

Metastatic Brain Tumor: A Case with Diagnostic Dilemma

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Metastatic brain tumor was first reported by Buchholz in 1898.¹ These tumors are neoplasms that originate in tissues outside the central nervous system and spread secondarily to the brain. In epidemiological studies, the annual incidence of brain metastasis is 11.1 per 100000 population.¹ In neurosurgical series, metastases may comprise from 14 to 22% of intracranial tumors.³ The lung is the primary site of approximately 70% of cancers that initially present with symptomatic brain metastases.² Clinical and autopsy data demonstrate that approximately half (50%) of the patients with unknown primary tumor have bronchial carcinoma as the primary source.³ Immunohistochemistry is helpful to establish the source of secondary deposits, particularly if the primary tumour has not yet been established.³

Metastatic brain tumor is a disease of elderly people. However, we report a case of occipital lobe metastasis from a primary lesion in lungs in a non-smoker young man who presented with headache and diminution of vision. The patient did not have any signs and symptoms regarding the lung disease. Though radiological diagnosis was tuberculoma and intraoperative diagnosis was meningioma, final histological evaluation suggested germinoma. Immunohistochemical evaluation suggested metastatic brain tumor from lung.

Reevaluation of patient was done clinically and radiologically. An enlarged supraclavicular lymphnode was found, the biopsy report of which suggested adenocarcinoma. Chest X ray showed a coin lesion in the right upper zone.

The diagnosis was reached retrospectively by immunohistochemistry and a search of primary focus after the former results arrived.

We had to overcome a lot of diagnostic hurdles that have been elaborated in the present case presentation.

Key words: brain metastasis, immunohistochemistry, lung cancer

Although the treatment of metastatic brain cancer results in a median survival of only three to six months, it does help to improve the quality of the remaining life of 70 – 80% of the patients and thus requires thoughtful planning.⁴

Case presentation

A 23 year old farmer from Morang came to the neurosurgical outpatient clinic with the chief complaint of headache and blurring of vision, the duration of both being about two to three months. However, he had no complaints regarding the respiratory system such as cough, breathlessness or chest pain.

On examination, his general condition was fair with stable vitals. He had normal higher mental function. However, his visual acuity from right and left eyes were 6/

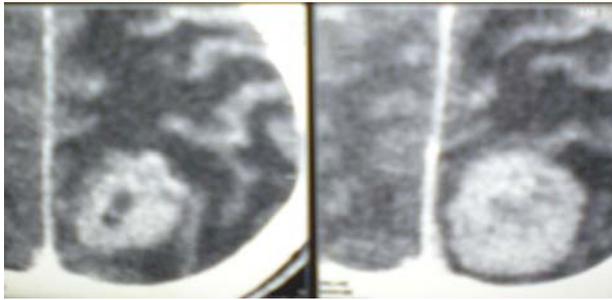


Figure 1. Computed tomography scan, contrast enhanced image, showing enhanced mass lesion with small cystic region in the centre with significant perifocal cerebral edema on left parietooccipital region.

12 and 6/36 respectively. Moreover, he had papilloedema bilaterally. He had no other focal neurological deficits or meningism.

Laboratory investigations were normal. However, perimetry showed enlarged blind spots suggesting homonymous hemianopia. Chest X-ray was reported as unremarkable. Computed tomography (CT) of head showed 3.5 x 3.5 cm left occipital enhancing mass (**Figure 1**). The mass had central cystic area with perifocal edema. Surgery was performed with preoperative provisional diagnosis of tuberculoma.

Left occipital craniotomy and excision of the mass was accomplished. The mass was well demarcated but was vascular. Thus the intraoperative diagnosis of meningioma was made excluding the possibility of tuberculoma. However, the pathologists reported it as germinoma (**Figure 2**). There was great confusion in the diagnosis, clinically, radiologically and histopathologically.

In the mean time the tissue sample was sent for immunohistochemical evaluation. Pancytokeratin was positive while placental alkaline phosphatase (PLAP) was negative. Thus, immunohistochemistry favored metastatic carcinoma of epithelial origin. Hence the patient was summoned and primary tumour was searched. Left supraclavicular lymph node was found to be enlarged and it was biopsied. Moderately differentiated adenocarcinoma was the histology report (**Figure 3**). The chest X-ray that was reported previously as unremarkable was reviewed and a coin lesion was found to be present in right upper zone. Hence, the working diagnosis was made- cerebral metastasis with primary adenocarcinoma of lung.

Discussion

Metastatic brain tumors are the most common in fifth to seventh decade of life.

Only six to eight percent of patients with cerebral metastasis are children and young adults. Secondary tumor may develop from any primary systemic cancer, but specific tumors and /or sites have a predilection for the brain. The most common primary sites include the

lungs (35-64%), breast (14-18%), skin (4-21%), kidneys and colon (5-9%) and unknown primary origin (5-11%) of the cases. In other words, the lung is the primary site of approximately 70% of the cancers that initially present with symptomatic brain metastasis.

Clinical and autopsy data demonstrate that approximately half (50%) of the patients with unknown primary tumor have bronchial carcinoma as the primary source. The incidence of the metastases also varies according to the histological type of the primary neoplasm: adenocarcinoma and small cell carcinoma of the lungs metastasize to the brain more commonly than squamous cell and large cell carcinoma.

