

Stereotactic Brain Biopsies in AIDS Patients - Early Local Experience

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ABSTRACT

Aim: To assess the usefulness of stereotactic brain biopsies in AIDS patients with cerebral lesions in Singapore.

Methods: A total of 10 patients with AIDS and cerebral lesions underwent stereotactic brain biopsies in the Department of Neurosurgery, Tan Tock Seng Hospital (TTSH) between September 1997 and September 1998. The patients were referred from the Communicable Diseases Centre (CDC), TTSH. These patients either failed a trial of therapy for toxoplasmosis encephalitis (TE) or had CT/MRI scans which did not suggest TE. Four were CT-guided and six were MRI-guided stereotactic biopsies. The Radionics Cosman-Robert-Wells (CRW) stereotactic apparatus was used for all cases.

Results: The male to female ratio was 9:1. Histological diagnosis from biopsy was lymphoma (5), metastatic adenocarcinoma (1), TE (1), abscess (1), encephalitis (1) and granulomatous tissue (1-presumed tuberculosis).

Conclusion: The early experience is that stereotactic brain biopsy is useful in patients with AIDS and cerebral lesions. The etiology is confirmed in the majority of cases and impacts on management decisions and prognostication.

Keywords: stereotactic brain biopsy, HIV, cerebral lesions

Singapore Med J 2000 Vol 41(4):161-166

INTRODUCTION

The incidence of HIV and AIDS has increased in Singapore since the first case was reported in 1985. There were 173 residents with HIV infection reported in 1997, compared with 139 cases in 1996. The cumulative number of HIV infection in residents at the end of 1997 was 731⁽¹⁾. Cerebral lesions are common in HIV infections with up to 10% of patients having CNS involvement as the first sign of HIV infection.

Toxoplasmosis encephalitis (TE) and cerebral lymphomas were the 2 most common causes of such lesions^(2,3,4). While cerebral lesions may not be the direct cause of mortality, they do cause considerable morbidity ranging from change in mentation to focal neurological deficits. The differentiation between TE and lymphoma is often difficult. Imaging either by CT or MRI may not definitively differentiate between the 2 lesions^(2,3,5,6,7,8,9,10). Hence in cases where there is doubt, or where empirical treatment for TE was unsuccessful, a brain biopsy is advocated⁽¹¹⁾. If empiric treatment for TE fails to demonstrate any clinical or radiological improvement within 10-14 days, it is considered as unsuccessful treatment⁽¹²⁾. In a recent editorial Whittle and Lean⁽¹³⁾ reviewed the experience of 11 neurosurgical series of brain biopsies in AIDS patients and established that cerebral lymphoma, TE and progressive multifocal leukoencephalopathy (PML) were the most common findings. These studies also reported a median diagnostic tissue rate of 92%. The most common complication is intracerebral haemorrhage and it is also certainly the one that carries the most mortality. This paper describes our local experience with stereotactic brain biopsies in AIDS patients with cerebral lesions.

METHODS

A total of 10 AIDS patients with cerebral lesions underwent stereotactic brain biopsies under local anaesthesia in the Department of Neurosurgery, Tan Tock Seng Hospital between September 1997 and September 1998. The patients were all referred from the Communicable Diseases Centre (CDC), TTSH. These patients had AIDS and presented with either changes in sensorium, seizures or focal neurological deficits and were found to have brain lesions on CT or MR imaging. All patients subsequently had MRI brain scans performed. Prior to biopsy, nine of the ten patients received empiric therapy for TE (6), tuberculosis (3) or pyogenic infection (1). One patient received therapy for both TE and TB. One patient had biopsy done without any empiric treatment because the lesion was solitary and the anti-toxoplasma serology was negative. Patients who underwent stereotactic brain biopsies either failed

