Low-grade intracranial meningioma with bilateral pulmonary metastases incidentally detected postpartum: a case report and review of the literature

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Abstract

Introduction: Meningiomas are the most commonly encountered intracranial tumors, usually showing indolent behavior. Extra-axial spreading and distant metastases are seldom detected in these tumors, and lung metastasis from a low-grade meningioma is a rare event.

Case presentation: This case report aimed to present the clinical, imaging, and pathological features of a 37-year-old Caucasian pregnant woman with bilateral lung metastases incidentally detected during preoperative workup ahead of surgery for a primary intracranial meningioma. The possible metastatic routes and risk factors of dissemination to the pulmonary circulation were discussed as well.

Conclusion: Metastasis must be considered in patients with intracranial meningiomas accompanied by venous sinus invasion and extension through the calvarium. Thorough paraclinical investigations are suggested in such cases.

Keywords: Meningioma, Extra-axial metastasis, Lung, Pregnancy, Case report

Background

Meningiomas are extra-axial tumors that are derived from the meningothelial cells of the arachnoid membrane. They are the most common types of primary brain tumor, and females are affected more than males, with a 2:1 ratio. Ionizing radiation and genetic syndromes such as neurofibromatosis type 2 (NF2) have been considered as the risk factors for meningiomas.

Meningiomas are mainly slow-growing. However, they can be aggressive or may even undergo malignant transformation in a small proportion of cases [1, 2]. According to the 2016 classification of central nervous system tumors by the World Health Organization (WHO), meningiomas are classified into three grades; that is, I, II (atypical), and III (malignant). It has been reported that, in the course of the disease, 0.1–1% of all primary meningiomas develop metastases, with the lung being the most frequent site of distant metastatic spread [1–3]. The present study aims to report the case of a pregnant patient with bilateral metastatic pulmonary lesions incidentally detected ahead of resection of the primary brain meningioma.

Case presentation

A 37-year-old Caucasian female presented at 18 weeks of gestation with the complaint of a slow-growing scalp mass. She had no history of headaches, blurred vision, nausea, or vomiting. In her past medical history, she had
two pregnancies with no complications. On palpation, a well-defined round-to-oval mass was detected with hard consistency. However, the physical examination was unremarkable. Her full-term baby was delivered via cesarean section without any fetal or maternal complications. One month postpartum, the patient was visited by a general surgeon and a tissue biopsy was obtained from the scalp mass. The pathology result was in favor of a grade I meningioma with skull bone involvement. Hence, the patient was referred to the neurosurgery ward. Therein, a brain magnetic resonance imaging (MRI) was done, and an extra-axial $39 \times 33 \times 25$ mm mass isointense in T1, hyperintense in T2, was noted high in the parafalcine region of the left parietal lobe. The mass had a dural tail appearance. Adjacent hyperostosis and enhancement of the adjacent involved calvarium in the
The findings were suggestive of an intraosseous meningioma with both intra- and extracranial components (Fig. 1).

The patient’s brain meningioma was operated in the neurosurgery department. Right frontoparietal craniotomy was performed, and the tumor was released from the brain tissue ahead of the gross total resection of the mass as well as the involved scalp. The postoperative pathology result of the brain mass was also in favor of grade I/III meningioma. The patient was discharged from high parietal scalp were mentioned as well. The findings were suggestive of an intraosseous meningioma with both intra- and extracranial components (Fig. 1).

Fig. 2. Chest X-ray showing bilateral intraparenchymal lung lesions

Fig. 3. Chest CT scan of the lung mass (lateral view). Two well-defined lung masses are apparent

Fig. 4. Histopathology of the resected brain mass and the pulmonary lesion showing tumoral cells with whorled appearance without atypia and mitotic figures compatible with meningioma grade I (A). The same pattern is obvious in the lung (B) (hematoxylin and eosin x 100)
the hospital with no complications and no adjuvant cranial radiotherapy.

