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## RESEARCH ARTICLE

### CASE REPORT: HER2 POSITIVE ON RECURRENT INTRACRANIAL MENINGIOMA

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#### ABSTRACT

**Introduction:** Meningiomas are the most common intracranial primary neoplasm in adults. We report 39 years-old-female with recurrent meningioma, the patient had craniotomy tumor removal 1 year ago, and the patient had second craniotomy tumor removal, and we performed an immunohistochemical staining with HER2. HER2 is a member of the human epidermal growth factor receptor (HER/EGFR/ERBB) family. Amplification or over-expression of this oncogene has been shown to play an important role in the development and progression of certain aggressive types of cancer. Patient and observation: We report 39 years-old female with recurrent meningioma, the patient had craniotomy tumor removal 1 year ago with histopathologic result Meningothelial Meningioma (WHO Grade I), and then the patient complain with bulging defect 6 months after surgery. CT Scan contrast shows isodens lobulated lesion, with homogeny enhancement. The patient had second craniotomy tumor removal and histopathologic result Meningothelial Meningioma (WHO Grade I), based on second pathologic result, we performed an immunohistochemical staining with HER2, we use c-erbB-2 Oncoprotein (SP3) Rabbit Monoclonal Antibody with catalog number RMAB008R manufactured by Diagnostic BioSistemas. **Discussion:** HER2 is a member of the human epidermal growth factor receptor (HER/EGFR/ERBB) family. Amplification or over-expression of this oncogene has been shown to play an important role in the development and progression of certain aggressive types of cancer. HER-2 is a type of oncogene in human carcinoma, and many studies have indicated HER-2 overexpression in several types of cancer and is associated with a particularly aggressive form of the disease. **Conclusion:** HER2 expression plays a role in the development of more-aggressive meningiomas or not is a question that needs to be clarified in further studies. The results of our case report did not advocate this role for HER2. For the HER2 targeted cancer therapy, numerous strategies including the blockage of receptor dimerization, inhibition of the tyrosine kinase activity, and interruption of the downstream signal pathway will be summarized. For the targeted drug delivery to HER2 positive tumor cells, various targeting ligands and their delivery systems will be described in details. Successful development of the humanized monoclonal anti-HER2 antibody (Trastuzumab) for the treatment of breast cancer further spurred scientists to develop various HER2 specific antibodies, dimerization inhibitors and kinase inhibitors for cancer therapy. On the other hand, the high expression of HER2 and the accessibility of its extracellular domain make HER2 an ideal target for the targeted delivery of anti-tumor drugs as well as imaging agents.

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## INTRODUCTION

Meningiomas are the most common intracranial primary neoplasm in adults. Meningiomas arise from the arachnoidal cells surrounding the brain and are one of the most common tumors of the central nervous system. Meningiomas account for about 15-30% of all primary intracranial tumors. According to the 2007 WHO classification, meningiomas are divided into three grades (I, II and III) (David, 2007).

With this new gradingsystem, which Include the brain invasion into the diagnostic criteria for aggressiveness, the percentage of atypical meningiomas grew to 20–35% of newly diagnosed meningiomas. This classification is important because, together with the extension of resection, it may help in predicting the recurrence rate and thus the global prognosis.<sup>[2]</sup> Hormonal therapy and hormone-dependent conditions such as breast cancer, pregnancy, or obesity were in fact associated with a higher incidence of meningiomas. Cranial irradiation is also a recognized risk factor for developing meningiomas, usually with tumor having a more complex caryotype and a more aggressive behavior [Giulia, 2016] Several studies have reported higher recurrence rates for males than for females (Boldrey, 1971; Gupta, 1989; Mahmood, 1994; Perry, 1997).

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Figure 1. Head Ct-Scan Pre-Operation show parasagittal meningioma, with contrast homogenous enhancement

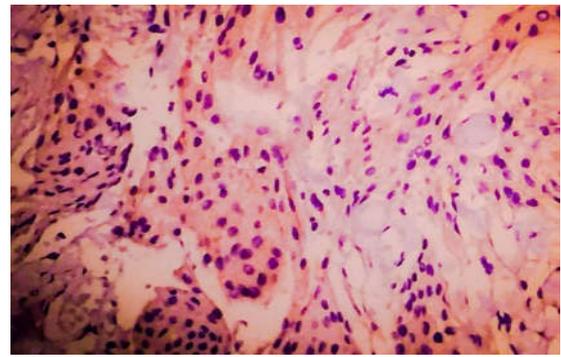


Figure 5. Show Photomicrograph immunohistochemical result.



