Sstr2A immunohistochemical expression in human meningiomas: Is there a correlation with the histological grade, proliferation or microvessel density?

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Abstract. Somatostatin anti-proliferative and anti-angiogenic activities, together with the expression of somatostatin receptors (sstrs), account for the use of somatostatin analogues in the treatment of human tumours. In the present study, sstr2A immunohistochemical expression was analyzed in grade II and III meningiomas and was compared with that revealed in grade I meningiomas. Thirty-five formalin-fixed paraffin-embedded meningiomas, comprising 13 grade I, 19 grade II and 3 grade III tumours, according to the WHO 2007 classification, were submitted to immunohistochemical assays for sstr2A. Moreover, in the same cohort of tumours, the immunohistochemistry of CD105, a specific marker for neo-angiogenesis, as well as the Ki-67 labelling index (LI), reflecting the proliferative activity of the meningiomas, were recorded. Sstr2A immunoreaction was evidenced in 26/35 cases and was localized at the cytoplasm and the plasma membrane in 12 and in 14 cases, respectively. Specifically, a positive staining was found in 7/13 grade I, in 16/19 grade II and in 3/3 grade III tumours, thus demonstrating that sstr2A is frequently expressed in high grade meningiomas. A significantly higher microvessel density (MVD), assessed by CD105 immunostaining and Ki-67 LI were evidenced in high grade meningiomas. A significant correlation was recorded between sstr2A expression and a high MVD of the meningiomas. The existence of a correlation between sstr2A expression and the entity of neo-angiogenesis provides the basis for the use of somatostatin analogue-based therapies in the treatment of meningiomas.

Introduction

Somatostatin is a 14- or 28-amino acid peptide hormone, which has been detected throughout the human body (1). It exerts an inhibitory function on a number of physiological processes, including pituitary hormone secretion (2) and the neurotransmission in the central nervous system (1). Anti-proliferative and anti-angiogenic activities have been attributed to somatostatin in human tumours (3-5). Somatostatin action is mediated by six specific somatostatin receptors (sstrs), named sstr1, sstr2A, sstr2B, sstr3, sstr4 and sstr5, which belong to a family of seven transmembrane domain G-protein coupled receptors, which are encoded on five different chromosomes (6). Among these receptor subtypes, sstr2A and sstr2B are encoded on chromosome 17 and are generated through the alternative splicing of sstr2 mRNA (7). The expression of sstrs has been demonstrated in a series of normal human tissues (8), including those of the adult and fetal central nervous system (9,10), as well as in many human tumours (11-13). Therefore the use of somatostatin analogues in the treatment of human neoplasms gets a rationale in sstr expression in neoplastic tissues together with the somatostatin inhibitory effect on proliferation and angiogenesis.

Among the central nervous system tumours, sstr expression has been evidenced in gliomas, with sstr2A as the most commonly expressed sstr (14). Moreover, a high frequency of sstr2A expression has been reported in medulloblastomas, paragangliomas and in neuroblastomas, with a cytoplasmic and membranous localization of this receptor (15). When sstr expression was investigated through immunohistochemistry or RT-PCR in meningiomas (14,16-18), a high density of these proteins or of their mRNA was found in these neoplasias, with sstr2A as the most frequently expressed sstr (18). It is well known that meningiomas are common central nervous system tumours, accounting for ~25% of the intracranial neoplasms (19). According to the WHO criteria (19), they are histologically classified into three grades of malignancy. The grade I meningiomas are the most frequent and are considered as benign, slowly growing and easily surgically removable tumours; by contrast, grade II and III represent ~20% of all meningiomas and are characterized by a worse clinical course (20) and a higher proliferation index (20) and microvessel density (MVD) (21,22). Thus far, all the studies that have evaluated sstrs expression in surgically resected meningiomas have mostly included cases histologically classified as grade I. On the contrary, only a small number (17,18), if not at all (14,16), of grade II and III meningiomas have been examined in these individuals.
In view of this, in the present study we aimed to analyze the immunohistochemical expression of sstr2A, the most frequent sstr in meningiomas, in a series of cases comprising of a higher number of grade II and III meningiomas in comparison to the other studies (14,16-18). In addition, we thought it would be of interest to investigate the correlation between sstr2A immunoeexpression and the histological grade as well as the proliferation index and the MVD of the tumours of our cohort.