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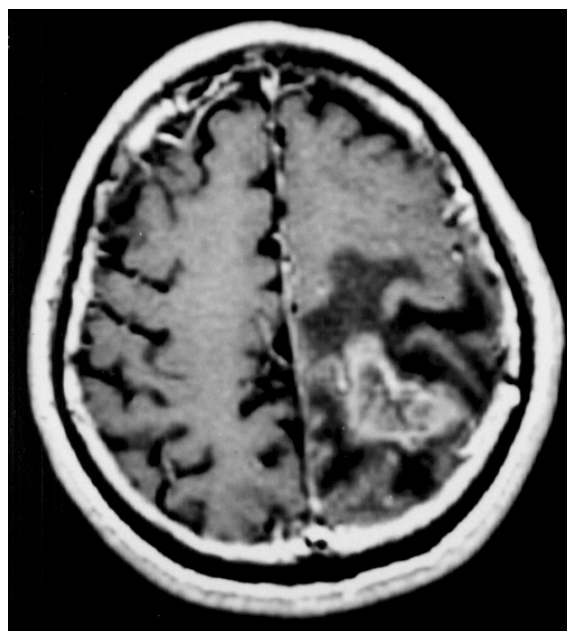
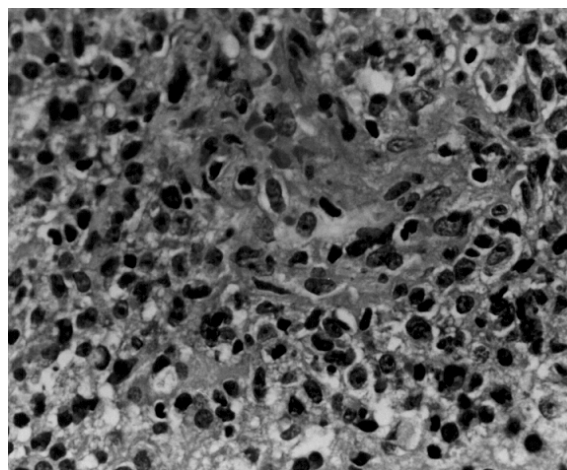
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Table I. Characteristics of the 10 patients

	Age/Sex/Race	Date of op	Initial treatment	Biopsy type	Diagnosis
1	57/M/C	29/9/97	For toxoplasmosis	CT-guided	Metastatic adenocarcinoma
2	35/M/C	4/11/97	For toxoplasmosis	CT-guided	High grade lymphoma
3	39/M/C	14/5/98	Not treated. Single lesion Toxoplasma serology negative	CT-guided	Malignant large cell lymphoma
4	59/M/C	8/12/97	For toxoplasmosis and tuberculosis	MRI-guided	Large cell lymphoma (B)
5	41/M/C	15/1/98	IV rocephine (for meningitis)	CT-guided	Cerebral abscess no AFB,TB, carcinoma
6	37/M/C	16/12/97	For toxoplasmosis	MRI-guided	Large cell lymphoma (B)
7	43/M/C	21/7/98	For tuberculosis	MRI-guided	Granulomatous reaction
8	32/M/C	18/8/98	For tuberculosis	MRI-guided	Encephalitis
9	30/F/Thai	17/12/97	For toxoplasmosis	MRI-guided	Large cell lymphoma (B)
10	29/M/C	11/9/98	For toxoplasmosis	MRI-guided	Toxoplasmosis

Table II. Further Characteristics of the 10 patients

	Number of lesions	Treatment after diagnosis	Survival after biopsy (up to 1 March 1999)	Diagnosis
1	Multiple.	Gamma knife radiosurgery and radiotherapy	3 months 2 days	Metastatic adenocarcinoma
2	Single. R frontal lobe.	Radiotherapy	5 months 5 days	High grade lymphoma
3	Single. R frontal parietal.	Died before radiotherapy	16 days	Large cell lymphoma B cell type
4	Single. L parietal mass.	Radiotherapy	1 month 24 days	Large cell lymphoma B cell type
5	Single, left periventricular region.	Antibiotics	2 months 9 days	Cerebral abscess no AFB,TB, carcinoma
6	Multiple.	Radiotherapy	4 months 15 days	Large cell lymphoma B cell type
7	Multiple.	Continued Anti-Tuberculous and Toxoplasma treatment	2 months	Granulomatous reaction
8	Multiple.	Continued antibiotics	2 months 3 days	Encephalitis
9	Multiple.	Radiotherapy	Alive	Large cell lymphoma B cell type
10	Single, Right caudate.	Continued Anti-Toxoplasma Treatment	Alive	Toxoplasmosis

