eNeurologicalSci 14 (2019) 13–15

Contents lists available at ScienceDirect

eNeurologicalSci

journal homepage: www.elsevier.com/locate/ensci

Case report

# Pituitary metastasis of breast cancer mimicking IgG4-related hypophysitis

Kanako Nose[a,1], Toshiyasu Ogata[a], Jun Tsugawa[a], Tooru Inoue[b], Kazuki Nabeshima[c], Yoshio Tsuboi[a,*]

[a] Department of Neurology, Faculty of Medicine, Fukuoka University, Japan
[b] Neurosurgery, Faculty of Medicine, Fukuoka University, Japan
[c] Pathology, Faculty of Medicine, Fukuoka University, Japan

ARTICLE INFO

*Keywords:*
Orbital apex syndrome
Pituitary metastasis
IgG4-related hypophysitis

ABSTRACT

IgG4-related hypophysitis, which is the pituitary gland inflammation caused by IgG4 positive lymphocytes, can affect cavernous sinus and orbital apex leading to developing cranial nerve related symptoms such as orbital apex syndrome (OAS). Here we report a case of hypopituitarism associated with OAS caused by pituitary metastasis of the breast cancer with elevated serum IgG4 level, who initially resembled to IgG4-related hypophysitis. Although this case had some features in common with igG4-related hypophysitis. The symptoms and pituitary enlargement were typical. However, steroid treatment did not improve her symptoms. Thus, we performed a tissue biopsy. Histopathologic examination of the hypophyseal tumor confirmed metastatic breast cancer in her pituitary. Pituitary metastatic tumor should be suspected if a case with OAS was once diagnosed as a cancer.

## 1. Introduction

IgG4-related hypophysitis, which is the pituitary gland inflammation caused by IgG4 positive lymphocytes, can affect cavernous sinus and orbital apex leading to developing cranial nerve related symptoms such as orbital apex syndrome (OAS). IgG4-related hypophysitis may be diagnosed in such cases with hypopituitarism, symptoms of headache and loss of visual acuity, and pituitary gland enlargement associated with the elevation of the serum IgG4 level. Prognosis of IgG4-related hypophysitis is often good because steroid treatment shows beneficial effect. OAS is a syndrome involving cranial nerves characterized by the disturbance of third, fourth, fifth (V1), sixth cranial nerves, and optic nerve disorder. It is frequently induced by inflammatory disorders, neoplasms, infection, trauma, and vascular disorders [1].

Here we report a case of hypopituitarism associated with OAS caused by pituitary metastasis of the breast cancer with elevated serum IgG4 level, who initially resembled to IgG4-related hypophysitis.

## 2. Case report

A 70-year-old woman had been diagnosed to have breast cancer in the right side and had undergone mastectomy with axillary lymph-node dissection at age 58. The histological examination revealed that the tumor was characterized by estrogen receptor-negative, progesterone receptor-negative and HER2-positive, which is generally regarded as refractory to hormonal therapy. The metastasis of interpectoral nodes (hilar lymph nodes, right axillary lymph nodes, adrenal glands and lung) was found at age 67, and she was treated with chemotherapy. After that, no recurrence had been identified for three years, which was considered to reach remission in general.

She was admitted to department of endocrinology of our hospital, because she suffered from anorexia and general malaise from 1 months before admission. Hypothyroidism was firstly pointed out. However, during the admission period, she developed headache, visual disturbance in the left eye, and diplopia. Then she referred to neurological department. Neurological examination revealed loss of visual acuity (counting fingers) and oculomotor palsy with dilated pupil and ptosis in her left eye. Facial sensory disturbance was not observed. Contrast-enhanced MRI showed a heterogeneously enhanced lesion in her pituitary (Fig. 1). Dura matter thickening around processus clinoideus anterior so called dural tail was also observed, while it is known as a common finding in IgG4-related hypophysitis. The laboratory tests showed elevated serum IgG4 of 178 mg/dL (normal: 4–108) and carcinoembryonic antigen of 8.2 ng/mL (normal: ≦2) with decreased level of pituitary hormones of thyroid stimulating hormone 0.147 μIU/mL (normal: 0.5–5.0), luteinizing hormone < 0.1 mIU/mL (normal:

