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STEREOTACTIC BIOPSIES OF BRAIN LESIONS

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Abstract – Objective: In the majority of cases, the correct treatment of brain lesions is possible only when the histopathological diagnosis is made. Several deep-seated lesions near eloquent areas are not safely approached by the classical neurosurgical procedures. These patients can get benefit by a minimally invasive procedure. **Method:** We present a series of 176 consecutive patients submitted to stereotactic biopsies due to a great variety of brain lesions. **Results:** Histological diagnosis found in this series: glioma in 40.1% of the patients, other neoplasms in 12.2% and infectious or inflammatory diseases in 29.1 %. The result was inconclusive in 5.2% of the procedures. One patient died (0.6%) and two (1.2%) presented operative complications. The criteria, advantages and risks of the stereotactic biopsies are discussed. **Conclusion:** The efficacy of the method is adequate and morbid-mortality rates were low.

KEY WORDS: brain biopsy, stereotaxy, brain lesions, cancer.

Biópsia estereotáxica de lesões encefálicas

Resumo – Objetivo: O diagnóstico anatomopatológico das lesões encefálicas é muitas vezes necessário para a instituição do tratamento adequado. Entretanto, muitas lesões localizadas profundamente no encéfalo ou em centros nervosos de grande importância funcional não podem ser acessadas sem riscos, com a aplicação dos procedimentos neurocirúrgicos habituais. **Método:** Apresentamos uma série de 176 doentes submetidos a biópsias estereotáxicas de lesões encefálicas. **Resultados:** Em 40,1% dos casos, o diagnóstico foi de glioma, em 12,2% de outras neoplasias e em 29,1%, de doenças infecciosas ou inflamatórias. O resultado foi inconclusivo em 5,2% dos doentes. Um (0,6%) doente faleceu e dois (1,2%) apresentaram graves complicações operatórias. Os critérios de seleção, as vantagens e os riscos da biópsia estereotáxica são discutidos. **Conclusão:** A eficácia do método é boa e a morbimortalidade das biópsias estereotáxicas é baixa.

PALAVRAS-CHAVE: biópsia encefálica, estereotaxia, lesões encefálicas, neoplasia cerebral.

The institution of an appropriate treatment plan for brain lesions demands a histopathological diagnosis[1-3]. Even when lesions are located deep in the brain or inaccessible by open surgery, the presumptive diagnosis, based solely on the clinical picture and subsidiary exams, is not a valid option.

In these cases, the stereotactic biopsy becomes an interesting choice[5-7]. Given the importance of sampling intracranial lesions, and the equivocal reports on the morbidity associated with stereotactic biopsy procedures continued evaluation of this technique is critical[8-11].

In the present study we reviewed our 5-year experience with stereotactic biopsy procedures, analyzing preoperative radiographic/neuroimaging predictors of non-diagnostic tissues, diagnostic yield and complication rates of frame-based technique.

METHOD

Patients

During 1994 to 1999, 176 patients with brain lesions identified by computadorized tomography (CT) or magnetic resonance (MRI) were submitted to stereotactic biopsy in the Hospital das Clínicas of University of São Paulo Medical School. Patient demographics, clinical presentations, radiological/neuroimaging studies, surgical variables, pathological diagnosis obtained through stereotactic biopsy procedures, and clinical outcomes were retrospectively reviewed in all cases. The patients mean age was 61,4 years old (7–82 yo, median of 65 yo). A hundred thirty three patients were male (65,7%), 128 were white, 22 afro-american and 1 asian descendant.

Procedures

The stereotactic apparatus fixation was done under local anesthesia (lidocaine 2%) associated with light sedation in 164

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patients (95.3%), and under general anesthesia in the remainder ones. The TM-Micromar (Micromar, Diadema SP, Brazil) stereotactic frame was used in all cases. The acquisition of stereotomographic images was accomplished after injection of intravenous non-ionic radiocontrast (Iopamiron®). The stereotactic calculus of the target was performed with the aid of MNPS software (Mevis, São Paulo SP, Brazil). The target was marked at the lesion core and the trajectory was calculated linking it to the most superficial point of the lesion, always avoiding vascular or eloquent structures. The trepanation was carried out under local (95.3%) or general (4.7%) anesthesia, at the closer and safer point to the lesion. The biopsies were performed with a Sedan biopsy tweezer (Micromar, Diadema SP, Brazil).

Tissue samples were collected from the lesion core and from the transition between normal brain and the pathologic area. Approximately 8-mm-long and 1-mm-thick tissue specimens were obtained and sent to the Pathology Department for frozen sectioning. If the pathological reading was non-diagnostic, additional samples were taken from another enhancing region of the lesion. When there was a clinical or radiological suspicion of infection, culture, Gram staining or direct mycological examination was performed. Specific staining methods and immunochemistry were employed whenever it was necessary for diagnosis confirmation. A post-biopsy CT scan within 4 hours of the procedure usually confirmed the location of the biopsy site within the mass by the presence of a small dot of blood or air.