**Fig. 1** Contrast-enhanced T1-weighted MRI brain scan of an AIDS patient for stereotactic biopsy showing an irregularly enhancing lesion at the left parietal lobe with adjacent vasogenic oedema.**Fig. 2** Histopathological slide of lymphoma showing numerous malignant lymphoid cells infiltrating blood vessel and surrounding neuroparenchyma.

a trial of empiric treatment (given by the CDC physician) or had CT/MRI scans which did not suggest toxoplasmosis. Failed treatment is defined as the lack of either clinical or neuroradiological improvement over a duration of 14 days. Four of the stereotactic biopsies were CT-guided and six were MRI-guided stereotactic biopsies (see Fig. 1). CT guidance was used if the lesion to be biopsied was well-delineated on the CT scan. The Radionics Cosman-Robert-Wells (CRW) stereotactic apparatus with the side-cutting Nashold biopsy instrument was used for all cases.

RESULTS

The results are as follows. (see Table I & II). There were 9 male patients and 1 female patient. This is consistent

with the male:female ratio of HIV notifications in Singapore. Age range was 29 to 59 years. There were 5 lymphomas (see Fig. 2), 1 metastatic adenocarcinoma, 1 toxoplasmosis, 1 abscess, 1 encephalitis and 1 granulomatous tissue (presumed tuberculosis). As can be seen, 9 out of 10 cases were treated prior to biopsy. This included 6 for toxoplasmosis, 2 for tuberculosis and 1 for meningitis. Of the 10 patients, 5 (50%) had single lesions while 5 had multiple lesions. 3 of the 5 with single lesions had cerebral lymphoma while 1 had an abscess and the last had toxoplasmosis. Of the 5 who had multiple lesions, 2 had cerebral lymphoma, 1 had metastatic adenocarcinoma, 1 had encephalitis while the last was reported as granulomatous reaction.

The only patient who had toxoplasmosis had the brain biopsy done because it was a solitary lesion on the CT and MRI scan and the anti-toxoplasma serology was negative. The patient did not have a 2 week course of anti-toxoplasma treatment before the biopsy. Of the patients with lymphoma, only one is still alive after 1 year while the other 4 died within 6 months. Of the non-lymphoma patients, only the patient with toxoplasmosis is still alive as of 1 March 1999, just short of 6 months.

The site of the cerebral lesions was diverse. There were no complications in this series of patients.

DISCUSSION

Cerebral lesions are fairly common in patients with AIDS. They may be either infective in nature, such as toxoplasmosis and TB, or malignant neoplasms e.g. lymphoma. Toxoplasmosis and primary central nervous system lymphoma are the 2 most common lesions. Unfortunately, it is sometimes difficult to differentiate between cerebral lymphoma and toxoplasmosis (see Figs. 3, 4).

Hence non-radiological investigations are frequently used to aid in diagnosis and treatment. The most common include toxoplasma serology and brain biopsies. The current practice in Singapore is to manage patients based on an algorithm⁽¹⁴⁾. Essentially, treatment centers around 3 factors: (1) Presence of anti-toxoplasmosis serology (2) CT or MRI scan findings (3) Brain biopsy results. The current treatment protocol is simplified below (see Fig. 5).