During the preoperative workup ahead of brain surgery, bilateral lung masses were detected as an incidental finding on chest X-ray and high-resolution computed tomography (HRCT) scan (Figs. 2, 3). There was no history of cough, chest pain, hemoptysis, or difficulty breathing. Heart and lung physical examinations were unremarkable. Preoperative laboratory evaluation including routine complete blood tests, electrocardiogram, and spirometry were unremarkable as well.

A wedge resection of the left lobe lesion (4 × 5 cm) was performed along with a Tru-Cut biopsy of a pleural-based mass in the right lower pulmonary lobe. The histological feature of the lung tumor was the same as that of the brain mass, and the diagnosis of metastatic meningioma was confirmed by immunohistochemistry (IHC). Accordingly, the tumor cells were positive for EMA, PR, and Ki67 (low) and negative for P63, TTF1, and chromogranin (Figs. 4, 5). Bilateral lesions were resected through staged thoracotomy with no postoperative complications. The patient did not require radiotherapy and chemotherapy. She was followed up via brain and chest CT scans after 2 months, revealing satisfactory residual respiratory function and no evidence of pulmonary relapse.

Discussion

Meningioma is a common primary slow-growing, intracranial, extra-axial neoplasm with attachment to the dura mater. It is composed of neoplastic meningothelial cells, and its usual growth rate is less than 1 cm/year, ranging from 0.03 to 2.62 cm/year [4]. Metastases may develop in less than 0.1% of patients, and lungs, liver, lymph nodes, and bones are the most common sites [5]. Pregnancy has been found to be associated with an increased incidence of symptomatic meningiomas in females, suggesting an increased tumor growth during this period [6]. On the other hand, attenuation of clinical symptoms and shrinkage of tumors have been reported during the postpartum period [2, 7].

Estrogen, progesterone, and prolactin levels are elevated during pregnancy, and the expression of the estrogen receptor (ER) and progesterone receptor (PR) has been found in a significant percentage of meningiomas [8]. These findings suggest that female sex hormone-induced cell proliferation is the simplest explanation for the growth of meningioma during pregnancy. On the other hand, exogenous estrogen therapy has not been associated with an increased risk of meningioma, and no change has been detected in the tumor size during the follicular phase of menstruation when estrogen levels are highest [8, 9].

Lusis et al. conducted a study on the pathology specimen of meningiomas during pregnancy and disclosed that the frequency of PR positivity was similar to that of the control group [10]. Although PR expression was found in 70–95% of meningiomas, the same level of expression was observed in tumoral tissues of children and males with minimal progesterone levels [10, 11]. Additionally, the grade of meningioma did not change during pregnancy [10].

Recently, Telugu et al. explored the expressions of ER and PR in meningioma specimens via IHC and assessed their correlations with gender, histological subtypes, and grade. The expression rates of ER and PR were 2% and 66%, respectively. No significant correlation was detected between the positivity of PR and the above-mentioned variables [12]. Therefore, the levels of sex hormones and expressions of receptors in tumoral tissues alone cannot justify the growth of meningiomas during pregnancy.

