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Brain metastasis mimicking a cavernous angioma as initial presentation of papillary thyroid carcinoma

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Summary

Brain metastases as the first clinical presentation of a papillary thyroid carcinoma (PTC) are exceptional, while cavernous angiomas are common cerebral malformations. We report the case of a 36-year-old male with an incidental brain lesion mimicking a cavernous angioma on MRI. Gamma knife radiosurgery was performed, but after 6 months, the patient developed neurological symptoms, and a repeat brain MRI revealed a significant increase in the mass. The patient underwent neurosurgery, and the histological examination of the lesion revealed metastatic carcinoma of thyroid origin. PET–CT and neck ultrasound, subsequently performed, were concordant for the presence of a right lobe nodule and ipsilateral lymph nodes, both with ultrasound features suspicious of malignancy. Total thyroidectomy with central and right lateral neck dissection was performed, and histology confirmed an intrathyroidal multifocal PTC with lymph node metastases. Postoperative radioiodine was administered, and focal uptake within the thyroid bed, without distant metastases or brain remnants, was found on the post-therapeutic whole-body scan. At 2 years from diagnosis, the patient is in good health and undergoes clinical and imaging follow-up.

Learning points

- Brain cavernous angiomas are common cerebral vascular malformations that are usually diagnosed by MRI.
- Despite the high accuracy of MRI, the exam is not pathognomonic, and misdiagnosis cannot be excluded.
- Brain metastases from PTC are very rare; however, they can mimic a cavernous angioma. Therefore, the differential diagnosis should always be considered.

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Background

Distant metastases of papillary thyroid carcinoma (PTC) develop in less than 10% of cases (1). They are usually detected at the time of diagnosis or during follow-up, whereas they occur as a presenting symptom in less than 2% of the patients (2). Brain metastases as the first clinical presentation of PTC are extremely rare (3). Cerebral cavernous angiomas account for up to 13% of intracranial vascular malformations, and their cystic variant can cause diagnostic and therapeutic dilemmas (4).

We report the case of a 36-year-old male in whom an incidental brain lesion initially diagnosed as a cavernous angioma, which was later revealed to be a brain metastasis from papillary thyroid carcinoma. Notably, the brain metastasis was the only distant metastasis detected.

Case presentation

A 36-year-old Caucasian male was diagnosed with a patent foramen ovale (PFO) and underwent brain MRI to detect silent ischemic brain lesions. MRI showed a space-occupying lesion in the convexity of the parasagittal region of the left frontal lobe. The mass was characterized by a cystic lesion with regular, clear margins, measuring 2 cm, and a mural nodule with calcifications, measuring approximately 1.2 cm adhering to the falx cerebri (Fig. 1). A neurological examination was unremarkable. The MRI features of the mass were considered consistent with a cavernous angioma, and treatment with Gamma Knife radiosurgery was performed 6 months later. After 18 months, the patient began to experience progressive weakness and paraesthesia in the right hemisome.

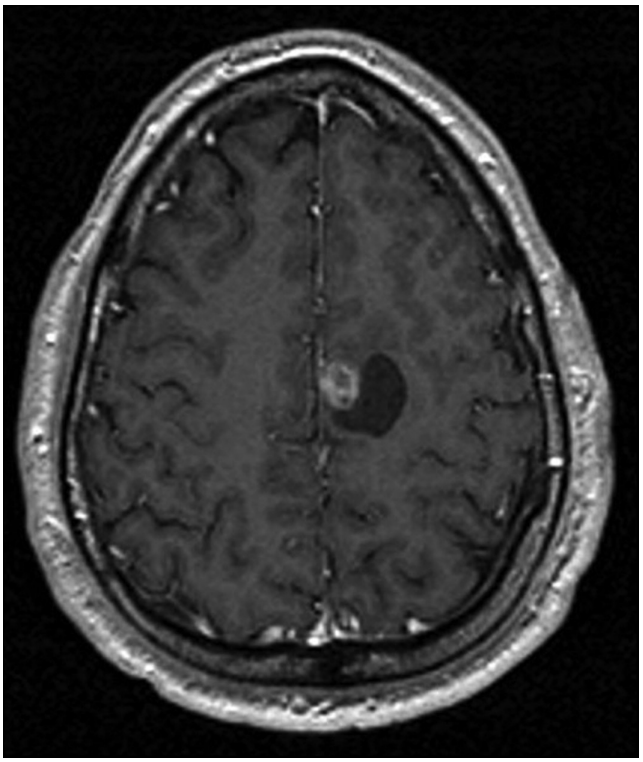

Figure 1

T1-weighted, post-contrast axial MRI image. Left frontal parasagittal mass consisting of a 2 cm cystic lesion with regular margins and a 1.2 cm mural nodule adhering to the falx cerebri.