Materials and methods

Thirty-five surgically resected meningiomas, obtained from an equal number of patients (22 female and 13 male patients; age range 31-84 years; mean age 64 years), were collected from the files of the Department of Human Pathology of the University of Messina, Italy. Specifically, 19 (54%) cases of meningiomas displaying a histological grade II and 3 characterized by a histological grade III (9%) were selected among meningiomas which occurred between 2006 and 2007.

Then, a comparable number of meningiomas with a histological grade I (13 cases; 37%) were collected. All the cases were histologically classified according to the criteria proposed in the WHO 2007 classification of central nervous system tumours (19). The cohort comprised 3 anaplastic or grade III meningiomas, 16 atypical, 1 clear cell and 2 chordoid meningiomas among the grade II tumours and 7 meningothelial, 1 transitional, 2 fibrous, 1 secretory and 2 microcystic meningiomas as grade I cases. For each case, the clinicopathological data, including the patient's age and gender, as well as the site, the histological grade and the Simpson grade of surgical resection (23) of the tumours were available. The tumour localization was subdivided into three sites: convexity (37%), parasagittal (37%) and basal (26%). On the basis of the subcellular site of the immunoreaction, specimens of human term placenta was tested as a positive control for the CD105 immunoreaction, whereas the syncytiotrophoblast present in specimens of human term placenta was tested as a positive control for the CD105 immunoreaction (25).

In parallel sections obtained from the same tissue blocks, the Ki-67 antigen was unmasked by retrieval procedures (10 nM, pH 6.0 sodium citrate buffer heated in a microwave oven for 3 cycles x 5 min) and then Ki-67 anti-serum (clone MIB-1, Dako, Glostrup, Denmark; w.d. 1:50) was applied for 30 min at room temperature.

Quantification and statistics. Immunostained sections were examined at light microscopy by two independent pathologists (V.B. and G.T) who were blinded to the clinicopathological data. In the discordant cases, consensus was achieved by using a double-headed microscope. Sstr2A expression was based on the presence of membranous and/or cytoplasmic staining.

In the evaluation of sstr2A immunohistochemical reaction, immunostaining intensity (IS) was graded as 0 (negative), 1 (weak), 2 (moderate), 3 (strong); the area of staining positivity (ASP), recorded as a percentage of positive cells, was graded as follows: 0 (<5%), 1 (5-25%), 2 (26-50%), 3 (51-75%) and 4 (76-100%), in accordance with the criteria proposed by Qiu et al (26). Then, an intensity distribution (ID) score was generated for each case by multiplying the values of IS and ASP. Cases displaying an ID score <1 were defined as negative. The median ID score value (ID score: 6) was used as the cut-off to discriminate between the cases with low (ID score: 1-4) and high (ID score 6-12) sstr2A expression.

On the basis of the subcellular site of the immunoreaction, positive cases were also subdivided into cases showing only a cytoplasmic staining and meningiomas displaying a cytoplasmic and membranous staining.

