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CASE REPORT

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Vascular flow empty shadow in pituitary neuroendocrine tumors: A case report and review of literature

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Key Clinical Message

To investigate the blood supply characteristics and surgical significance of pituitary neuroendocrine tumors with vascular flow void signal in tumors. The clinical data of one case of giant pituitary neuroendocrine tumor with vascular flow void signal were reported, and the related literature was reviewed. In this case of pituitary neuroendocrine tumor, the blood sinus from the superior pituitary artery was seen in the left rear of the tumor before the first operation, showing irregular low signal. Subsequently, the tumor recurred 46 mm high, grew upwards, and had no cystic degeneration. The blood vessels that showed flow voids signal in magnetic resonance imaging originated from the inferior pituitary artery. The tumor was removed through the frontal lobe through the lateral ventricle approach, and desirable results were obtained. Vascular flow void signals in giant pituitary neuroendocrine tumors are rare, which suggests a sufficient and rich arterial blood supply. Arterial blood supply from below such tumors should be properly handled during the operation.

KEYWORDS

Giant pituitary neuroendocrine tumor, magnetic resonance imaging, vascular flow void signal

1 | INTRODUCTION

Pituitary neuroendocrine tumors are generally considered benign, and they account for 10%–25% of intracranial tumors[1]; their arterial blood supply is mainly delivered by superior and inferior pituitary arteries. For giant pituitary neuroendocrine tumors with a diameter of more than 4 cm, blood supply from the superior pituitary artery is often lacking; thus, the blood supply mainly or only originates from the inferior pituitary artery and becomes prone to cystic degeneration in the upper part of the tumor.[2,3] No study has reported intratumoral vascular flow void signal in recurrent giant pituitary neuroendocrine tumors observed in magnetic resonance imaging (MRI) worldwide. This article reports such a case and analyzes it in combination with the literature.

2 | CASE DATA

A 60-year-old female patient was admitted to the hospital in 2014 due to "recurrent headache, dizziness with walking instability for half a year and aggravation for 10 days." Physical examination showed normal vision and no visual field defects. Pituitary MRI showed pituitary neuroendocrine tumors growing suprasellarly, with slightly high

signal intensity on T2-weighted image (T2WI) and substantially heterogeneous enhancement after enhanced scanning (Figure 1A–C). Pituitary neuroendocrine tumor resection via the transsphenoidal approach was performed on March 4, 2014. Postoperative immunohistochemistry revealed a polyhormonal pituitary neuroendocrine tumor (expressing follicle-stimulating hormone and progesterone). During follow-up, 3 months after surgery, MRI and computed tomography (CT) showed a mass shadow in the sellar region (Figure 2A–C). On September 6, 2022, the patient returned to our hospital due to "intermittent headache for 3 months." Physical examination showed a tubular visual field in the right eye and a temporal visual field defect in the left eye. Auxiliary examination revealed an FT4 of 11.16 pmol/L, and other hormone levels showed no abnormalities. Pituitary MRI: Pituitary neuroendocrine tumors grew suprasellarly, with a height of 46 mm. Both T1WI and T2WI showed mixed signal shadows (Figure 3A,B). Cord-like hypointense shadows in the mass were observed on sagittal T2WI, and they arose from the median position of the lower part of the tumor and extended longitudinally along the tumor's long axis. The shadows measured approximately 33 mm in length and 1 mm in width and exhibited several signs of branching (Figure 3C), T2WI coronal tumor left rear visible low signal cord shadow (Figure 3D). On September 14, 2022, right frontal craniotomy was performed under general anesthesia to remove the pituitary neuroendocrine tumor through the frontal lobe and lateral ventricle. Intraoperative findings showed enlargement of the interventricular foramen, grayish-white tumor located in the third ventricle, a texture between soft and tough, rich blood supply, and several areas with slightly increased bleeding. The tumor base was closely related to the interpeduncular fossa vessels, with considerable adhesions. During the operation, the tumor was subtotally resected, and only slight residuals were observed at the pituitary fossa. Immunohistochemically, a gonadotropin cell tumor with Ki-67 of 1% was observed. Thirty days after the operation, the patient reported remarkable relief of headache symptoms and recovered well from the operation. After evaluation of her condition, the patient was discharged from the hospital. During follow-up 6 months after the operation, the patient took care of herself and experienced no evident abnormality in visual field coarse measurement. Reexamination by MRI showed small soft tissue shadows in the sellar region (Figure 4A–C).