Investigation

A repeat brain MRI revealed an enlargement of the previously described mass, measuring 6 × 6.6 × 4.5 cm, with an increase of the cystic lesion and the appearance of a fluid component within the mural nodule (Fig. 2). Compression of the left ventricle and corpus callosum was also observed. The patient was referred to the neurosurgery unit and underwent a craniotomy for mass resection. Post-surgery recovery was uneventful, and the patient was started on antiepileptic medication. Histopathology showed a metastatic carcinoma, likely of thyroid origin, positive for thyroid transcription factor 1, cytokeratin AE1–AE3, and thyroglobulin (Fig. 3). A post-surgery MRI showed a surgical cavity of approximately 13 mm with a fluid-type signal and gliotic-malacic characteristics. Total-body PET–CT with ^{18}F-Fluorodeoxyglucose (FDG) subsequently detected focal uptake in the right thyroid lobe (SUVmax 4.3) and in III level of the right lateral neck compartment (SUVmax 4.29).

Neck ultrasound using high-frequency real-time ultrasound equipment (13 MHz) showed a 2.5 cm heterogeneous hypoechoic nodule with irregular margins and micro- and macrocalcifications in the right lobe, as well as a 1 cm hypoechoic nodule with rim calcification in the isthmus. Additionally, right-sided suspicious cervical lymph nodes were detected, measuring up to 1.6 cm. Fine-needle aspiration cytology (FNAC) of the thyroid nodules and lymph nodes was not conclusive. FNAC of the largest lymph node did not show epithelial cells, and the thyroglobulin (Tg) in the washout fluid was 1.18 ng/mL. Nevertheless, considering the histological, ultrasound, and PET-CT findings, the patient was referred to surgery.

Treatment

A total thyroidectomy with dissection of the central (VI and VII levels) and right lateral (II–V levels) neck compartments was performed. Histopathology showed an intrathyroidal multifocal PTC, consisting of one nodule measuring 2 cm and multiple foci measuring 1–3 mm in the right lobe, and a 2.2 cm nodule in the

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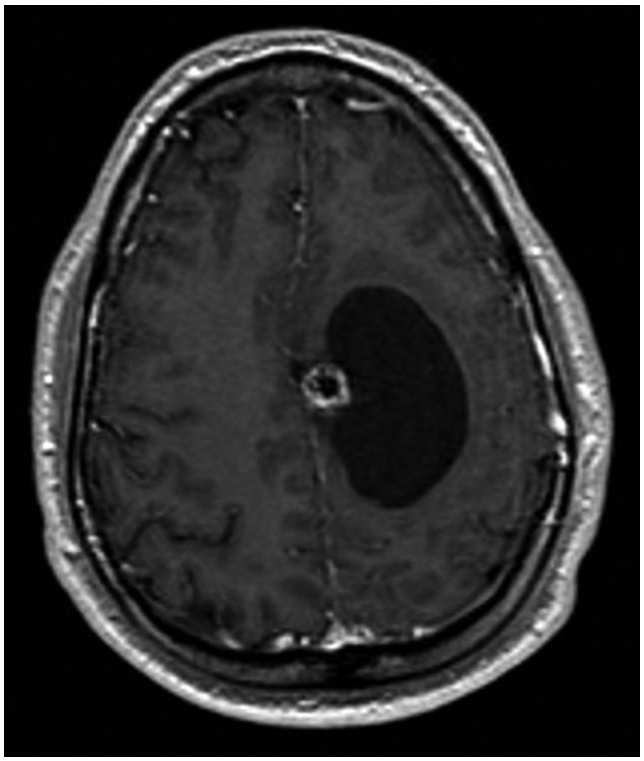

Figure 2

T1-weighted, post-contrast axial MRI image. Significant increase of the cystic component and appearance of a fluid component in the mural nodule.