Ten patients (5.8%) presented with lesions located in the infratentorial compartment: 2 in the fourth ventricle (1.6%), 2 at the tentorium of cerebelum (1.6%), 3 in the brainstem (1.7%), 1 in the brain peduncle (0.6%) and 2 in the cerebellum (1.6%). At the supratentorial compartment, one biopsy was located in the pineal gland region, one in the sellar region and the rest were located in the brain lobes.

Indications

CT-guided stereotactic biopsy was considered for patients with parenchymal lesions that were deep-seated, in eloquent areas of the brain (such as those close to the sensorimotor area), or multiple. While most of the lesions had significant mass effect, some ill-defined lesions with minimal or no mass effect were also studied. Usually, we avoided a stereotactic biopsy of obvious extra parenchymal masses such as meningiomas.

RESULTS

The results of the histopathological diagnosis of the biopsies of 176 patients are shown in the Table.

In the present series, glioma was the most common diagnosis, representing 40.1% of cases (sixty nine patients): 23 (33.8%) were classified as glioblastoma multiforme (WHO IV), 13 (19.1%) as anaplasic astrocytoma (WHO III) and 11 as low grade astrocytomas (10%). Two patients (1.2%) had their lesions classified as probable low grade astrocytoma and one (0.6%) as oligodendroglioma.

Table. Histopathological diagnosis of the biopses of 176 patients with brain lesions.

Diagnosis	N	%
Neoplasia	89	51.7
Glioma (2 HIV positive patients)	69	40.1
Linphoma (2 HIV positive patients)	12	7.0
Metastasis	4	2.3
Germinoma	2	1.2
Epidermoid cyst	1	0.6
PNET	2	1.2
Non HIV related inflammatory or infeccious process	28	16.3
Nonspecific chronic inflammatory process	11	6.4
Neurocysticercosis	8	4.7
Multiple sclerosis	2	1.2
Herpetic encephalopathy	2	1.2
Brain abscess	2	1.2
Granuloma *(Paraccidodosis brasiliensis, Cryptococcus neoformans)*	2	1.2
Arteritis	1	0.6
HIV related inflammatory or infeccious process	22	12.8
Nonspecific chronic inflammatory process	17	9.88
Multifocal leucoencephalopathy	3	1.7
Neurotoxoplasmosis	2	1.2
Others	17	9.9
Reactional gliosis	5	2.9
Necrosis	6	3.5
Cystic lesion (non parasitic or neoplasic)	1	0.6
Radionecrosis	1	0.6
Xanthomatous macrophagic proliferation	1	0.6
Ischemic tissue (stroke)	1	0.6
White matter edema	1	0.6
Alzheimer disease	3	1.7
No histopathological abnormalities	17	7.0
Total	176	100

The rest of tumors (12.2%) were classified as: lymphomas (7%), metastasis (2.3%), germinomas (1.2%), epidermoid cyst (0.6%) and primitive neuroectoderm tumor (1.2%). Metastasis were originated from pulmonary carcinoma, kidney and colon. Only one case ended in undifferentiated carcinoma as the diagnosis. Two HIV positive patients had B-cell non-Hodgkin lymphomas. From the other 10 HIV negative patients, 5 had the same B-cell non-Hodgkin lymphoma, 1 T-cell lymphoma, 2 high grade non-Hodgkin lymphoma, 1 primary brain lymphoma and 1 a Reed- Steinberg variance of Hodgkin's disease.

An inflammatory or infectious process was the diagnosis of brain lesions in 50 patients (29.1%). Twenty eight patients (16.3%) were HIV negative, 7.1% of them had fungus granulomas (*Paracoccodioidis brasiliensis* and *Cryptococcus neoformans*) and the other had herpetic encephalopathy. From those 22 (12.8%) HIV positive patients, 17

(77.3%) had chronic unspecific inflammatory processes, 3 (13.6%) had progressive multifocal leucoencephalopathy and 2 (9.1%), neurotoxoplamosis.

The non-diagnostic biopsies were classified as either negative or inconclusive biopsies. A biopsy was deemed to be negative if the tissue obtained failed to indicate the nature of the mass. Typically, the samples showed necrosis, gliosis, calcified material, or normal brain tissue. A biopsy was considered inconclusive in those samples where there was representative tissue but a definitive diagnosis could not be made. This category includes samples from inflammatory masses that show inflammation, but an etiological agent cannot be identified in spite of different stains and microbiological studies. Also, biopsies from neoplasms that showed evidence of an undifferentiated malignant process but could not be further categorized were considered inconclusive.

Diagnosis was not established in 30 patients (17.4%): 12 patients had negative biopsies (collected tissue with no abnormality) and 17 had inconclusive ones (ranging from reactional gliosis, necrosis, edematous tissue to chronic unspecific inflammatory process). Therefore, our biopsies results were converted to a clinical diagnosis in 83.6% of cases.

Complications

Eleven patients had complications due to the procedure (6.4%). Three of them had serious ones: 1 patient with a chronic granulomatous inflammatory process died after an increased edema near the biopsy site leading to increased and fatal intracranial hypertension; another patient with an anaplastic astrocytoma was submitted to a frontal craniotomy and lobectomy in the second post-biopsy day due to neurological deterioration caused by brain edema; the latter patient worsened his neurological deficits due to hemorrhage in the biopsy site. Four patients had seizures during the procedure with no consequences.