* Corresponding author at: Department of Neurology, Faculty of Medicine, Fukuoka University, 7-45-1, Nanakuma, Johnan-ku, Fukuoka 814-0180, Japan.
*E-mail address:* tsuboi@cis.fukuoka-u.ac.jp (Y. Tsuboi).
[1] Present address: 7-45-1 Nanakuma, Jonan-ku, Fukuoka 814-0180, Japan.

https://doi.org/10.1016/j.ensci.2018.11.014
Received 13 October 2018; Accepted 17 November 2018
Available online 22 November 2018

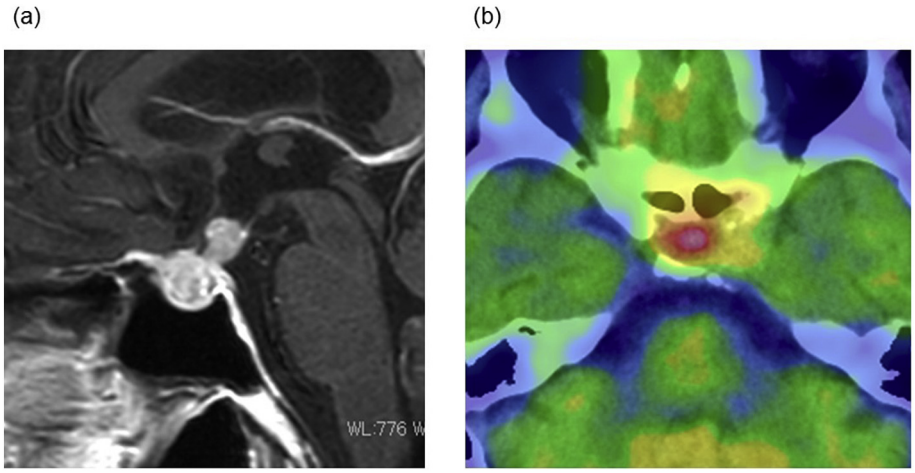


**Fig. 1.** (a) Contrast-enhanced MRI on admission revealed a heterogeneously enhanced lesion in the pituitary with thickened pituitary stalk (b) FDG-PET/CT revealed abnormal accumulation in the pituitary accompanied by osteoclasis.