When a HIV patient presents with neurological signs suggestive of an intracerebral lesion, CT or MRI brain scans and anti-toxoplasmosis IgG serology will be done. If there are multiple cerebral lesions or if anti-toxoplasmosis serology is positive, the patient will be treated as for toxoplasmosis without a need for biopsy. If there is no clinical improvement in 10-14 days, or if there is clinical deterioration in 3 days despite therapy, a brain biopsy is indicated. If the CT or MRI shows a

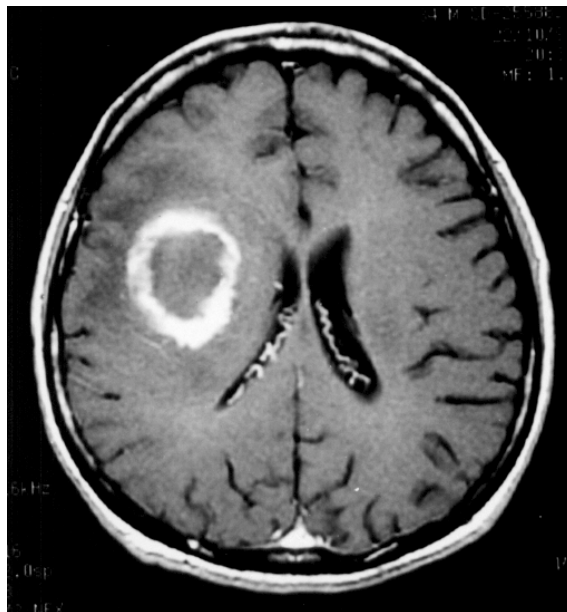


Fig. 3 Contrast-enhanced T1 weighted MRI brain scan shows a ring enhancing lesion in the right frontal lobe with vasogenic oedema and mass effect. Biopsy proved this to be a lymphoma.



Fig. 4 Contrast-enhanced T1 weighted MRI brain scan showing a ring-enhancing lesion with mass effect at the region of the left basal ganglia. Biopsy proved this to be toxoplasmosis.

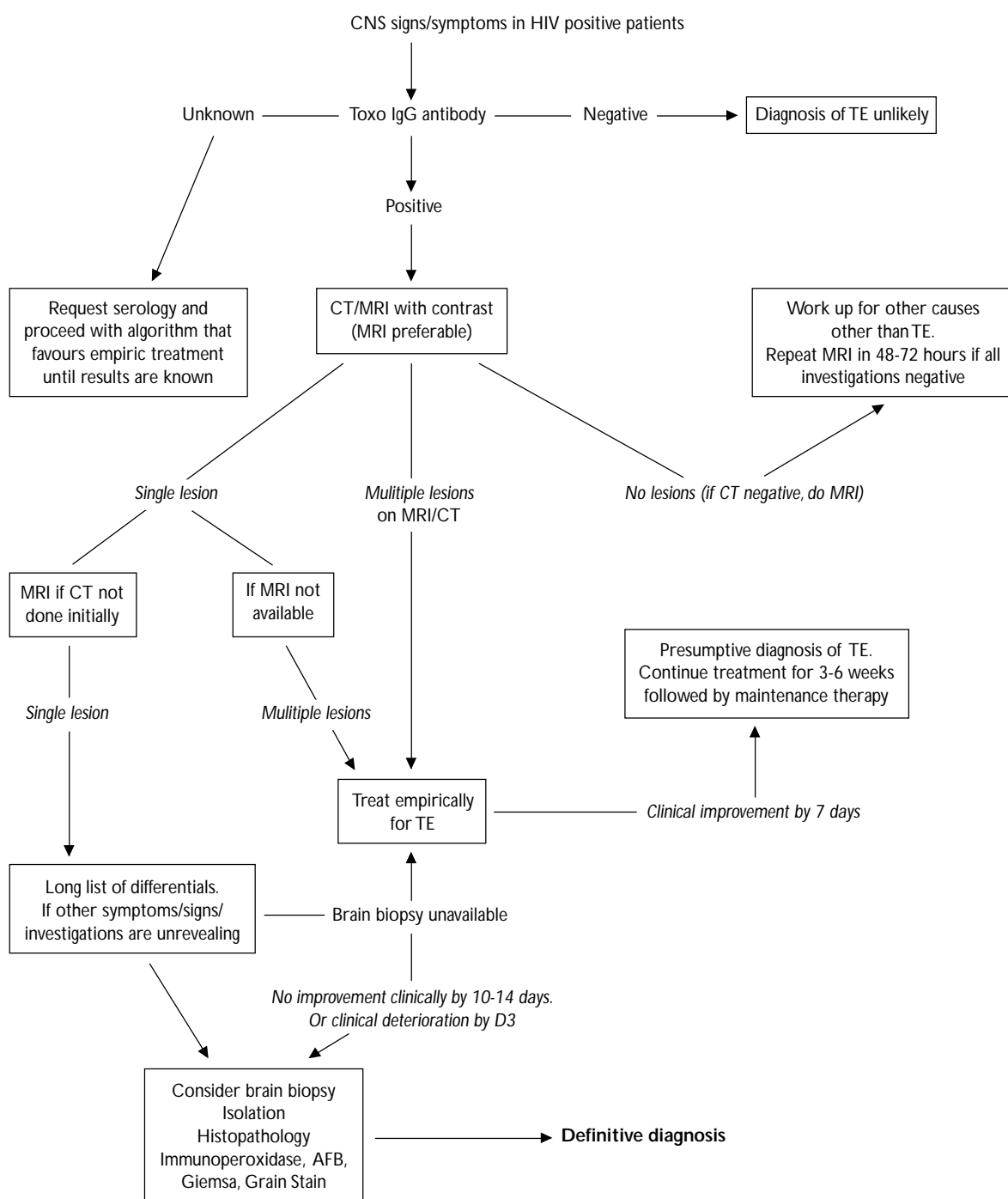
single lesion, then the patient is investigated for other diagnoses. These investigations may include a brain biopsy. As can be seen, our local experience shows that there were 9 out of 10 definitive diagnoses, including 2 which revealed encephalitis and abscess but without the exact infective organism being identified. The last result of granulation tissue was in a patient with proven tuberculosis who had undergone anti-tuberculous treatment.