3 | DISCUSSION

The blood supply of the adenohypophysis is mainly from the anterior and posterior branches of the superior hypophyseal artery originating from the superior clinoid segment of the bilateral internal carotid artery, and about 10 % from the inferior hypophyseal artery originates from the cavernous segment of the internal carotid artery.[2,3] Studies suggest that the arterial blood supply of pituitary neuroendocrine tumors is derived from the superior and inferior pituitary arteries.[4] Ogawa et al. showed the C-arm cone-beam CT imaging of a giant parenchymal pituitary neuroendocrine tumor, in which vascular were observed inside the adenoma; these shadows originated from the inferior pituitary arteries on both sides and ran inferiorly and superiorly, without blood supply coming from the superior pituitary artery.[5] Zhang J et al. observed that giant pituitary neuroendocrine tumors easily compress the diaphragmatic foramen sellae and block the blood supply from the superior pituitary artery and portal system, which results in easy cystic degeneration in the upper part of the tumor due to ischemia.[6] In this case, an irregular low signal shadow was seen in the left rear of the tumor before the first operation of pituitary neuroendocrine tumor. MRI T1 enhancement showed cord signs. There was no high-density signal shadow in brain CT after operation. Therefore, it can be inferred that this low signal shadow is a blood sinus with a fast flow rate, excluding the possibility of

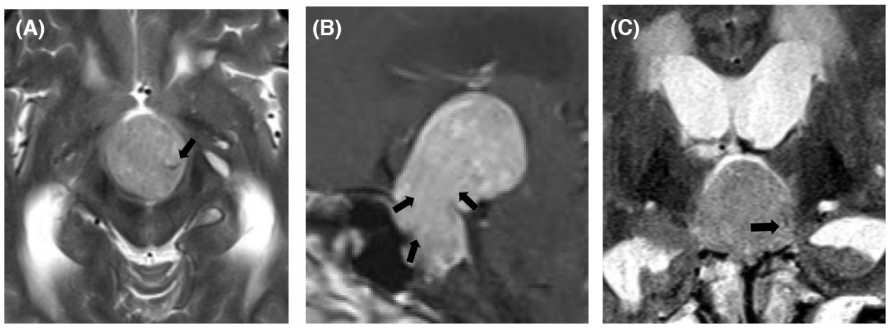

FIGURE 1 MRI findings before the first operation. (A). T2WI transverse position, an irregular hypointense shadow (arrow) was observed in the left posterior part of the tumor; (B). T1WI enhanced scan sagittal position, the tumor showed irregular enhanced signal, beaded hyperintense cord sign (arrow) was observed in the upper part; (C). T2WI coronal position: hypointense cord shadow (arrow) was observed in the left posterior part.

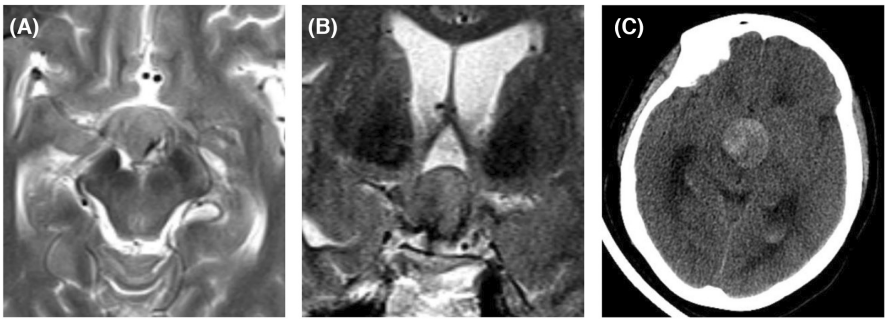

FIGURE 2 Imaging findings 3 months after the first operation: (A). MRI T2WI transverse position; (B). MRI T2WI coronal position visible saddle area mass, uneven signal, partial residual tumor; (C). The CT saddle area showed a round-like mass with a slightly higher density.