The quantification of microvessels was performed according to the procedure described by Weidner et al (27), already applied in our previous study on MVD in meningiomas (22). More specifically, the three most vascularized areas detected by CD105 were initially selected (so-called hot spots) under x40 field. Then microvessels were counted in each of these areas under a x400 field. Serial parallel sections were successively incubated at 4°C overnight with the primary polyclonal antibody against

sstr2A (Biotrend, Germany; w.d. 1:3500) and with the primary monoclonal antibody against CD105 (Dako Corporation, Denmark, clone SN6h, w.d. 1:50). The bound primary antibodies were visualized by avidin-biotin-peroxidase detection using the Vectastain rabbit/mouse elite kit, according to the manufacturer's instructions. In order to reveal the immunostaining, the sections were incubated in darkness (24) for 10 min with 3-3' diaminobenzidine tetrahydrochloride (Sigma Chemical Co., St. Louis, MO, USA), in the amount of 100 mg in 200 ml 0.03 % hydrogen peroxide in phosphate-buffered saline (PBS). Nuclear counterstaining was performed by Mayer's haemalum. Specificity of the binding was assessed by omitting the primary anti-serum or replacing it with normal rabbit serum or phosphate-buffered saline solution (PBS, pH 7.4). Moreover, islet cells within pancreatic human samples were used as positive controls for the sstr2A immunoreaction, whereas the syncytiotrophoblast present in specimens of human term placenta was tested as a positive control for the CD105 immunoreaction (25).

The quantification of microvessels was performed according to the procedure described by Weidner et al (27), already applied in our previous study on MVD in meningiomas (22). More specifically, the three most vascularized areas detected by CD105 were initially selected (so-called hot spots) under x40 field. Then microvessels were counted in each of these areas under a x400 field. Single endothelial cells or clusters of endothelial cells, with or without a lumen, were considered to be individual vessels. The mean value of three x400 field (0.30 mm²) counts was recorded as the MVD of the section. Then the MVD value was converted into the mean number of microvessels/mm² for the statistical analyses. The
median MVD value (MVD: 23.33 microvessels/mm²) was used as the cut-off point to discriminate between cases with a low and a high MVD.

The Ki-67 labelling index (LI) was calculated as a mean percentage by counting the stained nuclei of tumour cells for 1,000 cells in three representative neoplastic fields; each degree of nuclear staining intensity was taken into consideration. A Ki-67 value of 4% was utilized as a cut-off point to determine low and high Ki-67 expression, as suggested by Perry et al. (28).

Mann-Whitney and Chi-squared tests were applied to assess the correlation between the histological grade and the MVD or Ki-67 LI of the meningiomas. Grade II and III tumours were all put together in an attempt to obtain statistically comparable groups.

Fisher exact and Chi-squared tests were carried out to analyze the correlations between sstr2A expression (negative versus positive; low expression versus high expression; cytoplasmic versus membranous and cytoplasmic) and the clinicopathological variables, including the gender and age of the patients, the histological grade, site, Simpson grade and proliferative index of the meningiomas as well as the MVD of the tumours.

The Mann-Whitney test was further used to analyze the correlations between sstr2A expression and patterns of staining and the MVD of the tumours. A p-value <0.05 was considered statistically significant. Data were analysed using the SPSS package version 6.1.3 (SPSS Inc., Chicago, IL, USA).

Results

The clinicopathological variables, the sstr2A immunoreaction, and the MVD counts related to the analyzed meningiomas are shown in Table I.

A sstr2A positive immunoreaction, with a variable ID score ranging between 1 and 12, was found in 26/35 (74%) cases. In particular, sstr2A positive cases included 7/13 (54%) grade I, 16/19 (84%) grade II and 3/3 (100%) grade III meningiomas. Among the positive cases, a low sstr2A expression (ID score: 1-4) was recorded in 8/26 (31%) meningiomas, whereas a high sstr2A expression (ID score: 6-12) was evidenced in 18/26 (69%) cases. Specifically, 4/7 (57%) grade I, 12/16 grade II (75%) and 2/3 grade III (66%) meningiomas were characterized by a high sstr2A expression. Moreover, among the sstr2A positive tumours, 12/26 (46%) displayed a cytoplasmic staining in the neoplastic cells (Fig. 1a), whereas a cytoplasmic and membranous staining (Fig. 2) was evidenced in 14/26 (54%) cases (Table I).

