incomplete ring and restored the continuity of the aorta with the end-to-side anastomosis.

In summary, the described technique allowed us to avoid compression of the retroaortic innominate vein and create a widely open aortic anastomosis. Embryology gives a useful clue to understanding of the surgical anatomy of this rare malformation.

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CASE REPORTS

Development of Brain Metastasis 5 Years Before the Appearance of the Primary Lung Cancer: "Messenger Metachronous Metastasis"

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We report a patient with a brain metastasis that presented 5 years before the primary adenocarcinoma of the lung from which it originated. The metastasis and the primary tumor were removed. To confirm their common origin, we used comparative genomic hybridization. We have named this type of metastasis "messenger metachronous metastasis." The patient remains well 79 months after the brain metastasectomy and 18 months after the lung surgery.

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Bronchogenic carcinoma is the most common malignant tumor diagnosed in the United States, and the development of a brain metastasis during the natural history of non–small cell lung cancer is a common and devastating event. The median survival from the diagnosis of brain metastasis to death is approximately 1 month without treatment and 14 to 24 months in combined brain–lung resection cases [1,2]. The prognosis of a metachronous metastasis is better according to some investigators [3], but others have found no significant difference in survival between patients with synchronous and metachronous lesions [1]. We present an unusual case of brain metastasis from non–small cell lung cancer, which we term "messenger metachronous metastasis," and which appeared 5 years before the discovery of the primary lesion. We treated both lesions aggressively, and the patient remains well.

In 1995, a 51-year-old woman was evaluated for a 1-month history of decreased motor strength in the left lower extremity and for personality changes. Neurologic examination revealed left hemiparesis, and computed tomography (CT) demonstrated a 2-cm tumor in the right parietal area. After surgical removal of the tumor, pathologic evaluation suggested an adenocarcinoma metastasis from the lung; however, meticulous examination by chest CT and bronchoscopy did not disclose a primary lesion. The patient did not receive postoperative whole-brain irradiation. Over the next 4 years, the patient underwent chest CT every 6 months, which revealed no abnormality. At 5 years, after a delay in scanning because of patient neglect, a mass appeared in the hilum of the left upper lobe (cT3 to T4N0). The 8-cm central lung tumor was treated with 25×2 Gy neoadjuvant irradiation. The preoperative staging revealed a 5-mm metastasis in the right cerebellum without any symptoms, but this area was not accessible to surgical removal; accordingly, the patient received 10×3 Gy whole-brain and 5×2 Gy tumor bed irradiation. Because of the good physical status of the patient, we opted to perform left upper lobectomy. The histology demonstrated a T2N0 adenocarcinoma of the lung.

To confirm the common origin of the brain tumor and the lung adenocarcinoma, we used comparative genomic hybridization. After genomic DNA isolation from the paraffin-embedded tissues, we performed amplification and labeling steps as described previously [5]. For comparative genomic hybridization, we used human cDNA microarrays containing 800 random cDNA fragments (amplified and spotted in house) in duplicate. Relative DNA losses and gains were determined by normalizing intensity values to intensities after hybridization with labeled probes obtained from normal lymphoid tissue. We found and located several sequence gains and losses, which were common in both malignant tumors (Table 1). In three cases, brain-specific losses were also demonstrated (Table 1). From these results, we conclude that the two tumors are derived from the same clone. Eighteen months after the lung surgery, the patient was doing well. She had had no neurologic or chest symptoms, and chest radiography did not show any recurrence. Brain magnetic resonance revealed that the brain metastasis had completely disappeared.

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Table 1. Results of Comparative Genomic Hybridization for Molecular Comparison of the Two Tumors

Location	Accession No	Clone Name	Change	Lung[a]	Brain[a]
1 p12–13.3	AI017264	EST	Gain/gain	7.1	5.71
1 p13–p21	AF000148	ATP binding cassette transporter	Gain/gain	4.1	3.09
1 p34.2	BC017196	Adenyl cyclase-associated protein	Loss/loss	−5.56	−12.88
1 p36.31	AI015184	EST	Loss/loss	−3.09	−10.00
3 p16.3	L34408	Clone B3B3E13	Gain/gain	6.9	6.06
5 q27	D00761	Proteasome component C5	Loss/loss	−3.28	−3.75
6 p15.3–7p14	AA971315	EST	Loss/loss	−3.26	−3.7
9 p11.2	D14497	Proto-oncogene c-cot	Loss/loss	−3.85	−6.1
11 q22	L04731	Zinc finger protein HRX	Gain/gain	4.5	4.91
19 p13.2	U69141	Glutaryl-Coenzyme A dehydrogenase	Loss/loss	−2.1	−4.26
19 p13.2	L20965	Phosphodiesterase 4A	Gain/gain	8.8	10.34
19 q13.4	U09414	Zinc finger protein 137	Loss/loss	−6.25	−6.3
19 q13.4	AF004230	Lysozyme	Loss/loss	−4.6	−6.93
1 q21	U16954	AF1q	Normal/loss	−1.06	−4.54
13 q32.2	AB008430	CDEP	Normal/loss	−1.64	−13.11
18 q21.3	X98307	UV-B repressed, HUR 7	Normal/loss	−1.05	−4.37

[a] Normalized to normal lymphoid tissue.

ATP = adenosine triphosphate; EST = expressed sequence tag.

Comment

In this case, at the first emergence of the malignancy, a TxNxM1 adenocarcinoma of the lung was diagnosed upon removal of a brain metastasis. It would appear to be a metachronous metastasis, with more than 60 months between the appearance of the metastatic lesion and the primary, but, in this case, the metastasis preceded the appearance of the primary cancer, as a "messenger."

According to The Lung Cancer Study Group [4], 95% of brain metastases develop from nonsquamous cell cancer and most frequently from an upper lobe tumor [2]. Therefore, we expected an adenocarcinoma of the lung to appear in one of the upper lobes. Ultimately, a cT3 to T4N0M1 lesion was discovered in the left upper lobe, with a recurrent brain metastasis at the same time.

Because of the inoperable recurrent brain metastasis (5 mm) located in the right cerebellum, removal of the lung tumor was debated. Because complete resection rather than stage of locoregional primary lung disease is the primary determinant of survival in patients undergoing brain metastasectomy [1], and because the situation is the same in patients receiving cranial irradiation only to control the metastasis [6], we opted to proceed. To control the recurrent brain metastasis, the patient received 30 Gy whole-brain and 10 Gy tumor bed irradiation. For control of the primary tumor, after the neoadjuvant irradiation (50 Gy) to the central lung cancer with good regression, left upper lobectomy was performed without any complication. Despite the neoadjuvant irradiation, the removed tumor contained viable tumor cells.

The mean survival after combined brain–lung resections is 14 months [1]. In our case, survival after the brain metastasectomy is 79 months at the last follow-up. The median survival interval after lung resection and irradiation to the brain metastasis was 5.1 months [2]. In our case, with the lung resection and irradiation to the recurrent brain metastasis, the survival after the lung resection is 18 months at the last follow-up, and the patient is disease free.

In rare cases, brain metastasis can develop from a subclinical tumor many years before the appearance of the primary lesion ("messenger metachronous metastasis"). The favorable clinical course in our patient suggests that the process of the malignancy may be different from that in the typical case of metachronous brain metastasis, with longer survival. Thus, aggressive treatment is indicated for both the primary and the metastatic lesion. Presentation of this type of "messenger brain metastasis" from lung cancer has not been previously reported in the literature.

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