Invasive Meningioma: A Tumour with High Proliferating and “Recurrence” Potential

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Summary

A study was undertaken to investigate the correlation between histological invasiveness and proliferating potential and clinical recurrence in meningioma. In 39 meningiomas, the histological findings at the tumour-brain interface zone were classified into 3 types, consisting of 29 cases of non-invasion (NON), 7 cases of nodular invasion (NOD), and 3 cases of intermingled invasion (INT). Proliferating cell nuclear antigen (PCNA) and argyrophilic nucleolar organizer region (AgNOR) indices were studied. PCNA indices (mean ± standard error) of NON, NOD, and INT were 1.7 ± 0.1%, 5.2 ± 0.5%, and 7.5 ± 0.7%, respectively, and the AgNOR indices (dot number/nucleus) were 1.50 ± 0.03, 2.00 ± 0.04, and 2.22 ± 0.07, respectively. Significant differences were found among the three types in both parameters. Clinically, tumour recurrence was observed in 1/29 NON, 4/7 NOD, and 2/2 INT cases, indicating a higher incidence of recurrence in invasive meningiomas (NOD plus INT). Four of 32 patients who underwent gross total removal of the tumours showed recurrence, and all of these four tumours were invasive meningiomas. The results of the present study showed that tumour invasiveness as measured by PCNA + AgNOR indices correlated well with high proliferative potential and clinical recurrence.

Keywords: Argyrophilic nucleolar organizer regions (AgNORs); invasiveness; meningioma; proliferating cell nuclear antigen (PCNA).

Introduction

Although meningiomas are encapsulated benign tumours amenable to surgical resection, several unresolved problems still remain. One of these is tumour recurrence. Considerable evidence shows that recurrence occurs in about 10% of the cases in which total resection has been performed grossly [4, 8, 29, 30]. In addition, not rarely, it has been mentioned in the literature that the initial specimens from some recurrent cases do not exhibit histologically malignant features.

Generally, invasion of a tumour into the surrounding tissue is considered to be a feature showing malignant behaviour. In meningioma, however, the relationship between tumour invasiveness and biological behaviour has remained unexplained in the literature [7, 11, 19, 23, 29, 31]. Accordingly, we undertook a study to investigate the correlation between histological invasiveness and proliferating potential and clinical recurrence in meningiomas.

Materials and Methods

Patient Population

Thirty-nine meningiomas, in which the boundary area between the tumour surface and the brain was available in the initial surgical specimens obtained at Kitasato University Hospital between July 1985, and May 1991, were selected for use in this study. The patients consisted of 9 males and 30 females with ages varying from 12 to 78 years with a mean age of 52.5 years. The location of the tumour was the convexity in 9 cases, the parasagittal area in 8 cases, the falx in 4 cases, the sphenoid ridge in 6 cases, the tuberculum sellae in 3 cases, the olfactory groove in 6 cases, the cerebello-pontine angle in 2 cases, and the lateral ventricle in 1 case. With the exception of one case who died from postoperative pulmonary infarction, 38 patients were followed from 8 to 84 months, with a mean follow-up period of 51.8 months. Local recurrence at the site of origin from the dura mater was found in 7 cases, but neither extracranial metastasis nor subarachnoid dissemination was observed. The tumours were totally removed in 33 cases and subtotally in 6 cases.

Histopathological Study

Histopathological examination of the resected specimens was performed with haematoxylin and eosin stain. Twenty-one tumours were meningothelial, 13 fibrous, 2 transitional, 1 angiomatous, 1 microcystic, and 1 xanthomatous.

Haemangiopericytic, papillary meningioma and meningeal sarcoma were not found in the present series. The boundary zone between the tumour surface and the brain was classified into 3 cat-
categories: (1) non-invasion type (NON) in which a continuous capsule consisting of some layers of spindle cells existed between the tumour and the brain, (2) nodular invasion type (NOD – Fig. 1) in which the capsule had partially disappeared and the tumour had penetrated through the capsule into the superficial layer of the cortex in a nodular fashion, and (3) an intermingled invasion type (INT – Fig. 2) in which the capsule was almost entirely absent and both tumour and superficial brain tissues were intermingled at the boundary zone.

We also examined the tumour tissues to see if they had histological features indicative of malignancy, such as loss of architecture, frequent necrosis, high cellularity, nuclear atypia, and frequent mitoses. Frequent mitoses were defined as 5 or more mitotic cells in 10 high-power fields.

Proliferating Cell Nuclear Antigen (PCNA) Indices

All of the specimens were fixed in 10% formalin (Masked Formalin A, Japan Tanner, Kobe) immediately after sampling, then embedded in paraffin within 48 hours. The specimens were used to prepare 3 µm thick sections, which were then deparaffinized and incubated with 0.3% hydrogen peroxide in methanol and reacted with anti-PCNA monoclonal antibody (PC10-murine IgG2, Novocastra, Newcastle-upon-Tyne, UK) diluted 1:100. Biotinylated secondary antibody and peroxidase-labelled streptavidin were added in that order, diaminobenzidine was used as chromogen and the samples were lightly counterstained with haematoxylin. PCNA indices were randomly examined in 6 or more high-power representative fields to score more than 1000 tumour cell nuclei for computation of the percentage of the positively stained cells.

Argyrophilic Nucleolar Organizer Region (AgNOR) Indices

The serial sections contiguous to that used for the PCNA study were deparaffinized in xylene and rehydrated. A solution consisting of 1 volume of 2% gelatin in 1% aqueous formic acid and 2 volumes of 50 aqueous silver nitrate solution, was instilled onto the surface of the sections. After the sections were reacted with the solution in the dark at room temperature for 30 min, they were washed well with de-ionized water, dehydrated and mounted in a synthetic medium. No counterstain was applied. Using an oil-immersion objective lens with 100-fold magnification, the number of silver dots for AgNORs was randomly counted in 200 nuclei by focusing up and down. The mean number of dots per nucleus was used as the AgNOR index.

Statistical Analysis

The data obtained for each invasion type as described above were expressed as mean ± standard error (SE). Statistical analysis was conducted by the Mann-Whitney test. Furthermore, the correlation between PCNA and AgNOR indices was evaluated by Spearman’s correlation coefficient by rank. The level of statistical significance was taken to be p < 0.05.

Results

Histopathological Features

The NON cases did not show any histopathological features indicative of malignancy. All invasive meningiomas (NOD + INT) were meningothelial and their extent of invasiveness was limited to the superficial cortex of the brain. NOD was seen in 7 cases, 6 of whom did not exhibit histological features indicative of malignancy at all, and 1 of whom showed only high cellularity in a limited area. Of 3 cases of INT, 1 did not exhibit malignant features, whereas the other 2 cases displayed loss of architecture, frequent necrosis, high cellularity and frequent mitosis, in some areas of the tumours (Table 1).

PCNA Indices

Nuclei positive for PCNA showed diffuse and granular staining. In the NON cases, the PCNA indices were 0.6–3.7% with a mean of 1.7 ± 0.1%. The NOD cases showed indices of 3.8–7.5% with a mean of 5.2 ± 0.5%. The INT cases revealed PCNA indices