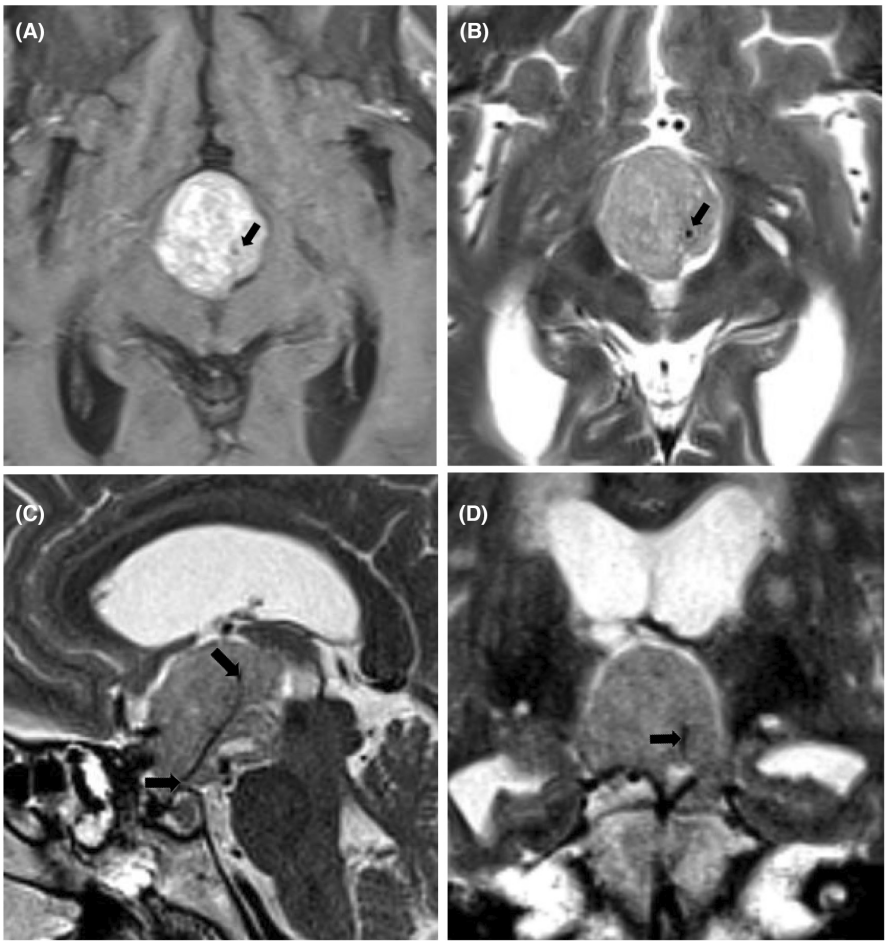

FIGURE 3 MRI findings before the second operation: (A). T1WI enhanced scan transverse position, a round soft tissue mass was observed in the suprasellar region, significantly enhanced, clear boundary, an unenhanced circular dot shadow (arrow) was observed in the left posterior part of the tumor; (B). T2WI transverse position, the tumor showed slightly high signal intensity mixed with signal intensity, a low signal intensity round vascular flow void (arrow) was observed in the left posterior part; (C). T2WI sagittal position, a low signal intensity shadow about 33 mm in length was observed in the tumor, roughly distributed along the long axis of the tumor (arrow), showing several branches; (D). T2WI coronal position, the tumor grew suprasellar, and an unenhanced cord shadow (arrow) was observed in the left posterior part of the tumor.

surgical scar and calcification. The first operation removed 2/3 of the lower part of the tumor, and no ischemic cystic change was observed in the upper part of the residual tumor. Thus, the upper part of the residual tumor still had blood supply coming from the superior pituitary artery. Combined with the preoperative image blood findings, these results demonstrated that the tumor had a rich blood supply. Before the second operation, a hypointense shadow approximately 33 mm in length was observed in the tumor, and it was roughly distributed along the long axis of the tumor. In addition, several branches were observed in the upper part of the tumor, which indicates that its arterial blood supply came from the inferior hypophyseal artery. The main trunk of the lower segment is mainly blood vessels, and the bifurcation of the upper segment is blood sinus. Coarse arterial blood vessels (flow void) appear in the tumor and run from bottom to top, which fully ensures the blood supply of the tumor. This result also confirmed the axial growth of the tumor rather than the pattern of lateral growth.