CD105 positive vessels were identified in 32/35 (91%) meningiomas. In the positive cases, CD105 immunoreaction was observed in the endothelial cells of the stained vessels (Fig. 1b). A high MVD (MVD ≥23.33 microvessels/mm²), quantified through CD105 immunostaining was observed in
Table I. Clinicopathological data, sstr2A immunoexpression profile and MVD counts of the 35 analyzed meningiomas.

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LI, Labelling index; IS, intensity of staining; ASP, area of staining positivity; ID, intensity distribution; M, membranous and C, cytoplasmic.
16 high grade (grade II- and III), in 2 microcystic and in 1 meningothelial meningiomas (Table I).

Variously represented Ki-67 nuclear reactivity was found in meningiomas (Fig. 1c), with a rate of stained cells ranging from 0.5 to 30% (mean value 7%). All grade II and III meningiomas displayed a Ki-67 LI >4% (Table I).

A significant correlation was found between a high MVD and a high histological grade (II-III) (P=0.0185) or Ki-67 LI (Ki-67 >4%) (P=0.0039).

When meningiomas were subdivided on the basis of sstr2A expression, sstr2A positive cases were found to display a significantly higher MVD than sstr2A negative cases (P=0.0183) (Table II). The statistically significant association between sstr2A positive immunoreaction and a high MVD (≥ 23.33 microvessels/mm^2) was confirmed through the Fisher exact test (P=0.022) (Table III). Even if statistical significance was not reached, an association was evidenced between sstr2A expression and a high histological grade or Ki-67 LI (P=0.05) (Table III). When sstr2A expression was correlated with the histological grade and Ki-67 LI of the meningiomas of our series excluding the microcystic ones, which emerged as grade I highly vascularized tumours both of which expressed sstr2A (Fig. 3), a significant correlation was evidenced between a positive sstr2A immunohistochemical reaction and a higher histological grade (II-III) and growth fraction (Ki-67 LI> 4%) (P=0.033).

When only the sstr2A positive cases were taken into consideration, no significant correlation emerged between the subcellular site of staining (cytoplasmic versus cytoplasmic and membranous) or the rate of sstr2A immunoreactivity (low ID score versus ID score) and the clinicopathological parameters as well as the MVD of the tumours (Table IV and V).

### Table II. Statistical correlations between the sstr2A immunohistochemical pattern and the tumour MVD investigated through the Mann-Whitney test.

<table>
<thead>
<tr>
<th>sstr2A</th>
<th>n</th>
<th>Mean rank</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>9</td>
<td>11.0556</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>26</td>
<td>20.4038</td>
<td>0.0183</td>
</tr>
<tr>
<td>Cytoplasmic</td>
<td>12</td>
<td>12.2917</td>
<td></td>
</tr>
<tr>
<td>Membranous and cytoplasmic</td>
<td>14</td>
<td>14.5357</td>
<td>0.4558</td>
</tr>
<tr>
<td>Low ID score (1-4)</td>
<td>8</td>
<td>13.500</td>
<td></td>
</tr>
<tr>
<td>High ID score (6-12)</td>
<td>18</td>
<td>13.500</td>
<td>1.00</td>
</tr>
</tbody>
</table>

### Table III. Statistical correlations between sstr2A immunohistochemical expression and the clinicopathological variables of the 35 analyzed meningiomas.

