

30. Wang XX, Wang X, Li ZL, et al. Anterior maxillary segmental distraction for correction of maxillary hypoplasia and dental crowding in cleft palate patients: a preliminary report. *Int J Oral Maxillofac Surg* 2009;38:1237–1243
31. Dedeoglu N, Altun O, Kucuk EB, et al. Evaluation of the anatomical variation in the nasal cavity and paranasal sinuses of patients with cleft lip and palate using cone beam computed tomography. *Bratisl Lek Listy* 2016;117:691–696

OPEN

Familial Tuberculum Sellae Meningiomas

Peng Zhou, PhD,* Li Wei, MM,† Jia Shi, MM,* and Naiyuan Shao, MM*

Objectives: The aim of this study was to study and explore the genetic mechanism of familial meningiomas through 3 cases of familial tuberculum sellae meningioma.

Methods: A retrospective analysis of clinical data of 3 cases of familial tuberculum sellae meningioma patients, and the pathological results of types and immunohistochemical results of the 3 patients were compare.

Results: Three cases of postoperative pathology were meningiomas (mixed type), immunohistochemical examination showed that Vimentin, epithelial membran antigen, and Ki67 were positive.

Conclusions: The occurrence of meningiomas is associated with ≥ 1 chromosomal deletions, and the absence of certain tumor suppressor genes may be the genetic basis for the familial growth of meningiomas.

Key Words: Familial, tuberculum sellae meningiomas

This report focuses on a family of 7 siblings, with 5 sisters and 2 brothers. Among the sisters, 3 suffer from tuberculum sellae meningiomas, which has been confirmed via pathological analysis. The remaining 4 siblings all underwent brain magnetic resonance

imaging (MRI) scanning while they accompanied their sisters to hospital, and no meningioma was found. The 3 cases of familial tuberculum sellae meningioma are detailed in the following section.

CLINICAL STUDY

Patient 1, female, age 71. The patient was admitted to the Department of Neurosurgery at the First People's Hospital of Changzhou in July 2011 after repeated episodes of intermittent dizziness, ongoing for 2 months. A brain MRI scan suggested meningioma in the sella area. Right pterional craniotomy was performed to remove the tumor. Follow-up visits to the hospital in the subsequent 4 years found no neurological dysfunction. Post-surgery pathologic analysis showed the mixed meningioma rich in cells and actively growing. Immunohistochemistry assays revealed negative staining of the glial fibrillary acidic protein (GFAP) and human hematopoietic progenitor cell antigen (CD34), and positive staining of Vimentin, epithelial membran antigen (EMA), and proliferation marker Ki-67 ($< 2\%$).

Patient 2, female, age 69. The patient was admitted to the Department of Neurosurgery at the First People's Hospital of Changzhou in July 2015 after progressive vision loss in the left eye for 30 years with acute headaches during the preceding 2 months. A brain MRI scan suggested bilateral sella meningiomas. Presurgical examinations showed no perception of light in the left eye and 4.8 vision in the right eye. Right pterional craniotomy was performed to remove the tumors. During follow-up visits during the subsequent 6 months, the patient still had no perception of light in the left eye and 4.8 vision in the right. Post-surgery pathologic analysis showed mixed meningioma with abundant cells and angiogenesis. Immunohistochemistry assays revealed negative staining of monoclonal anti-Pan-Cytokeratin (AE1/AE3), GFAP, and S-100, and positive staining of CD34, EMA, Vimentin, and Ki-67 ($< 2\%$).

Patient 3, female, age 68. This patient was the first to be diagnosed with meningioma among the 3. She was admitted to the Huashan Hospital of the Fudan University in November 2005 due to progressive loss of vision in both eyes for 10 years. A brain MRI scan suggested meningioma in the sella area. Presurgical examinations showed only the right eye capable of light perception and 4.5 vision in the left eye. Craniotomy was performed to remove the tumor. In the subsequent 6 years of follow-ups, the patient had no perception of light in the right eye and 4.4 vision in the left. The post-surgery pathologic analysis showed mixed meningioma, part of which had abundant cells and was actively growing. Immunohistochemistry assays revealed negative staining of GFAP and positive staining of Vimentin, EMA, CD34, and Ki-67 ($< 2\%$).

All 3 cases of tuberculum sellae meningioma had soft tumors, medium supply of blood, and a mixed histological type according to the post-surgery pathology reports.