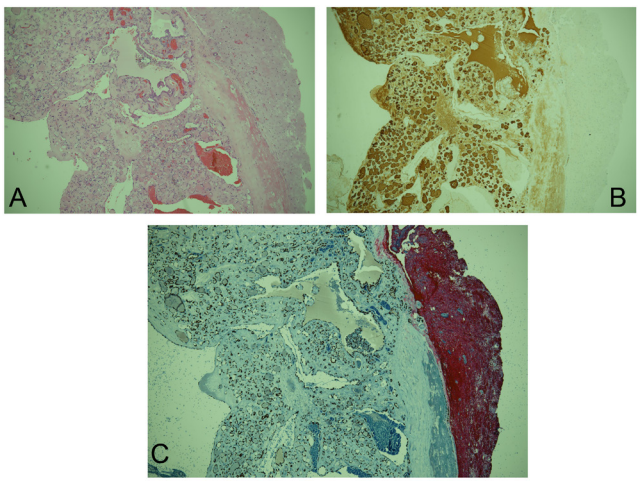

Figure 3

(A) Brain tissue showing a well-circumscribed, partially encapsulated metastasis from a follicular-patterned tumor filled with colloid-like material (hematoxylin-eosin stain, 4×– magnification), (B) same field stained with Thyroglobulin, and (C) same field double stained with TTF1 (brown) and glial fibrillary acidic protein (red).

isthmus (pT2). The tumor showed features of classic PTC. Areas with stromal fibrosis and calcifications, minimal extrathyroidal extension, and focal peritumoral vascular invasion were described. Histopathology of the left lobe was unremarkable. Metastases not larger than 1.5 cm were detected in eight lymph nodes of the central compartments and in four lymph nodes of the right lateral compartments. Molecular analysis revealed the BRAF V600E mutation both in the brain metastasis and in the thyroid PTC. Levothyroxine (L-T4) suppressive dose was started. Three months after surgery, the patient underwent radioactive iodine adjuvant therapy (RAI) with 150 mCi ^{131}I after L-T4 withdrawal. Prior to radioiodine administration, endogenous TSH-stimulated Tg was 3.9 ng/mL (TSH = 131 mU/L); and anti-Tg autoantibodies (Tg-Ab) were absent. The post-therapy whole-body scan showed two foci of iodide uptake within the thyroid bed. L-T4 suppressive therapy was reintroduced.

Outcome and follow-up

At the first post-radioiodine neck ultrasound, three round lymph nodes lacking a fatty hilum, measuring 4 mm, and one measuring 10 mm were found in the right lateral compartment. A total-body PET-TC with ^{18}F-FDG did not show any areas of increased uptake. Starting from 5 months after RAI, serial unstimulated Tg ranged between 0.15 and 0.2 ng/mL. Tg-Ab were always undetectable.

Repeated neck ultrasounds at 6-month intervals confirmed the findings without a significant increase in the size of the lymph nodes. FNAC of the larger lymph node was not conclusive, Tg in the washout fluid was <0.1 ng/mL. After 2 years of follow-up, neck ultrasound findings were substantially unchanged. Recombinant human TSH-stimulated Tg was 0.4 ng/mL, and ^{18}F-FDG PET-TC did not show areas of increased uptake. Six-month interval MRI and neurosurgical examinations did not show signs of remnant and/or recurrent tumor (Fig. 4).

Discussion

The case herein reported has some characteristic features. The brain metastasis was the presenting feature of PTC, which is an extremely rare condition described in the literature mainly as case reports (5). Furthermore, the brain metastasis was the only distant metastasis detected, a condition observed in few patients (3, 5, 6). Indeed, brain metastases are usually associated with lung, bone, and liver metastases (1). A possible explanation for this peculiarity is the presence of PFO in our patient. Indeed, it has been hypothesized that the presence of PFO can promote the passage of metastatic cells from the right side to the