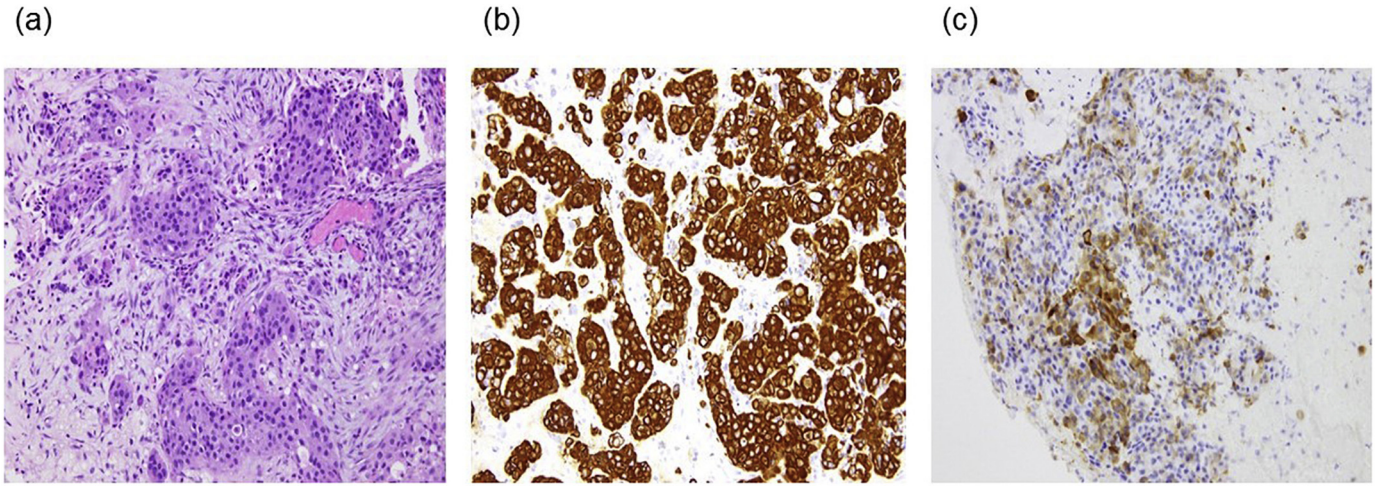


**Fig. 2.** (a) Tumor cells have large hyperchromatic nuclei and eosinophilic cytoplasm. The tumor showed invasive growth pattern arranged in irregular nests and clusters, accompanied by fibrous stroma. (hematoxylin & eosin, ×200). (b,c) Immunohistochemically, the carcinoma cells are diffusely and strongly positive for cytokeratin AE1/AE (×200) (b) and focally positive for mammaglobin (×200) (c).

5.2–62.0), follicle stimulating hormone 3.6 mIU/mL (normal: 26.7–133.4), adrenocorticotropic hormone 6.1 pg/mL (normal: 7.2–63.3), indicating possible diagnosis as IgG4-related hypophysitis. Cerebrospinal fluid examination was normal including the cytological evaluation. Contrast-enhanced CT did not exhibit the other organs' involvements. Although she was treated with steroid for IgG4-related hypophysitis, her neurological symptoms were deteriorated, leading to complete loss of left visual acuity and restricted left eye movement except for abduction. FDG-PET/CT scan revealed the abnormal accumulation of her pituitary as well as osteoclasis superior orbital bone (Fig. 1). Thus, we suspected her to have malignant tumor and performed a tissue biopsy. Histopathologic examination of the hypophyseal tumor confirmed metastatic breast cancer (Fig. 2) in her pituitary. According to the immunostaining finding, it was proved to have the same histology as the one diagnosed at age 58. There were no IgG4 positive lymphocytes in the biopsy specimen. She received the treatment of chemoradiotherapy. But the cancer had metastasized to the cervical spine. She wasted away physically and died 16 months after.

## 3. Discussion

Our case demonstrated OAS associated with headache, high level of serum IgG4, pituitary gland enlargement, and inflammation of cavernous sinus. We initially considered that the patient's condition might be due to IgG4-related hypophysitis because the patient fulfilled the diagnostic criteria of IgG4-related autoimmune disease [2]. However, steroid treatment did not improve her symptoms, regardless of the fact that steroid reactivity was one of the characteristics of IgG4-related hypophysitis. The contrast enhanced T1-weighted image of our case revealed dumbbell-type shaped implicating unusual findings as IgG4-related hypophysitis. Furthermore, the osteoclasis seen in CT scan also suggested the possibility of metastatic tumor rather than IgG4-related hypophysitis, and histological examination confirmed it was the same type of tissue as the breast cancer 12 years ago. Metastatic tumors in the pituitary was extremely rare, although it may occur in cases with lung, breast and kidney cancer [3]. Therefore, pituitary metastatic tumor should be considered in the case with OAS, even if > 10 years passed since the diagnosis of the breast cancer [4].

## 4. Conclusion

We experienced the case with pituitary metastatic tumor mimicking IgG4-related hypophysitis. Although this case had some features in common with igG4-related hypophysitis, a careful observation did not correspond to it, and the case was finally confirmed pituitary metastatic tumor. Pituitary metastatic tumor should be suspected if a case with

OAS was once diagnosed as a cancer.

## References

[1] R.E. Warburton, C.C. Brookes, B.A. Golden, et al., Orbital apex disorders: a case series, Int J Oral Maxillofac Surg 45 (2016) 497–506.
[2] P. Leporati, M.A. Landek-Salgado, I. Lupi, et al., IgG4-related hypophysitis. A New addition to the hypophysitis spectrum, J Clin Endocrinol Metab 96 (2011) 1971–1980.
[3] M. Habu, H. Tokimura, H. Hirano, et al., Pituitary metastases: current practice in Japan, J Neurosurg 123 (2015) 998–1007.
[4] G.P. Spinelli, G. Lo Russo, E. Miele, et al., Breast cancer metastatic to the pituitary gland: a case report, World J Surg Oncol 10 (2012) 137.