The great majority of brain metastasis is of hematogenous origin, through the arterial circulation. The brain metastasis occur approximately 80% in cerebral hemispheres, 10-15% in the cerebellum and 2-3% in the brainstem. Frontal and parietal lobes are more frequently involved than the temporal and occipital lobes.

Adenocarcinoma is the most common histological subtype in women and non smokers. It invades lymphatic and blood vessels relatively early in their natural history though it is a slow growing cancer. So, the patients with adenoarcinoma have poorer survival than squamous cell carcinoma.⁶

Immunohistochemistry is useful to establish the source of secondary deposits, particularly if the primary tumor has not yet been established. Cytokeratins (ck7 and 20) are positive in cancers of epithelial origin whereas PLAP is positive in cancer of germ cell origin tumors. ck7 has 100% sensitivity in lung cancer especially adenocarcinoma.³ Since ck7 was positive and PLAP was negative in the present case, we finally made the diagnosis of metastatic brain tumor secondary to adenocarcinoma of lung.

The prognosis of patient with brain metastasis is poor, with median survival typically less than one year.³ A recent large series of 1292 patients reported as overall median survival time of 3.4 months, with only four percent of patients alive at two years after the diagnosis of brain metastasis.²

The aim of therapy is palliative and qualitative prolongation of life. Radiation therapy oncology group (RTOG) in 1980 defined the prognostic factors in patients with brain metastasis. They are: Karnofsky Performance Score more than 70, controlled primary lesion, age less than 60 years and metastasis limited to brain. In terms of improved symptoms, (published) response rate ranges from 70-90%. Combined surgery of isolated metastasis and whole brain radiotherapy (WBRT) appear to prolong survival and decrease neurological morbidity.⁵ Multiple randomized trials have also proved that WBRT with or without surgery is effective and prolongs the survival from weeks to at least 4 months.

The median survival time for untreated patients with brain metastasis is about four weeks, while with doses of

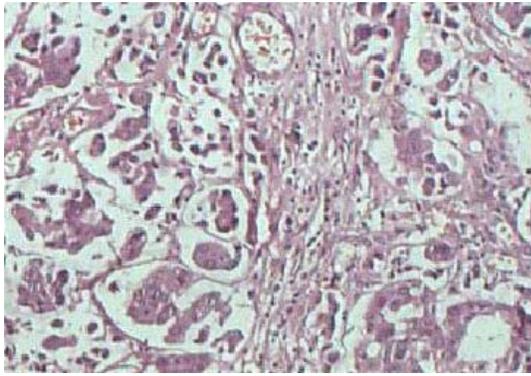


Figure 2. Histological picture showing the histology of brain tumor.

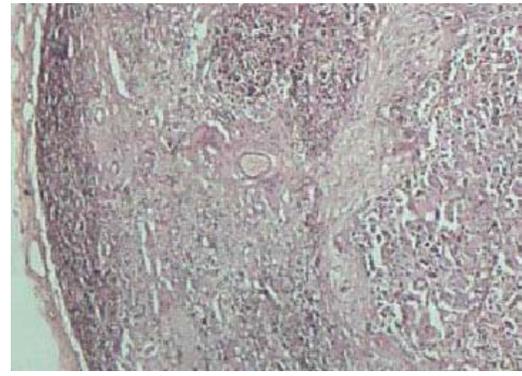


Figure 3. Histological picture showing histology of lymph node.

30 to 50 gray in 3 to 5 weeks, overall median survival of four to six months is seen with symptomatic improvement in 60-80% of patients.⁴

Most of primary tumors metastasizing to the brain tend to be chemoresistant. In 1954 Chao and coworkers were first to report WBRT for brain metastasis. Patients younger than 60 years had a higher frequency of brain metastasis than older patients. Patients with initial performance status above 60% and patients responding to chemotherapy had higher risk for developing brain metastasis during treatment than other patients.

Surgical excision is usually indicated in cases of solitary and sub cortical brain lesion with localized stage I lung tumor, non small cell lung cell carcinoma (NSCLC) (less than 3 cm without nodal involvement).

Radiosurgery namely gamma knife radiosurgery (GKS) is another option especially in cases of cerebral lesion smaller than 3cm in size. Overall median survival time after radiosurgery is about 15 months from the diagnosis of brain metastasis. The GKS offers effective local tumor control.

Although chemotherapy is a reasonable option for many patients in advanced adenocarcinoma of lung, it is not the choice in case of NSCLC as most of them are relatively chemo resistant. However, it can be offered to patients with good performance scale and without significant weight loss. Several studies on chemotherapy for metastatic brain tumor have shown beneficial effect. With the advent of newer chemotherapeutic agents like Temozolamide and implantable gliadel wafer, there is some hope for patients with brain metastasis.

Conclusion

Metastatic brain tumors are rare in children and young adults. If they are afflicted by this condition a diagnostic dilemma can be encountered. Immunohistochemistry, if

available, seems to be helpful in clinching a diagnosis. With all the modern diagnostic tools at hand, a good history and clinical examination are fundamental.

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