Brain metastasis localized to the same area of infarction: illustrative case

Oday Atallah, MD, MBA1 and Bipin Chaurasia, MS2

1Department of Neurosurgery, Hannover Medical School, Hannover, Germany; and 2Department of Neurosurgery, Neurosurgery Clinic, Birgunj, Nepal

BACKGROUND Ischemic stroke and tumor account for a disproportionate share of deaths and disabilities among the elderly. Patients with a tumor who develop recurrent acute neurological deficits after a stroke can be at risk for tumor-related stroke. In contrast, brain metastases (BM) are common causes of neurological symptoms and are associated with a poor prognosis in patients with both malignancy and ischemic stroke.

OBSERVATIONS The authors report a rare case of metastatic melanoma that manifested in the same region as a previous ischemic infarction. A 22-year-old female presented at our emergency department with right hemiparesis and sensory difficulties. Infarction in the left frontoparietal and basal ganglia regions was found on a computed tomography scan of the brain. A decompressive hemicraniectomy was performed urgently. After 16 years, a biopsy taken from her chin revealed malignant melanoma. Hemorrhagic metastasis on the frontal lobe of the brain was detected with magnetic resonance imaging and was histopathologically confirmed upon resection.

LESSONS In addition to recurrence, BM may be considered when a person with ischemic stroke and a cancer such as melanoma has new neurological problems in one area that cannot be explained by the stroke.

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KEYWORDS brain metastasis; stroke; melanoma

Brain metastases (BMs) will be present in up to 15% of the predicted 1.44 million Americans who will receive a cancer diagnosis this year.1,2 The primary tumors with the highest rates of BM are lung, breast, and melanoma. These are followed by kidney (i.e., renal cell carcinoma [RCC]), colon, pancreas, and other urological/gynecological cancers.3,4 Approximately 80% of BMs come from the cerebral hemispheres, 15% from the cerebellum, 5% from the brainstem, and 10%–15% from the deep or eloquent parts of the brain.1,2,5 Ischemic stroke and tumor are the two most common conditions that result in mortality and disability in the elderly.6,7 People with systemic cancer frequently experience cerebral vascular issues. In fact, 14.6% of tumor patients showed symptoms of cerebrovascular dysfunction, according to an autopsy study.8 Furthermore, ischemic stroke is particularly hazardous in the first few months after a cancer diagnosis.9 Three percent to 5% of patients with ischemic stroke have a new cancer diagnosis within 2 years of the index stroke.10

It is exceedingly complicated how hemiparesis brought on by a stroke relates to tumor. Both illnesses are influenced by variables such as aging, cigarette use, and obesity. Some of the stroke reasons for tumor increases include atherosclerosis, small artery disease, and hypercoagulability.11 Both radiation treatment and chemotherapy for tumors have been associated with a higher risk of suffering from ischemic stroke.12 The microenvironment can also be altered by an ischemic stroke, leading to neovascularization and blood-brain barrier leakage, which can function as a distinct risk factor for metastatic malignancies.13 The brain and central nervous system (CNS) are particularly susceptible to melanoma spread, which results in significant morbidity and therapy resistance.14

In patients with ischemic stroke and concurrent tumor, recent research has concentrated on the pathomechanisms and treatments for cancer-related stroke. However, we should not ignore distant metastases, including BMs, as their incidence may increase with longer life expectancies as a result of advances in cancer treatment. Despite the fact that the underlying processes in this group have not been adequately studied, metastases are associated with a poor prognosis.15,16

ABBREVIATIONS BDNF = brain-derived neurotrophic factor; BM = brain metastases; CNS = central nervous system; CT = computed tomography; MRI = magnetic resonance imaging; PET = positron emission tomography; RCC = renal cell carcinoma; VEGF = vascular endothelial growth factor.

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Illustrative Case
A 22-year-old female presented to our central emergency department with right hemiparesis and sensory disturbances. The patient was known to have an antiphospholipid syndrome and systemic lupus erythematosus. For further elucidation of the symptoms, a brain computed tomography (CT) scan (Fig. 1) was obtained, revealing an infarct in the left middle cerebral artery with midline shift to the right. Then, an emergency decompressive hemicraniectomy was performed.