DISCUSSION

Meningiomas are neoplasms that arise from the meninges and the subarachnoid space. They may grow from cells of the dura mater, the pia mater, and in most cases, the arachnoid mater, and may be present in any area that contains arachnoid cells. Meningiomas are not caused by any single factor, but may correlate with internal changes and gene mutations. Familial meningiomas are not common, and 3 cases within 1 family with tumors in the same area are extremely rare.

These 3 cases of familial tuberculum sellae meningioma were all confirmed to be of mixed type by pathological analysis, and they all had positive staining of Vimentin, EMA, and Ki-67 in immunohistochemistry assays. Vimentin is an important cytoskeletal protein in mesenchymal cells. A multiphosphorylated form of this protein can be used as a discriminative marker for infiltrative and invasive

From the *Department of Neurosurgery; and †Department of Blood Transfusion, The Third Affiliated Hospital of Soochow University, Changzhou, China.

Received May 5, 2020.

Accepted for publication May 25, 2020.

Address correspondence and reprint requests to Naiyuan Shao, Department of Neurosurgery, The Third Affiliated Hospital of Soochow University, No. 185 Juqian Road, Changzhou 213003, PR China; E-mail: bingheyuan@sina.com

PZ, LW, and JS contributed equally to this work.

The authors report no conflicts of interest.

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Copyright © 2020 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of Mutaz B. Habal, MD.

ISSN: 1049-2275

DOI: 10.1097/SCS.00000000000006823

meningiomas.¹ Abnormal expression of Vimentin in tumor cells may lead to changes in quality and quantity of cytoskeletal proteins, which may enable the cells to float about, modify their mobility and affinity, and finally induce changes to their biological characteristics. A previous study showed decreased expression of EMA and increased expression of Vimentin with malignant progression of meningioma. Although Vimentin was found to be expressed in both benign and malignant meningiomas, it only increased in 20% of the anaplastic types.² Ki-67 has been shown to be associated with different histological types of meningiomas, that is, its expression is different in different types and the difference may be due to whether the tumor is benign or malignant. Therefore, Ki-67 can be used as a diagnostic marker for meningioma subtypes. Takeuchi et al³ found an increased risk of meningioma relapse when the Ki-67 labeling exceeded 2% even though the tumor was pathohistologically benign and thus, radiotherapy or stereotactic radiosurgery was recommended in this case.

Chromosomal aberration is an anomaly in chromosomes that is caused by missing, repetitive, or rearranged genetic material. It can be caused via atypical numbers of chromosomes or structural abnormalities. In meningiomas, chromosomal aberrations have been found in chromosomes 1, 3, 6, 7, 8, 10, 12, 14, 17, 18, 19, 22, X, and Y.⁴ Among these, abnormalities in chromosome 22 are the most common, and they include missing, translocated, monploidy, and polyploidy of the chromosome. The long arm of chromosome 22 contains the tumor suppressor gene *NF2*. A number of studies have suggested that mutations in *NF2* might be associated with the carcinogenic aberrations of chromosome 22.^{5,6} It has previously been proposed that missing chromosome 22 leads to *NF2* mutations, which in turn causes meningioma, and changes the other chromosomes in combination with gene mutations, thus aggravating histological grades of the tumor.⁶ Furthermore, Aavikko et al⁷ reported an incidence of five cases of meningiomas among siblings in one family, four out of which were multiple

meningiomas. With genome-wide linkage analysis and exome sequencing, the authors showed that a hereditary mutation in the tumor suppressor gene *SUFU*, predisposed to meningiomas, especially multiple meningiomas. The altered *SUFU* had significantly lower activity, resulting in abnormal expression of the Hedgehog signaling pathway, which might help explain the genetic etiology of familial meningiomas.⁷

Cranial injuries, radiation exposure, viral infection, and bilateral acoustic neuromas may all lead to mutations in chromosomes or acceleration in cell proliferation. Since each chromosome consists of thousands of genes, missing DNA on a single chromosome will result in loss of a considerable amount of genetic information. It is possible that meningioma is related to loss of one or multiple chromosomes and of tumor suppressor genes. We are currently trying to contact the 3 patients of tuberculum sellae meningiomas and the other members of their family. We plan to perform genome-wide sequencing of the whole family to search for genetic aberrations, underlying the meningiomas in the family. With in-depth analysis of molecular and genetic information, new paths and directions may be uncovered for the further exploration into mechanisms of meningioma occurrence and progression (Fig. 1).