Pituitary neuroendocrine tumors should be differentiated from primary posterior pituitary tumors with vascular flow void signals, which are also rare. The 2017 World Health Organization classification of pituitary neoplasms[7] classified primary posterior pituitary neoplasms as neoplasms having thyroid transcription factor-1-immunopositive single pathological lineages that can be

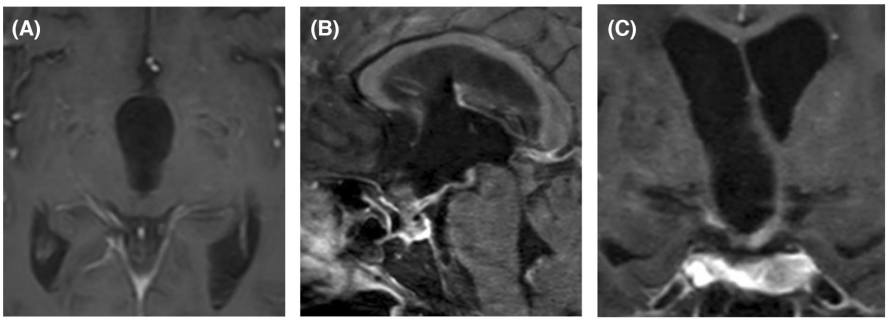

FIGURE 4 MRI findings 6 months after the second operation: (A). T1WI enhanced scan transverse position; (B). T1WI enhanced scan sagittal position, visible sellar region small film enhancement shadow; (C). T1WI enhanced scan coronal position, visible third ventricular floor a few enhancement shadows.

differentiated from pituitary neuroendocrine tumors by immunohistochemistry.

The blood vessels inside the tumor have important guiding significance for the selection of surgical methods. Giant pituitary neuroendocrine tumors tend to grow aggressively, and surgical resection is preferred in principle.[8] This case of pituitary neuroendocrine tumor considers that the illumination of the microscope through the transsphenoidal approach is tubular, relatively limited, and prone to blind areas in the sella. Especially for suprasellar and posterolateral surgery, the visual field of the sphenoid platform is poor, and the whole anatomical field of view of the sella region cannot be effectively obtained. In addition, the transsphenoidal surgery starts from the lower part of the tumor, and it is easy to encounter large blood vessels (thick inferior pituitary artery), and it is easy to cause the problem of fierce bleeding, which makes it difficult to stop bleeding at the beginning, and it is difficult to continue to advance the operation of tumor resection.[9] Moreover, transsphenoidal total resection is difficult for most giant pituitary neuroendocrine tumors that have extended to the suprasellar region,[10] if the upper part of the tumor is not removed during surgery, which results in residuals in the upper part of the tumor, postoperative "residual tumor apoplexy" is likely to occur due to the loss of arterial blood supply from the inferior part, and infarct hemorrhage may develop in the tumor area, which causes third-ventricle hemorrhage, acute hydrocephalus, and dramatic deterioration of the patient's condition. Neuroendoscopic surgery has a high rate of tumor resection, but the operation time is long, which requires high surgical skills, and is more difficult to stop bleeding after massive hemorrhage. Craniotomy has the following advantages: (1) the surgical field is relatively wide; (2) it enters the third ventricle through the interventricular foramen and begins to separate and resect from the upper part of the tumor, that is, electrocoagulation and resection of the tumor tissue from the distal end of the large intratumoral artery, which facilitates hemostasis and progresses inferiorly; the safety of the operation is high; and (3) even if the lower pole of the tumor cannot be removed, it does not cause postoperative "residual tumor stroke." Therefore, we used craniotomy and removed more than 95% of the tumor, which ensured the safety and overall efficacy of the operation.

Intratumoral blood vessels play an important role in tumor growth and metastasis.[11] Studies have suggested that pituitary neuroendocrine tumors may develop through a nonangiogenic and vascular endothelial growth factor-dependent pathway.[12] In this case, the pituitary neuroendocrine tumor with intratumoral vascular flow void may be due to the increase of blood supply required to maintain metabolism with the increase of tumor volume and height. Therefore, the blood supply vessels exhibit a thickened diameter and an increased number, which leads to the emergence of a flow void signal. Such cases are rare. A total of 4 (3.0%) out of 134 cases of pituitary neuroendocrine tumors reported by Okamoto et al. worldwide showed flow void signals in MRI,[13] and 9 of 72 pituitary neuroendocrine tumors (12.5%) reported by Kurosaki et al. showed presented void signals during MRI[14] (Only the flow void signal was found, and no obvious intratumoral flow void was found). These tumors were greater than 30 mm, which suggests that the blood supply of pituitary neuroendocrine tumors is related to tumor size. In addition, tumors with flow voids are larger than those without.[15]

For giant invasive pituitary neuroendocrine tumors, the use of dynamic enhancement and other imaging techniques is recommended to evaluate the regional blood supply. If the tumor blood supply is rich, the risk of transsphenoidal bleeding is great, which easily causes residual tumor and postoperative residual tumor infarction and bleeding. Thus, transcranial approach surgery is recommended.

