AND METHODS

From April 1985 to December 1991, 43 patients with a diagnosis of cryptococcal meningitis who had computerized tomographic (CT) examinations of the brain were reviewed. Proven cryptococcal meningitis was based on two of the following: a) cerebrospinal fluid (CSF) Indian ink stain positive; b) culture of CSF positive for *C. neoformans;* c) CSF cryptococcal latex antigen test positive.

RESULTS

There were 12 patients who had intracerebral mass lesions, 6 were males and 6 were females. Age incidence ranged from 25-66 years with a mean of 41 years. The clinical manifestations and clinical outcome are shown in Tables 1 and 3. Except patient no. 12, none had localizing signs such as hemiparesis or aphasia at initial presentation. Only one case (patient no. 8) had an associated condition (malnutrition). CT findings are shown in Table 2. All of them had hypodense mass lesions (single lesion in 8 cases, two lesions in 1 case, multiple lesions in 1 case and multiple lesions with poorly marginated lesions in 1 case. These occurred with and without ring enhancement at the various sites in the brain except for patient no. 4, who had hyperdense with poorly marginated hypodense lesions and diffuse small enhanced nodules. The sizes of the lesions varied from less than 1 cm to 2.5 cm in diameter. Patients no. 5 and no. 8 had normal CT finding and early cerebritis at initial presentation, respectively. Six cases responded to treatment (cure in 5 cases and improvement in 1 case) and 6 patients died. In the improving patient, visual impairment remained persistent while other clinical manifestations disappeared. On follow-up with a mean of 19 months, no living patient had relapsed. Of the 6 fatal cases, 5 died from progression of the disease; 3 cases (patients no. 1, 7, 8) died within 1-2 weeks during antifungal drug therapy. Patient no. 4 was treated with amphotericin B 1,800 mg but he developed right hemiparesis and a stuporous condition. Repeated CT scan revealed increased size and number of small enhanced lesions with an enlarged hypodense lesion of left parietal lobe (Fig 1A, B). Patient no. 5 developed drowsiness after treatment with am-

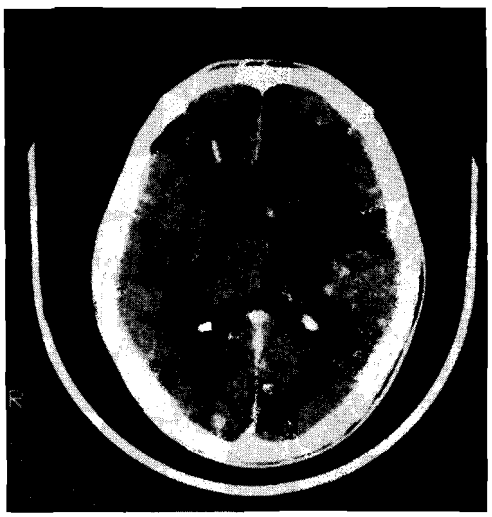
Table 1

Patient characteristics and clinical outcome of 12 patients with intracranial mass lesions.

Patient No.	Age/Sex	Symptoms	Signs	Other foci of infection	Antifungal drugs	Outcome
1	35/M	headache 3 months	stiffneck, bilateral papilledema	-	amphotericin B and flucytosine	death
2	32/F	fever and headache 1 month	T 38.2° C, stiffneck, unilateral 6th nerve palsy, bilateral papilledema	-	amphotericin B	death
3	25/F	headache 1 week	stiffneck, bilateral papilledema	-	amphotericin B and flucytosine 6 weeks	cure
4	51/M	headache 1 month, drowsiness and decreased vision 4 days	stiffneck, hand movement both eyes, bilateral papilledema	lung, skin	amphotericin B	death
5	39/F	headache 1 month	stiffneck, bilateral 6th nerve palsy, bilateral papilledema	-	amphotericin B (+surgical removal)	death
6	66/M	Fever, headache and confusion 5 days	T 39.0°C, stiffneck	lung	amphotericin B and flucytosine 6 weeks	cure
7	35/M	fever and headache 2 weeks	T 38.5°C, stiffneck	skin	itraconazole	death
8	31/F	fever and headache 3 days	T 38.2°C, stiffneck, malnutrition	lung, skin	amphotericin B and flucytosine	death
9	53/M	fever and headache 2 weeks, drowsiness 1 week	T 38.7°C, stiffneck	-	fluconazole 8 weeks	cure
10	45/M	headache 1 month, drowsiness 2 weeks	stiffneck, bilateral papilledema	-	amphotericin B and flucytosine 2 weeks, followed by itraconazole 8 weeks	cure
11	39/F	headache 1 month, drowsiness 2 weeks	stiffneck, bilateral 6th nerve palsy, 6/60 of both eyes, bilateral papilledema	-	amphotericin B and flucytosine 2 weeks, followed by itraconazole 8 weeks	improvement
12	47/F	fever and headache 10 days, drowsiness 3 days	T 38.0°C, stiffneck, positive rt cerebellar sign, bilateral papilledema	-	amphotericin B and flucytosine 2 weeks, followed by itraconazole 8 weeks	cure