<table>
<thead>
<tr>
<th>Variable</th>
<th>sstr2A</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>&lt;65 yrs</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>≥65 yrs</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Male</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>Female</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>Site</td>
<td>Convexity</td>
<td>Parasagittal</td>
</tr>
<tr>
<td>Convexity</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Parasagittal</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Basal</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Grade</td>
<td>I</td>
<td>II</td>
</tr>
<tr>
<td>I</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>II</td>
<td>3</td>
<td>19</td>
</tr>
<tr>
<td>Ki-67 LI</td>
<td>≤4%</td>
<td>&gt;4%</td>
</tr>
<tr>
<td>≤4%</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>&gt;4%</td>
<td>3</td>
<td>19</td>
</tr>
<tr>
<td>Simpson</td>
<td>1</td>
<td>2-3</td>
</tr>
<tr>
<td>1</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>2-3</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>MVD</td>
<td>Low (&lt;23.33 vessels/mm^2)</td>
<td>High (≥23.33 vessels/mm^2)</td>
</tr>
<tr>
<td>Low (&lt;23.33 vessels/mm^2)</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>High (≥23.33 vessels/mm^2)</td>
<td>2</td>
<td>18</td>
</tr>
</tbody>
</table>

16 high grade (grade II- and III), in 2 microcystic and in 1 meningothelial meningiomas (Table I).

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A significant correlation was found between a high MVD and a high histological grade (II-III) (P=0.0185) or Ki-67 LI (Ki-67 >4%) (P=0.0039).
Discussion

In human meningiomas, the expression of sstrs has been largely explored through different techniques such as in vitro autoradiography, immunohistochemistry and RT-PCR (14,16-18,29).

The majority of these tumours have been found to express a high density of sstrs compared to the surrounding tissue, which allows them to be readily visualized by in vivo receptor imaging methods using labelled somatostatin analogues such as octreotide (30). The demonstration of sstr expression in meningiomas provides a molecular basis for utilizing novel therapeutic strategies with somatostatin analogues in the treatment of these neoplasias (18). It has been shown that somatostatin exerts an anti-proliferative effect in vitro on meningiomas displaying sstr expression (18). Somatostatin anti-tumoural activity is not only due to its anti-proliferative action, but also to its ability to inhibit the neo-angiogenic process by reducing the tumour cell-derived VEGF secretion (3,4,31). In human meningiomas, the proliferation index and the MVD, which reflects the intratumoural neo-angiogenesis, appear to increase together with the histological grade (20-22). Thus meningiomas displaying a higher histological grade may represent a suitable candidate to therapies with somatostatin analogues. Nonetheless, the expression of sstrs, which represent the essential condition for such therapies to have an effect, has been barely evaluated in grade II and III meningiomas up to now (14,16-18). In view of this, in the present study we analyzed the expression of sstr2A in a series of grade II and III meningiomas and compared it with the data obtained in grade I cases in an attempt to evaluate whether the sstr2A expression is linked to a higher biological aggressiveness of meningiomas. Furthermore, we correlated the presence of sstr2A immuno-

Table V. Statistical correlations between the subcellular site of sstr2A immunohistochemical staining and the clinicopathological variables in the 26 sstr2A positive meningiomas.

<table>
<thead>
<tr>
<th>Variable</th>
<th>sstr2A staining</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cytoplasmic</td>
<td>Membranous and cytoplasmic</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 yrs</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>≥65 yrs</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>Gender</td>
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<td></td>
</tr>
<tr>
<td>Male</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Female</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Convexity</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Parasagittal</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Basal</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>II-III</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Ki-67 LI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤4%</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>&gt;4%</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>Simpson</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>2-3</td>
<td>4</td>
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<tr>
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</tr>
<tr>
<td>High (≥23.33 vessels/mm²)</td>
<td>3</td>
<td>10</td>
</tr>
</tbody>
</table>

Figure 3. A microcystic meningioma showing a strong immunohistochemical reaction to sstr2A with a cytoplasmic and membranous subcellular localization (sstr2A staining; original magnification x100).
labelling and its pattern with the proliferation index and the MVD of meningiomas in order to verify whether sstr2A positive tumours are characterized by a high growth fraction and neo-angiogenesis, which represent the targets for somatostatin analogue therapy.