REFERENCES

1. Bouamrani A, Ramus C, Gay E, et al. Increased phosphorylation of vimentin in noninfiltrative meningiomas. *PLoS One* 2010;5:e9238
2. Ikeda H, Yoshimoto T. Immunohistochemical study of anaplastic meningioma with special reference to the phenotypic change of intermediate filament protein. *Ann Diagn Pathol* 2003;7:214–222
3. Takeuchi H, Kubota T, Kabuto M, et al. Prediction of recurrence in histologically benign meningiomas: proliferating cell nuclear antigen and Ki-67 immunohistochemical study. *Surg Neurol* 1997;48:501–506
4. Lee JY, Finkelstein S, Hamilton RL, et al. Loss of heterozygosity analysis of benign, atypical, and anaplastic meningiomas. *Neurosurgery* 2004;55:1163–1173
5. Leuraud P, Dezamis E, Aguirre-Cruz L, et al. Prognostic value of allelic losses and telomerase activity in meningiomas. *J Neurosurg* 2004;100:303–309
6. Lim HS, Jung J, Chung KY. Neurofibromatosis type 2 with multiple plexiform schwannomas. *Int J Dermatol* 2004;43:336–340
7. Aavikko M, Li SP, Saarinen S, et al. Loss of *SUFU* function in familial multiple meningioma. *Am J Hum Genet* 2012;91:520–526

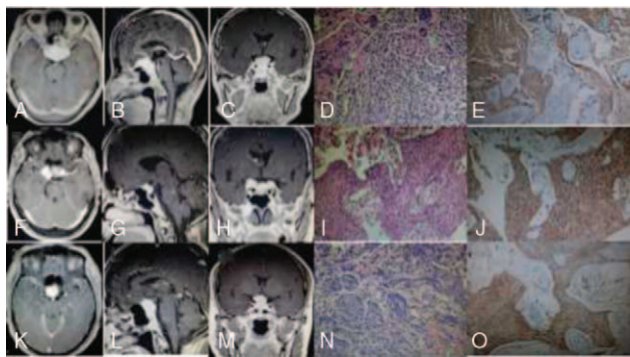


FIGURE 1. (A) Tumor in the sella area shown by contrast-enhanced magnetic resonance imaging (MRI) imaging of brain, case 1, transverse section. (B) Tumor in the sella area shown by contrast-enhanced MRI imaging of brain, case 1, sagittal section. (C) Tumor in the sella area shown by contrast-enhanced MRI imaging of brain, case 1, coronal section. (D) Post-surgery pathology staining (H&E staining 10 × 10) showed mixed meningioma, case 1. (E) Immunohistochemistry staining (EMA +), 10 × 10, case 1. (F) Bilateral tumors in the sella area shown by contrast-enhanced MRI imaging of brain, case 2, transverse section. (G) Bilateral tumors in the sella area shown by contrast-enhanced MRI imaging of brain, case 2, sagittal section. (H) Bilateral tumors in the sella area shown by contrast-enhanced MRI imaging of brain, case 2, coronal section. (I) Post-surgery pathology staining (H&E staining 10 × 10) showed mixed meningioma, case 2. (J) Immunohistochemistry staining (EMA +), 10 × 10, case 2. (K) Tumor in the sella area shown by contrast-enhanced MRI imaging of brain, case 3 transverse section. (L) Tumor in the sella area shown by contrast-enhanced MRI imaging of brain, case 3 sagittal section. (M) Tumor in the sella area shown by contrast-enhanced MRI imaging of brain, case 3 coronal section. (N) Post-surgery pathology staining (H&E staining 10 × 10) showed mixed meningioma, case 3. (O) Immunohistochemistry staining (EMA +), 10 × 10, case 3.

Implant-Supported Maxillary and Mandibular Rehabilitation in a Patient With Hallermann-Streiff Syndrome

Alfredo von Martens, MD,* Andres Perilla, MD,†
Schilin Wen, MD,‡ Pablo Acuña, MD,§ and Víctor Beltrán, MD§

Abstract: Hallermann-Streiff syndrome is a rare congenital abnormality involving multiple craniofacial malformations, such as micrognathia, prominent frontal and nasal bones, vision defects, and dental anomalies. In most patients, patients affected with this disease have multiple dental problems involving a severe loss of teeth and maxillary atrophy. Specialized individual and multidisciplinary treatments are often required in these patients. The objective of this report was to demonstrate the rehabilitation approach of a patient with Hallermann-Streiff syndrome using total