photericin B 1,800 mg. Repeated CT scan revealed an abnormal mass with marked perilesional edema (Fig 2). Surgical removal was performed without improvement. Histological finding of the mass was compatible with cryptococcal granuloma. Patient no. 2 improved during treatment with amphotericin B 3,000 mg but died from brain herniation resulting from obstructed ventriculo-peritoneal shunt.

Table 3 shows the clinical manifestations at initial presentation and outcomes of patients with



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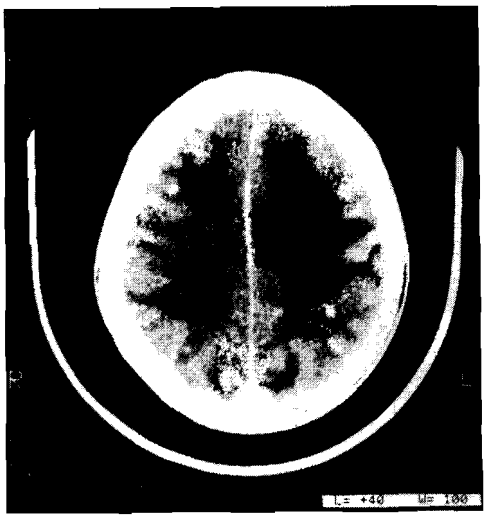

B

Fig 1—A, B (patient no. 4): CT scan showing diffuse small enhanced lesions and poorly marginated hypodense lesion.

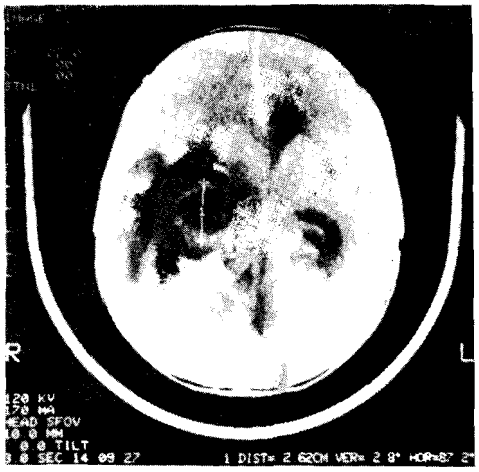

Fig 2—(patient no. 5): CT scan showing hypodense lesion with marked perilesional edema.

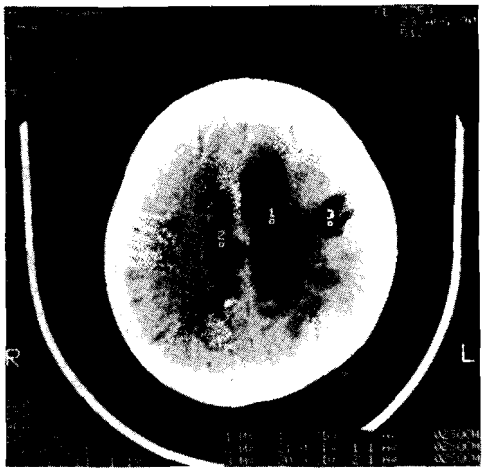

Fig 3—(patient no. 8): CT scan showing multiple hypodence with poorly marginated hypodense lesions.

and without intracranial mass lesions. Mortality seemed to be higher in patients with intracerebral mass lesions.

DISCUSSION

Fujita *et al* (1981) studied 55 cases of intracerebral cryptococcal mass lesions and found that the lesions were usually single. The lesions had a mean size of 4 cm diameter; 34 patients had an associated meningitis of which 6 (18%) had no characteristic symptoms or signs of a focal central nervous system lesion or increased intracranial pressure. Of 13 patients that had meningitis diagnosed during life, 9 patients died.