We found a high sstr2A immunohistochemical expression in the majority of the analyzed meningiomas and demonstrated that grade II and III tumours frequently express this receptor in their neoplastic cells (84 and 100% of cases, respectively). Moreover, in our series, the cases expressing sstr2A were found to exhibit a significantly higher MVD than the sstr2A negative meningiomas, thus suggesting that somatostatin analogues may be relevant in the treatment of meningiomas by reducing their blood supply. MVD was assessed by using an antibody against the specific marker for neo-angiogenesis CD105, which is a 180 kDa transmembrane glycoprotein (32), specifically expressed by cycling endothelial cells of newly formed vessels in inflamed or in regenerating tissues, or in tumours (32,33), all of which undergo active angiogenesis. By contrast, it is only weakly expressed or absent in the vessels of normal tissues (34). Thus it represents a powerful marker of neovascularization in human meningiomas, as well as in other types of tumours, in comparison to pan-endothelial markers, such as CD31 and CD34 (22,35-37).

Although we demonstrated the existence of a significant correlation between the MVD and the histological grade and Ki-67 LI of the analyzed meningiomas, no significant correlation between the latter two parameters and the sstr2A expression emerged in our study. Nonetheless, our series comprised two microcystic meningiomas, which, in spite of their histological grade I, are highly vascularized tumours (22,38). When the correlation between sstr2A expression and the histological grade and growth fraction of the meningiomas was investigated by excluding these cases, sstr2A expression appeared to be significantly associated with a high histological grade and Ki-67 LI of the tumours. Thus, sstr2A expression seems to parallel the existence of an extensive neo-angiogenic process rather than the malignant progression of meningiomas. As a consequence, somatostatin analogue therapies may be effective on highly vascularized meningiomas in spite of their histological grade.

A recent study has reported that only the membranous, rather than cytoplasmic, sstr2A immunostaining is correlated with the clinical response to somatostatin analogues in patients affected by neuroendocrine tumours (39). In previous studies describing sstr2A immunohistochemical expression in human meningiomas, the subcellular distribution of the immunoreaction was not clearly specified and discussed (14,16,17). In the present study, we stratified for the first time the sstr2A positive meningiomas according to their subcellular pattern of staining, in order to verify the frequency of membranous sstr2A staining and its eventual correlation with other parameters. In our series, a cytoplasmic co-expression existed in all cases which were characterized by a membranous one. None of the subcellular patterns of immunolabelling was prevalent in the sstr2A positive meningiomas. Moreover, we did not find any significant association between the subcellular localization of the immunoreaction and the clinicopathological characteristics, such as the histological grade and the growth fraction of the tumours, or their MVD. The observation of a cytoplasmic localization of sstr2A in almost half of the positive meningiomas raises the question whether these receptors remain accessible in vivo to somatostatin analogues and permit therapeutic applications. A recent pilot study described the progression-free survival at six months as a result of treatment with long-acting somatostatin in a subset of patients with recurrent meningiomas shown to overexpress sst2 by octreotide scintigraphy (40). However, the evaluation of sst2 by this technique does not allow the sstr subtype to be defined, in contrast to the immunohistochemical procedure. Thus, further investigations correlating the sstr2A immunohistochemical pattern and the sstr scintigraphy as well as the response to the therapy with somatostatin analogues are needed. Specifically, it would be worth examining whether such a therapy is effective only on meningiomas displaying a membranous sstr2A staining or also on those with a merely cytoplasmic immunoreaction.

In conclusion, the present study demonstrates the existence of a correlation between sstr2A expression and the entity of neo-angiogenesis in meningiomas, thus providing the basis for the use of somatostatin analogue-based therapies, which have an anti-angiogenic effect, in the treatment of these tumours. On the basis of our findings, the meningiomas characterized by a higher MVD, such as atypical, anaplastic and microcystic ones, appear as the most suitable candidates for such therapies, which may be used on recurring or partially resected tumours. We suggest to preliminarily test the tumour samples for sstr2A immunohistochemical reaction; indeed this receptor subtype is the one mediating the anti-proliferative and anti-angiogenic effects of somatostatin.

References