Figure 2.1. Month post operation head CT-Scan show mass on the right frontal

However, other studies, including ours, have found no significant difference based on gender.<sup>[7,8,9,10]</sup> Nakasuet al<sup>[11]</sup> and several other authors found no association between tumor development in young patients (<40 yrs) and a high likelihood of recurrence.<sup>[11,12]</sup> However, Perry and associates<sup>[7]</sup> found a significant difference between age and recurrence, while Adegbite and colleagues<sup>[11]</sup> could demonstrate no significant influence of sex and age on recurrence. Predicting the biological and clinical behavior of meningiomas remains a significant problem. Currently, the most reliable factors that are helpful in predicting recurrence of meningiomas are the extent of surgical resection and histological grade. The aggressiveness of meningiomas is unpredictable. HER2 represents a well-known prognostic factor in various tumors such as breast carcinomas. There are only a few studies on the relationship between meningioma and HER2 expression, and the results are different as well. The aim of this study was to determine this relationship.



Figure 3. Clinical photos show bulging defect on the head 1 year after surgery

**Patient and observation:** We report 39 years-old female with recurrent meningioma, the patient had craniotomy tumor removal 1 year ago with histopathologic result Meningothelial Meningioma (WHO Grade I), and then the patient complain with bulging defect 6 months after surgery. CT Scan contrast shows isodense lobulated lesion, with homogeneity enhancement. The patient had second craniotomy tumor removal and histopathologic result Meningothelial Meningioma (WHO Grade I), based on second pathologic result, we performed an immunohistochemical staining with HER2, we use c-erbB-2 Oncoprotein (SP3) Rabbit Monoclonal Antibody with catalog number RMAB008R manufactured by Diagnostic Bio Systems.

**DISCUSSION**

HER2 is a member of the human epidermal growth factor receptor (HER/EGFR/ERBB) family. Amplification or over-expression of this oncogene has been shown to play an important role in the development and progression of certain aggressive types of cancer. HER2 (also known as erbB-2) is a 185-kD transmembrane glycoprotein with tyrosine kinase activity. These tumors are known to be hormonally modulated and may occur in association with breast carcinoma. HER2 is highly expressed in a significant proportion of breast cancer, ovarian cancer, and gastric cancer. Since the discovery of its role in tumorigenesis, HER2 has received great attention in cancer research during the past two decades. HER-2 is a type of oncogene in human carcinoma, and many studies have indicated HER-2 overexpression in several types of cancer and is associated with a particularly aggressive form of the disease. In a study performed by Loussouran et al.



Figure 4.1 year after first operation show large lesion, with contrast enhancement

HER2 immunostaining was detected in 10 (28.5%) of 35 meningiomas. They also reported a significantly higher rate of tumor recurrence in HER2 positive than in HER2-negative meningiomas. They used different methods for assessment of HER2 immunoreactivity. In 2010, Wang et al., showed that high levels of HER2 expression correlated with increase of tumor grades and recurrence in meningiomas. There are only a few studies on HER2 expression in meningiomas. Torp et al. reported a higher ratio (63%) of HER2-positive meningiomas, but they applied immunostaining on frozen sections. They investigated a very small number of meningiomas and reported HER2 positivity in 12 of the 19 patients. While Andersson et al. demonstrated a high rate of HER2 expression in meningiomas, Potti et al. reported a very low rate of it in the same year and suggested that HER2 overexpression has no role as a prognostic factor in meningiomas.

## Conclusion

HER2 expression plays a role in the development of more-aggressive meningiomas or not is a question that needs to be clarified in further studies. The results of our case report did not advocate this role for HER2. For the HER2 targeted cancer therapy, numerous strategies including the blockage of receptor dimerization, inhibition of the tyrosine kinase activity, and interruption of the downstream signal pathway will be summarized. For the targeted drug delivery to HER2 positive tumor cells, various targeting ligands and their delivery systems will be described in details. Successful development of the humanized monoclonal anti-HER2 antibody (Trastuzumab) for the treatment of breast cancer further spurred scientists to develop various HER2 specific antibodies, dimerization inhibitors and kinase inhibitors for cancer therapy. On the other hand, the high expression of HER2 and the accessibility of its extracellular domain make HER2 an ideal target for the targeted delivery of anti-tumor drugs as well as imaging agents.

**Competing interest:** The authors declare no competing interest.

**Authors' contributions:** The author read and approved the final version of the manuscript.

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