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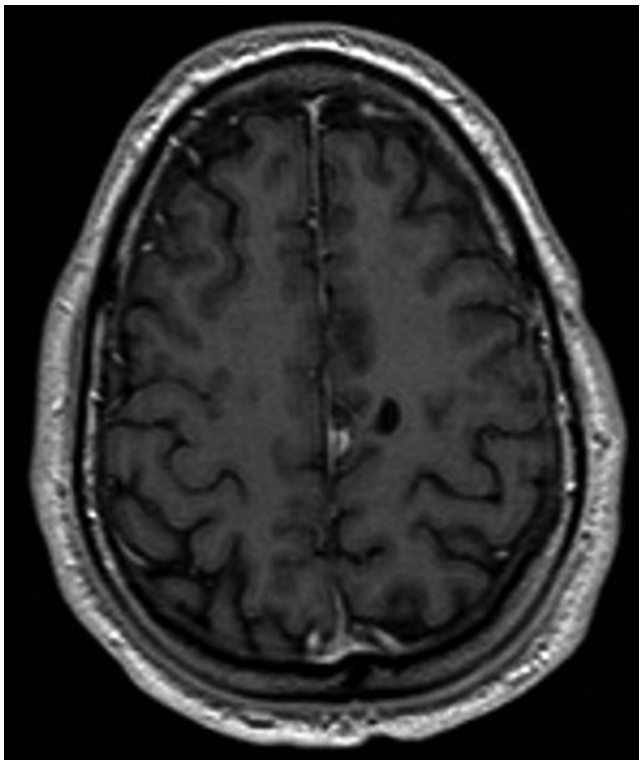

Figure 4

T1-weighted, post-contrast axial MRI image. Stable surgical cavity with gliotic features and millimetric hyperintense area consistent with radiation and surgery injury.

left side of the heart, bypassing the lungs and causing a paradoxical embolism, as described for cryptogenic stroke and brain abscesses (7).

A further peculiarity of the case presented is that the brain metastasis mimicked a cavernous angioma on MRI, leading to inappropriate treatment. The finding of cystic and hemorrhagic radiological features in brain metastases from PTC is not unusual (3, 5, 6); however, the mimicking of a cavernous angioma, to our knowledge, has been described in only three cases (8, 9, 10). Indeed, only one of the reported cases resembles our patient's history, a symptomatic solitary brain mass presurgically diagnosed as a cavernous angioma that was actually the sole distant metastasis of PTC (8). In the second case, the brain lesion, consistent with a cavernous angioma with hemorrhage, was associated with a large mass in the sternum in a patient without a history of thyroid carcinoma (9). In the third case, the brain lesion was diagnosed in a patient who had been treated with surgery and radioiodine for a low-risk PTC 7 years before (10). These observations indicate that metastatic thyroid cancer should be considered in the differential diagnosis of intracranial cavernous angioma, particularly if radiation therapy is planned, to avoid inappropriate treatment. Indeed, although MRI is the gold standard for the diagnosis of intracranial cavernous angioma, its diagnostic accuracy is not 100%.

Two further peculiarities of this case are the young age of the patient and the lack of aggressive histological features in the PTC. Indeed, brain metastases are associated with older age and aggressive histologic variants of PTC (6). However, the primary tumor presented the BRAF V600E mutation, a condition associated with a more aggressive clinical outcome. Unfortunately, we could not evaluate further mutations, such as in the telomerase reverse transcriptase, whose association with the BRAF characterizes PTCs with aggressive behavior.

In conclusion, the present case has several peculiar features that deserve to be underlined. Although PTC usually has an excellent prognosis, the possibility of distant metastases exists, and in rare cases, they can be present at the time of diagnosis or, as in our patient, they can be the first clinical manifestation of the disease. Furthermore, brain metastasis from thyroid tumors can mimic a cavernous angioma on MRI; therefore, caution should be used before starting radiation treatment based solely on this data. Indeed, the radiation therapies indicated for cavernous angioma can have only a transient effect in reducing the growth of the brain metastasis and can delay the definitive diagnosis, as in the case described herein.

Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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Patient consent
Written informed consent for the publication of its clinical details and clinical images was obtained from the patient.

Author contribution statement
IB, CG, GDD, GN: clinical and endocrinological evaluation, contributions to the conception and design of the work, literature review, drafting the work, final approval of the version to be published. DI, DZ: performed neurosurgery and neurological follow-up. AI: performed the pathology studies of the brain metastasis. LP: performed thyroid surgery.

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