After 16 years, a biopsy revealed that a brownish lesion on the right jawline was malignant melanoma. The patient presented to the emergency department 8 months later with regurgitation, nausea, and decreased vigilance. As part of the diagnostic process, we performed brain magnetic resonance imaging (MRI; Fig. 2), which revealed a hemorrhagic metastasis in the left frontotemporoparietal region with midline displacement. The metastasis was subsequently removed via craniectomy. Histopathological analysis confirmed the presence of metastasis.

When the patient was discharged, she was conscious and contactable, but her general and nutritional states had deteriorated. Furthermore, she had a right-sided hemiparesis.

Patient Informed Consent
The necessary patient informed consent was obtained in this study.

Discussion
Observations
Infarcted tissue-specific BMs are extremely rare. To our knowledge, this is the first case of metastasis in a patient with malignant melanoma after a stroke. In one report in the literature, such metastases were documented in a patient with uterine cervical cancer. After the initial stroke, a patient with RCC had a rare case of BM of the cancer (Table 1).

The seed and soil hypothesis describes the complex relationship between tumor cells (the seed) and the environment of the host organs (the soil). Recent research has focused more on the metastatic niche than on the seed characteristics that contribute to tumor progression and growth, which is thought to be a fruitful environment appropriate for the colonization and proliferation of metastatic seed. The metastatic niche serves a number of similar purposes, including as anchoring, prosurvival signaling support, defense against outside threats, and proliferation.

Neovascularization and rupture of the blood-brain barrier are potential consequences of cerebral infarction. In the infarcted tissues, numerous capillary-sized blood vessels are surrounded by distended endothelial cells. Experimental research suggests that neovascularization and hyperemia may be related. These properties may make it easy for circulating tumor cells to target the newly formed vascular network of infarcted regions and penetrate the brain parenchyma. In addition, a considerable number of metastatic tumor cells may be

FIG. 1. Head CT scans (A–F) show medial infarction on the left side and partial infarction of the anterior cerebral artery on the left. Midline shift to the opposite side with a shift of the right foramen of Monro by about 12 image mm to the right. The right lateral ventricle is clearly narrowed, as is the right temporal horn. The basal cisterns are no longer delimitable. The fourth ventricle is preserved. The outer cerebrospinal fluid spaces have completely elapsed, and the gyri and sulci are no longer visible.
absorbed by the compartmentalized space created by the ischemia injury. A modified microenvironment of infarcted tissue could resemble the qualities of fruitful soil and serve as a metastatic habitat.

The brain goes through a complicated series of processes after a stroke as part of the recovery process. Vascular endothelial growth factor (VEGF) and brain-derived neurotrophic factor (BDNF) are two examples of growth factors that are secreted as a result of these processes. These growth factors are essential for the survival and development of brain blood vessels and neurons. Increased levels of VEGF and BDNF can contribute to the formation of a metastatic focus at the site of injury after a stroke. VEGF’s main job is to encourage the growth of new blood vessels (angiogenesis) in response to damaged or ischemic (not enough blood flow) tissue. However, this elevated VEGF level may unintentionally help metastatic

FIG. 2. Head MR images (A–F) show inhomogeneous, marginal contrast-affine and hemorrhagic formation based on a known parenchymal defect on the left frontal side, with a high probability of neoplastic origin and compatible with metastatic, previously known malignant melanoma with hemorrhages.

TABLE 1. Summary of case reports of BM localized to the same area of an ischemic infarction

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Age at Dx of Stroke/Sex</th>
<th>Localization of Stroke</th>
<th>Metastasis Location</th>
<th>Histological Features</th>
<th>Duration From Stroke to Metastasis</th>
<th>FU (mos)</th>
<th>Cause of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nielsen &amp; Posner, 1983&lt;sup&gt;17&lt;/sup&gt;</td>
<td>50/F</td>
<td>Territory of MCA</td>
<td>Frontal, parietal, &amp; superior temporal lobes</td>
<td>Metastasis from carcinoma of uterine cervix</td>
<td>9 mos</td>
<td>Death after 2 mos of discharge</td>
<td>Acute pulmonary edema &amp; shock</td>
</tr>
<tr>
<td>Gwak et al., 2021&lt;sup&gt;18&lt;/sup&gt;</td>
<td>48/M</td>
<td>Territory of MCA &amp; PCA</td>
<td>Frontal &amp; temporal region</td>
<td>Metastasis from RCC</td>
<td>8 mos</td>
<td>Death w/in 6 mos of discharge</td>
<td>Refusing further radiation therapy</td>
</tr>
<tr>
<td>Present case</td>
<td>22/F</td>
<td>Territory of MCA &amp; ACA</td>
<td>Frontal, parietal, temporal, &amp; basal ganglia regions</td>
<td>Metastasis from malignant melanoma</td>
<td>16 yrs</td>
<td>Death w/in 8 mos of discharge</td>
<td>Refusing further radiation &amp; chemo</td>
</tr>
</tbody>
</table>