The criteria for brain biopsy in HIV patients with cerebral lesions has been discussed in numerous other papers^(3, 6, 15, 16, 17). The above algorithm considers the fact

that brain biopsy carries with it a certain morbidity and mortality. Stereotactic brain biopsy allows localization of cerebral lesions with MRI or CT to be biopsied accurately with minimal damage to surrounding structures as opposed to open brain biopsy. The experience of other centres has also shown that the use of stereotactic brain biopsy has proven to be accurate and useful in diagnosing brain lesions in HIV patients who fail a trial of anti-toxoplasmosis

treatment^(17, 18, 19, 20). Their experience also shows that stereotactic brain biopsy is generally safe but there are still small risks of complications, the most devastating being that of intracerebral hemorrhage. Hence the presumptive anti-toxoplasmosis treatment if toxoplasma serology is positive and MRI/CT brain scan is suggestive. While there was no case of post-operative intracerebral hemorrhage with subsequent mortality in this series, in the literature the rate of

Fig. 5 Clinical Algorithm for HIV patients suspected to have toxoplasma encephalitis (TE)¹¹. Modified from Wong SY and Remington JS: Toxoplasmosis in the setting of AIDS, Textbook of AIDS medicine. 1st edition. Baltimore, Williams & Wilkins, 1994, pp244



haemorrhagic complications rate ranges from 4-20%⁽¹³⁾ in HIV-positive patients.

MR spectroscopy may be used as an adjunctive diagnostic imaging tool (see Fig. 6a, b; 7a, b). It may prove useful in helping to make more accurate radiological differentiation between cerebral toxoplasmosis and lymphoma⁽⁷⁾.

Whittle and Lean⁽²⁴⁾ commented that brain biopsies, although diagnostic, did not make an impact on the median survival time⁽¹³⁾, and as such, questioned the need for brain biopsies in HIV-positive AIDS patients. Of the 5 patients with cerebral lymphoma, one is still alive after 1 year, while the other 4 died within 6 months. The mean survival time is 90 days for these 4 patients. Our study is too small to make any other generalisations. On the other hand, with advances in the treatment of both AIDS (especially with new anti-retroviral regimes), and for lymphomas, it could be argued that the clear diagnosis of cerebral lesions in AIDS

patients may eventually result in improved survival rates that is currently not evident with current therapeutic options.