Another hypothesis that prevails to date is that meningioma growth is associated with vascular changes during pregnancy such as intratumoral hypervascularity and tissue edema [10]. The exact mechanism of edema is
| Reference            | Age, years | Interval, years | Location                                      | Histology | Treatment                                      | Outcome                                      |
|----------------------|------------|-----------------|-----------------------------------------------|-----------|-----------------------------------------------|-----------------------------------------------|
| Aumann et al. [13]   | 45         | 5               | Left frontal parasagittal                      | I         | Total resection                               | NA                                            |
| LeMay et al. [14]    | 56         | 10              | NA                                            | I         | Partial resection                             | Died of disease 3 years after thoracotomy    |
| Hishima et al. [15]  | 25         | Prior to intracranial tumor | Right parietal region adjacent to the falx | I         | Partial resection                             | NA                                            |
| Murrah et al. [16]   | 53         | 10              | Left frontal hemispheric convexity             | NA        | Partial resection                             | Alive with disease 2 years after thoracotomy  |
| Adlakha et al. [17]  | 39         | 6               | Left parietal parasagittal                     | II        | Partial resection and gamma knife radiosurgery| Died of disease 10 years after initial presentation |
| Figueroa et al. [18] | 50         | 5               | Left cranial fossa                             | I         | Total resection and radiotherapy for metastases| Alive with disease 32 years after radiotherapy |
| Travitzky et al. [19]| 41         | 19              | NA                                            | III       | Total resection and radiotherapy              | No evidence of disease 6 months after doxil-induced regression of metastases |
| Erman et al. [7]     | 34         | 8               | Left frontal-parasagittal                      | II        | Partial resection and radiotherapy            | Died of disease shortly after thoracotomy, radiotherapy, and chemotherapy of the metastasis |
| Psaras et al. [20]   | 65         | 15              | Falx cerebri and superior sagittal sinus       | I         | Total resection and radiotherapy              | No evidence of disease 12 months after thoracotomy |
| Alexandra et al. [21]| 26         | NA              | Multiple supratentorial                         | III       | Partial resection                             | NA                                            |
| Ocque et al. [24]    | 44         | NA              | Right frontal                                  | NA        | Total resection                               | NA                                            |
| Frydrychowicz et al. [25]| 45   | 5               | Left frontal                                   | II        | Surgery and radiotherapy                      | NA                                            |
| Dalle Ore et al. [26] | 69    | 5.4            | Cerebellum                                     | III       | No intervention                               | Alive after 5 months F/U                     |
|                     | 75         | 9.2             | Falx, parasagittal                              | II        | No intervention                               | Alive after 1.5 months F/U                   |
|                     | 64         | 10.8            | Parasagittal                                   | III       | Hydroxyurea, EBRT                             | Alive after 13 months F/U                    |
| Vakil et al. [1]     | 91         | 1               | Left frontoparietal                            | III       | Radiotherapy with sunitinib                   | Alive after 13 months F/U                    |
| Sathirareuangchai et al. [27]| 59  | Concurrent | Left occipital convexity                        | I         | Surgery                                       | NA                                            |
| Wang et al. [2]      | 54         |                 | Left middle cranial                            | I         | Surgery                                       | NA                                            |
| Som et al. [38]      | 53         | 5               | Right sphenoid wing                            | I         | Surgery                                       | NA                                            |
| Kodama et al. [33]   | 61         | 19              | Cerebellar                                     | I         | Surgery                                       | NA                                            |
| Tao et al. [40]      | 32         | 18              | Right frontal                                  | I         | Surgery                                       | NA                                            |
| Shin et al. [37]     | 53         | 9               | Left frontal                                   | I         | Surgery                                       | NA                                            |
| Tworek et al. [41]   | 50         | 6               | Left frontal                                   | I         | Surgery                                       | NA                                            |
| Baisden et al. [29]  | 71         | 13              | Right middle cranial fossa                     | II        | Surgery                                       | NA                                            |
unclear, but an increase in the expression of aquaporin (a water channel protein) during pregnancy and a positive effect of progesterone on vascular dilatation have been suggested [10]. It seems that, during pregnancy, due to hemodynamic changes, a preexisting meningioma may present with the clinical symptoms of elevated intracranial pressure, including headache, nausea, and vomiting. After pregnancy, shrinkage of the tumoral tissue may occur and the mass size may decrease on its own.