ACA = anterior cerebral artery; chemo = chemotherapy; Dx = diagnosis; FU = follow-up; MCA = middle cerebral artery; PCA = posterior cerebral artery.
cells. After the metastatic cells have traveled to the site of the stroke-induced injury, the elevated levels of VEGF can encourage angiogenesis and the development of new blood vessels. This procedure may pave the way for metastatic cells to settle into a new environment with an adequate blood supply and proliferate after an injury. Additionally, BDNF is a neurotrophic factor that promotes the growth, survival, and maintenance of neurons in the brain. After a stroke, the lack of oxygen and nutrients causes damage to the brain's neurons and cell death. In this situation, the neural survival- and regeneration-promoting BDNF is secreted. Inadvertently, though, more BDNF could help metastatic cells live and multiply. Different types of cells, including cancer cells, can rely on BDNF for survival. For this reason, it is possible that the increased BDNF levels at the site of a stroke-induced injury provide a favorable environment for metastatic cells to survive and proliferate.24

Metastatic melanoma refers to the spread of primary melanoma cells to distant organs such as the lymph nodes, lungs, liver, brain, and bones.25 Metastatic melanoma has a poor prognosis. Only 10% of patients are expected to live for 5 years, and the prognosis is worse for distant metastases than for local spread. Metastasis locations include the skin, lungs, liver, and central nervous system. The prognosis could be impacted by where clinical metastases are found.25

Staging is done in accordance with the recommendations of the American Joint Committee on Cancer after clinical findings and histopathologic confirmation of a melanoma diagnosis.25 CT or positron emission tomography (PET) scans can be used to check for metastases. Radiodense areas can be seen on a CT scan of subcutaneous tissue, which contrasts sharply with radiolucent fat. A PET scan is more reliable than a CT scan for identifying metastases to the subcutaneous tissue and determining lymph node involvement.16 Both CT and MRI were performed in our patient. The second most frequent cause of mortality from metastatic melanoma is CNS involvement. Patients with BMs from melanoma bleed.14 MRI with contrast is more beneficial than CT because of its remarkable ability to identify acute, chronic, and subacute hematomas. Additionally, when imaging the spinal cord, meninges, and brainstem, MRI is more sensitive.14 In our case under consideration, MRI of the brain (Fig. 2) indicated a hemorrhagic metastasis.

Surgical removal of the tumor, either through broad excision or Mohs micrographic surgery, is the only proven treatment for primary melanoma.27 Whole-brain radiation therapy can be used as either the primary treatment for individuals with BMs or as an adjuvant treatment following resection.28 The metastases in our patient were subsequently resected via craniectomy. The histology report confirmed the presence of metastases.

Lessons
Our study is limited in that it is based on only a case report; however, we did perform histological confirmation of the BMs. Despite this limitation, our finding of metastatic tumors solely in the regions of previous cerebral infarctions is consistent with both the seed and soil concept and the notion that infarcted tissue could serve as a metastatic habitat. BMs can also be considered in addition to recurrence when individuals with ischemic stroke and concomitant malignancy like melanoma have new localized neurological deficits.

With this knowledge, we can manage these patients more effectively by imaging them frequently to detect any new BMs or recurrences. This is particularly important for younger stroke patients, who may be at greater risk of developing these complications. In conclusion, it is crucial to recognize the link between ischemic stroke and BMs so that we can provide optimal treatment for these patients.

References


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

Author Contributions
Conception and design: Atallah. Acquisition of data: Atallah. Analysis and interpretation of data: both authors. Drafting the article: both authors. Critically revising the article: both authors. Reviewed submitted version of manuscript: both authors. Approved the final version of the manuscript on behalf of both authors: Chaurasia. Administrative/technical/material support: Atallah. Study supervision: both authors.

Correspondence
Bipin Chaurasia: Neurosurgery Clinic, Birgunj, Nepal. trozexa@gmail.com.