CONCLUSION

There is a useful role for stereotactic brain biopsy in patients with AIDS and cerebral lesions. This is especially so in patients who fail a trial of anti-toxoplasma treatment. The etiology is made clear in the majority of cases and impacts greatly on management decisions and prognostication. Our findings in Singapore are comparable to previous reports in other centres.

ACKNOWLEDGEMENTS

We would like to thank Dr P L Ong for his kind support, Ms Mary Heng for her secretarial assistance, and all the histopathologists who have helped to read the slides of the patients in this study.

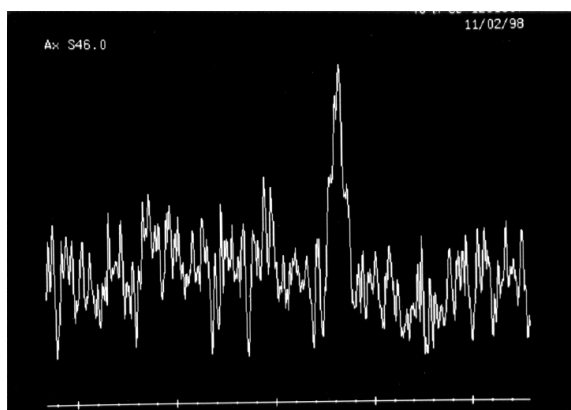


Fig. 6a & b MRS (Magnetic Resonance Spectroscopy) of biopsy – proven toxoplasmosis shows peak of breakdown products at 1.3 ppm position.

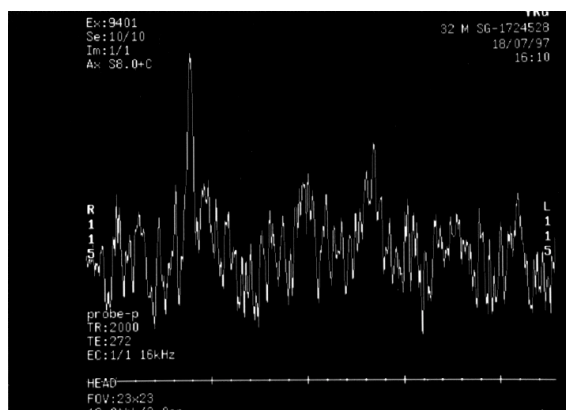
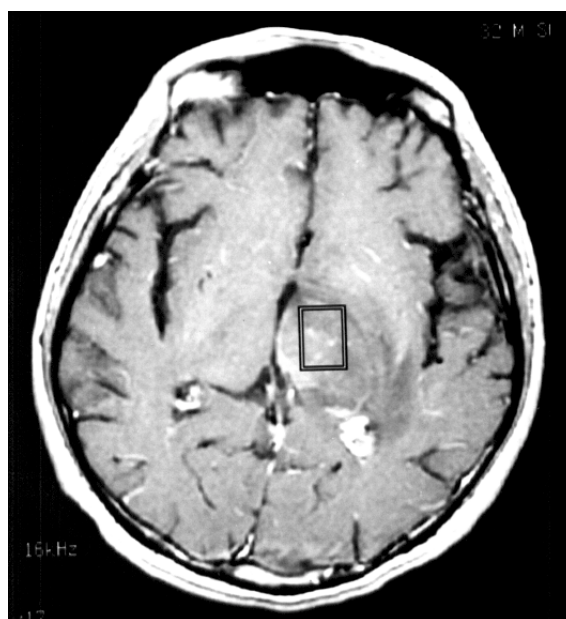


Fig. 7a & b MRS (Magnetic Resonance Spectroscopy) of biopsy – proven lymphoma shows elevated choline peak at 3.2 ppm with small peak of breakdown products at 1.3 ppm position.

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