Although meningiomas are more common among females, metastasis has not been reported to be more common in this population. To the best of our knowledge, 33 such cases have been reported in the literature (Table 1) [1, 2, 7, 13–41]. The median age of the patients was 50 years (age range 26–91 years). In addition, the interval between the detection of the primary meningioma and the detection of lung metastases ranged from 9 to 19 years. In two cases, the lung mass was found concurrently with the primary brain tumor. Generally, lung metastases rarely cause symptoms such as cough and hemoptysis. In the present case, bilateral pulmonary nodules were found incidentally and the patient had no respiratory symptoms. The exact mechanism of multiple lung metastases from an intracranial tumor is not clear yet. Higher histological grades (II/III), venous sinus invasion, prior surgery for resection of the primary tumor, and tumor recurrence have been reported as the predictive factors for multiple lung metastases. Dissemination of tumor cells by hematogenous and lymphatic vessels or by cerebrospinal fluid (CSF) seeding have also been suggested as the underlying mechanisms of metastasis [42]. Tumor invasion to dural venous sinuses and cranial veins facilitate the hematogenous spread of tumoral cells to the pulmonary circulation [42]. The present case had a large mass with the invasion of the superior sagittal sinus and extension through the calvarium and scalp. Genetic abnormalities such as loss of heterozygosity at 9p, 1p, and 22q have also been considered the predictors of lung metastases [1].

Surgical resection is the current standard of care for primary low-grade meningiomas. For high-grade lesions, surgical resection is combined with adjuvant radiotherapy to prevent local recurrence. Thoracotomy to surgically excise the lung mass is the treatment of choice for metastatic lung masses. Due to the rarity of metastatic meningiomas, few clinical trials have been performed and no standard treatment is available. Previous studies assessed the efficacy of hydroxyurea, external beam radiation, and sunitinib in treatment of high-grade metastatic cases [43, 44].

Conclusion
In patients with intracranial meningiomas accompanied by venous sinus invasion and extension through the calvarium, metastasis must be considered and thorough paraclinical investigations are suggested. From a practical point of view, these seemingly benign lesions may not be as they appear, which emphasizes the importance of follow-up for such lesions beyond the scope of neurosurgery.

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Authors’ contributions
NA drafted the article. AA and SP collected the data and participated in drafting the article. PM, AS, MV, and SHY performed the surgical operation, were in charge of the patient’s status, obtained consent, collected the clinical data, and helped draft the manuscript. MHA performed the pathological

Table 1. (continued)

| Reference          | Age, years | Interval, years | Location            | Histology WHO grade | Treatment     | Outcome |
|--------------------|------------|-----------------|---------------------|---------------------|---------------|---------|
| Kovoor et al. [34] | 40         | 2               | Left parietal       | I                   | Surgery       | NA      |
| Pramesh et al. [36]| 29         | 9               | Right occipital     | I                   | Surgery       | NA      |
| Fabi et al. [31]   | 57         | 1               | Right frontal       | III                 | Surgery       | NA      |
| Ascoli et al. [28] | 58         | 12              | NA                  | I                   | Surgery       | NA      |
| Brennan et al. [30]| 74         | 22              | Parasagittal        | II                  | Surgery       | NA      |
| Kanzaki et al. [32]| 67         | 15              | NA                  | II                  | Surgery       | NA      |
| Lambertz et al. [35]| 65         | 12              | Right frontal       | II                  | Surgery       | NA      |
| Tao et al. [39]    | 51         | 1               | Right lateral ventricle | III              | Surgery       | NA      |
| Kansaki [32]       | 67         | 15              | NA                  | II                  | Surgery       | Alive   |
| Current case       | 34         | Concurrent      | Left parafalcine    | I                   | Surgery       | Alive   |

NA not available
examination and revised the article. PM and AS equally participated in the management of the case and have been considered as co-first authors. All authors read and approved the final manuscript.

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**Availability of data and materials**
No additional datasets were used for the creation of this manuscript. All information is available from the standard documentation in the patient's electronic medical record.

**Declarations**

**Ethics approval and consent to participate**
This study was approved by the Ethics Committee of Namazi Hospital. In addition, written informed consent was obtained from the patient.

**Consent for publication**
Written informed consent was obtained from the patient for publication of this case report and the accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of the journal.

**Competing interests**
The authors declare that they have no competing interests.

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