AUTHOR CONTRIBUTIONS

Jiansheng Zhong: Writing – original draft. **jun Li:** Writing – review and editing. **shousen Wang:** Funding acquisition; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from Fuzhou 900th Hospital. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from the authors with the permission of Fuzhou 900th Hospital.

CONSENT STATEMENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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REFERENCES

1. Moller MW, Andersen MS, Glintborg D, et al. Pituitary neuroendocrine tumor. *Ugeskr Laeger*. 2019;181(20):V05180331.
2. Stanfield JP. The blood supply of the human pituitary gland. *J Anat*. 1960;94:257-273. doi:10.1016/j.wneu
3. Cironi KA, Decater T, Iwanaga J, Dumont AS, Tubbs RS. Arterial supply to the pituitary gland: a comprehensive r eview. *World Neurosurg*. 2020;142:206-211. doi:10.1016/j.wneu
4. Dawson B. The blood vessels of the human optic chiasma and their relation to those of the hyp ophysis and hypothalamus. *Brain*. 1958;81:207-217. doi:10.1093/brain/81.2.207
5. Ogawa Y, Sato K, Matsumoto Y, Tominaga T. Evaluation of fine feeding system and angioarchitecture of giant pituitary neuroendocrine tumor-implications for establishment of surgical strategy. *World Neuros Urg*. 2016;85:244-251. doi:10.1016/j.wneu2015.09.087
6. Zhang J, Gu J, Ma Y, et al. Uneven distribution of regional blood supply prompts the cystic cha nge of pituitary neuroendocrine tumor. *World Neurosurg*. 2017;103:37-44. doi:10.1016/j.wneu2017.03.109
7. Lopes MBS. The 2017 World Health Organization classification of tumors of the pituitary glan d: a summary. *Acta Neuropathol*. 2017;134(4):521-535. doi:10.1007/s00401-017-1769-8
8. Chen Y, Xu X, Cao J, et al. Transsphenoidal surgery of giant pituitary neuroendocrine tumor: results and exp erience of 239 cases in a single center. *Front Endocrinol*. 2022;13:879702. doi:10.3389/fendo.2022.879702
9. Shibin S, Wenjin Q, Shenting W, et al. Effect analysis of endoscopic transsphenoidal pituitary neuroendocrine tumor resection in the treatment of pituitary neuroendocrine tumor [J]. *J Chin Clin Med*. 2021;21(13):2252-2255. doi:10.11655/zgywylc2021.13.006
10. Nishioka H, Hara T, Usui M, Fukuhara N, Yamada S. Simultaneous combined supra-infrasellar approach for giant/large multilobulated pituitary neuroendocrine tumors. *World Neurosurg*. 2012;77(3–4):533-539. doi:10.1016/j.wneu.2011.07.013
11. Goel A, Shah A, Jhawar S, et al. Fluid–fluid level in pituitary tumors: analysis of management o f 106 cases. *Neurosurgery*. 2010;112:1341-1346. doi:10.3171/2009.11.JNS091083
12. Takano S, Akutsu H, Hara T, Yamamoto T, Matsumura A. Correlations of vascular architecture and angiogenesis with pituitary neuroendocrine tumor histotype. *Int J Endocrinol*. 2014;2014:989574. doi:10.1155/2014/989574
13. Okamoto K, Ito I, Furusawa T, Sakai K. Intratumoral void flow in pituitary neuroendocrine tumors. *Am J Roentgenol*. 1996;167:1070-1071. doi:10.2214/ajr.167.4.8819423
14. Kurosaki M. Endonasal transsphenoidal surgery in department of neurosurgery, Tottori University. *J Yonago Med Ass*. 2017;68:1-8.
15. Xuzhu C, Shaowu L, Tao J, et al. Correlation between nodule size and vascular flow void in angioreticuloma. *Chin Neurosurg J*. 2007;23(11):880. doi:10.3760/j.issn1001-2346.2007.11.024

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