CT scan is very useful technique for defining intracerebral lesions. Non-contrast CT scans in cryptococcal meningitis may show poorly or sharply marginated, low density lesions with or without surrounding edema. Contrast CT scans may show

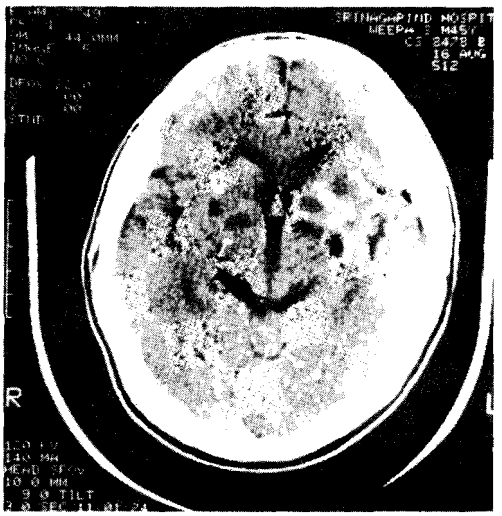

Fig 4—(patient no. 10): CT scan showing multiple hypodense lesions.

little or no enhancement, ringlike enhancement, or homogeneous areas of enhancement (Garcia *et al,* 1985; Lee, 1987; Zee *et al,* 1988). However these abnormalites are not specific for cryptococcosis. Other infectious diseases such as cysticercosis, tuberculosis, and neoplasms have also been reported to give similar findings.

Of the pathologic features of cryptococcal intracerebral mass lesions, 4 types have been reported: abscess, gelatinous mass, fibrogranulomatous mass and mixed-type.

Up to now there is no established treatment for cryptococcal intracerebral mass lesions. The lesions may persist, decrease or undergo complete resolution; progression, or development of new lesions may occur with medical treatment. Fujita *et al* (1981) suggested that a prolonged course of medical therapy alone may be adequate as the initial mode of therapy in patients with small mass lesions,

Table 2

Computed tomographic findings of 12 patients with intracranial mass lesions.

Patient No.	Number of lesion	Density before contrast enhance	Enhancing characteristics	Size of the lesion	Surrounding hypodensity	Site of the lesion	Evolution of CT after treatment
1	1	hypodense	mininal rim enhancement	2.2 cm	-	lt. basal ganglia	ND
2	1	hypodense	rim enhancement	1 cm	-	rt. temporal lobe	ND
3	1	hypodense	rim enhancement	1.7 cm	-	lt. parietal lobe	not changed
4	1	hypodense	non enhancement,	< 1 cm	-	rt. thalamus	progression
	1	poorly marginated, hypodense				lt. parietal lobe	
			(with diffuse small enhanced lesion in both hemisphere)				
*5	1	hypodense	rim enhancement	2.5 cm	+ + +	rt. temporo-pareito-occipital region	ND
6	1	hypodense	non-enhancement	< 1 cm	-	rt. cerebellum	ND
7	2	hypodense	non-enhancement	1 cm	-	both cerebellar hemispheres	ND
*8	multiple	hypodense with poorly marginated, hypodense	non-enhancement	< 1 cm	-	both parietal lobes	ND
9	1	hypodense	non-enhancement	< 1 cm	-	posterior limb of lt. internal capsule	ND
10	multiple	hypodense	non-enhancement	< 1 cm	-	both basal ganglias	ND
11	1	hypodense	non-enhancement	< 1 cm	-	rt. temporo-parietal region	ND
12	1	hypodense	non-enhancement	1 cm	-	rt. cerebellum	ND

- = no, + + + = large or marked, ND = not done

* initial CT scan showed normal finding and cerebritis at Lt parietal lobe respectively.

Table 3

Comparison of patients with and without intracranial mass lesions (initial presentation).

	With lesions (n = 12)	Without lesions (n = 31)
Age (mean), years	41	42
Sex (males), n	6	15
Duration of symptoms (mean), days	24	36
Fever, n	6 (50%)	13 (41%)
Mental impairment, n	6 (50%)	14 (45%)
Papilledema, n	8 (66%)	19 (61%)
Eye ocular movement abnormality, n	3 (25%)	11 (35%)
Decreased vision, n	2 (16%)	11 (35%)
Decreased hearing, n	0	1
Other foci of cryptococcal infection, n		
lung	3 (25%)	10 (32%)
skin	3 (25%)	1 (3%)
Localizing signs, n		
cerebellar sign	1	0
Associated diseases, n	1 (8%)	3 (9%)
Death, n	6 (50%)	9 (29%)

and surgical intervention should be considered when the lesions reached a size greater than 3 cm in diameter, if located in surgically accessible areas. Futher study is warranted.

This investigation showed that the initial clinical manifestations of cryptococcal meningitis patients with intracerebral mass lesions usually presented without focal neurological deficits, depending on the size of the lesions. Most of them had small lesions without surrounding edema. New lesions or progression of existing lesions occurred in some cases during medical therapy. The mortality depended on the severity of the meningitis and the size of the lesions. From our experience we suggest that in cryptococcal meningitis patients who had no signs of focal neurological deficits, mental impairment or papilledema, CT scan of the brain is useful though not mandatory.

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