In the presented series, the morbid-mortality index was 1.7%. The most common complication was hemorrhage or intracranial hypertension due to edema in lesions with a great mass effect, like glioblastoma multiforme. Post procedure CT scan demonstrated intracranial hemorrhage in 6 patients: 2 patients (1.2%) had worsened their neurological deficits, 1 patient died after the procedure, and the other 4 patients had no clinical repercussion.

DISCUSSION

Based on the literature, stereotactic biopsy may provide the diagnosis in 80 to 99% of cases[5-9] . In the present study, 93% of samples demonstrated histopathological alterations and a clinical diagnosis was achieved in 83.6% of patients. Soo et al.[10] carried out 518 biopsies: 8.4% of them had no definitive diagnosis and 1.4% of samples demonstrated normal tissue. Hall et al.[11] evaluated by metaanalysis, 7500 biopsies of the 17 largest series and concluded that the diagnosis was established in 91% of cases. Whereas negative biopsies may reflect technical or operator error or instrument failure, an inconclusive result is more of an inherent limitation of the procedure[8,10]. The accuracy of most stereotactic systems has been calculated to lie within 1 mm of the selected target. Thus, negative biopsies can only be attributed to factors other than instrument failure. Technical errors, incorrect choice of targets, heterogeneity of the tumor, consistency of the tumor, migration of masses away from the probe, and the tiny fragments of tissue in the biopsy itself can either singly or in combination lead to a negative biopsy.

Our results match with the literature in a variety of aspects. The majority of biopsies (51.7%) in our series had neoplasia as the histopathological diagnosis, followed by inflammatory or infeccious process as observed in other seriers[11,12]. The diagnosis was achieved in 92.9% of the HIV positive patients, corresponding with Chappell et al.[13] (88%), Incoangeli et al.[14] (92%) and Luzzati et al.[15] or Nasser et al.[16] (100%).

In seven patients (25%) of 28 HIV positive patients and 21 (14.56%) of the 144 HIV negative ones, the histopathological diagnosis was different from the initial impression. Diagnosis ranged from neoplasia as the initial MRI impression to desmyelinating disease as the final histopathological diagnosis; astrocytoma to a granuloma due to Cryptococcus neoformans; craniopharyngioma to an anaplasic astrocytoma. Therefore, the stereotactic biopsy has reduced indications of unnecessary open surgeries, consequentially reducing the morbid- mortality[1,4,5].

Although frame-based biopsy morbidity is low, it has its singularity. In the present series, one patient (0.6%) developed increased intracranial pressure with worsen of his neurological deficits and died in the first day after the biopsy. Our previous series and other authors demonstrated similar results. Teixeira et al.[17] observed a mortality rate of 1.6%. In 140 stereotactic biopsies, Kaakaji et al.[18], mortality was found in 0.8% of cases. Bernstein and Parrent[19] demonstrated 1.7% of mortality. Some authors found even lower rates[20]. The most probable cause of this variance is the heterogeneity of cases and patient selection. Prediction of post-procedure edema is a key factor in managing patients with great mass effect lesions, especially those temporal ones. These patients must be followed closely after the biopsy, but the safe hospital discharge time has to be determined by future studies. We usually keep our patients in intensive care unit one day and 2 to 3 days in the infirmary.

Post procedure CT scan demonstrated intracranial hemorrhage in 6 patients in the present series. In another

series, Teixeira et al.[17] reported hemorrhage in 12.5% of 63 patients submitted to stereotactic biopsy. In this series if was also found that the Sedan biopsy tweezer was more suitable for this kind of procedures than the grasper type tweezer because it is related to less hemorrhagic complications and provides a more adequate tissue sample in the majority of the cases. We usually use the grasper type only in procedure involving very delicate regions as brain stem regions in lesion that do not have the aspect of rich vascularization. Other authors have already reported similar complication rates. Luzzati et al.[15] found 11.5% of hemorrhages and Gildennberg et al.[21], 12.5%. Field et al.[12] observed hemorrhage in 40 patients (8% of 500 biopsies) after 15 minutes of the stereotactic operation seen by CT scan images. As in our series, the worsening of neurological deficit was noticed in the minority of patients with intracranial hemorrhage. Two patients presented with neurological deficits after 48 hours of the procedure, although their 15 minutes post-biopsy CT scan were normal. Our control CT scan was performed after a mean time of 4 hours after the operation and no late neurological deficits were observed in patients with initially "normal CT scans". The exact timing for control images has to be established in future controlled studies as there is still lot of controversy in the literature.

In conclusion, the stereotactic biopsy represents a minimally invasive method that provides an accurate diagnose compared to conventional techniques. It does not change the feasibility of a future cytoreduction surgery and it modifies the therapeutic orientation by providing a precise histologic diagnosis, that can be different from the iconological and laboratory tests[22,23]. The method is safe and efficient, and it is associated with low morbid-mortality.

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