ORIGINAL RESEARCH PAPER

Volume-7 | Issue-11 | November-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

CENTRAL NERVOUS SYSTEM MANIFESTATIONS OF SYSTEMIC MALIGNANCY IN A TERTIARY HOSPITAL

Neurology

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ABSTRACT

Background - Neurologic complications occur frequently in patients with systemic cancer. Index of suspiscion for diagnosis of these complications should be high as they present with similar neurological symptoms and signs as other neurological disorders.

Objectives - To study the various central nervous system (CNS) manifestations in patients with systemic malignancy.

Methodology: A total of 54 cancer patients who presented with CNS manifestations were included in the study from February 2015 to January 2018.

Results - The most common malignancy with CNS manifestations is lung carcinoma followed by haematological malignancy.

Conclusion – Neurologic complications occur frequently in patients with cancer. Spinal cord metastases are more common compared to cerebral metastases. The index of suspicion should be high which can lead to early diagnosis.

KEYWORDS

Central nervous system (CNS) metastases, Epidural spinal cord compression (ESCC), posterior reversible leucoencephalopathy (PRES).

INTRODUCTION

Neurological complications occur frequently in patients with systemic malignancy. The incidence is on the rise partly due to improved treatment options for cancer patients, thereby increasing their survival period, and partly because of the better diagnostic tools available for detection of systemic metastasis. These complications can involve any part of the neuraxis – central or peripheral nervous system. Brain metastases are the most common neurological complication of systemic cancer [1]. The most frequently implicated tumors are those from the lung, breast, colon, rectum, prostate gland, head and neck, as well as haematological malignancies like leukemia and lymphoma 2. Neurological complications can manifest in two ways - a patient with known systemic cancer presents with neurological symptoms and signs or a patient without known cancer has a neurological disorder caused by an undiagnosed cancer3. Systemic cancer can directly involve central nervous system(CNS) in the form of brain metastases, epidural spinal cord compression and leptomeningeal metastases. Indirect effects of systemic cancer include vascular disorders, infections, metabolic abnormalities and paraneoplastic syndromes. Here, we describe the details of cancer patients with central nervous system(CNS) manifestations referred to our hospital from February 2015 to January 2018.

PATIENTS & METHODS

All patients with systemic cancer, presenting with neurological symptoms who were referred from cancer hospital were included in the study. Few patients who presented with neurological symptoms and on evaluation found to be metastatic lesions were also included in the study. The study period was from February 2015 to January 2018. Demographic details, details of the systemic cancer, presenting neurological problem were noted. Further, patients were examined and advised investigations if necessary, details of which were noted on follow up.

RESULTS

A total of 54 patients were included in the study. 2 patients presented with neurological symptoms, who on evaluation were found to have cerebral metastases. 31 patients were males and 23 were females. Of the 54 patients, 23 had spinal cord metastases and 21 patients had cerebral metastases, and rest of the 10 patients had indirect effects like infections, vascular and paraneoplastic manifestations. Spinal cord metastases were more common accounting for 43% of the total patients. Out of the 10 patients who had indirect effects, 3 patients had stroke, 2 had tuberculomas, 1 patient had Posterior Reversible Encephalopathy Syndrome (PRES), 2 patients had paraneoplastic cerebellar syndrome, 1 patient had cough syncope and 1 had tuberous sclerosis. Carcinoma lung was the commonest systemic malignancy to present with neurological illness followed by haematological malignancies. Breast carcinoma accounted for only 9.2% of the cases. Most common presenting symptom was headache of raised intracranial pressure, followed by back pain. MRI was diagnostic in all patients with metastatic disease. The unusual manifestations included – dystonic seizures, cough syncope with seizures. One patient had involvement of Central Nervous System (acute transverse myelitis), followed by Periphral Nervous System (CIDP).

DISCUSSION

Brain metastases are the most common neurological complication of systemic cancer in adults4. In the United States, these metastases occur in 20 to 40 percent of cancer patients who are over 20 years of age5. Epidural spinal cord compression (ESCC), the most dreaded sequela of spinal column metastasis, is relatively common, occurring in 5 to 14 percent of patients with systemic cancer6,7. In the present series, spinal cord metastases(43%) were more common than brain metastases (39%). This is in contrast to the previous studies which have shown brain metastasis as more frequent compared to spinal cord metastasis8. In adults, metastases to the brain most commonly arise from primary tumors of the lung (50–60%), breast (15–20%),skin (melanoma) [5–10%], and gastrointestinal (GI) tract (4–6%)9,10. In our series, lung cancer accounted for 66% of brain metastasis, whereas breast cancer was the cause in only 5% of brain metastasis i.e., breast cancer was less common compared to previous studies. This might be the reason for brain metastasis being less frequent than spinal cord metastasis. As in other studies, lung cancer was the most common systemic cancer to cause neurological complications. CNS metastases were more common in males compared to females, which is also consistent with previous studies.

Of the brain metastasis, carcinoma lung accounted for most cases i.e., 66% of the brain metastases (Table 1). This is similar to previous studies11. Most common presentation was headache associated with vomiting, which is also consistent with previous studies12. Seizure was the next most common neurological manifestation after headache. Focal weakness, which is commonly reported as manifestation of brain metastasis was noted in only 7.4% of patients in this series. Other manifestations which were noted are dyarthria, cerebellar ataxia, cough syncope associated with seizures and episodic dystonia. The patient with cough syncope had primary lung cancer with severe bouts of cough followed by seizures. Another patient with basal ganglia metastasis presented with episodic dystonia involving right upperlimb and right face. Two patients of ovarian carcinoma presented with cerebellar ataxia. MRI did not show any metatstasis and CSF was negative for malignant cytology, therefore were labelled as paraneoplastic cerebellar ataxia syndrome. CT scan and MRI (Figures 1& 2) are highly sensitive for detecting brain metastasis,13 and were diagnostic in 95% of the patients in this series.

Table 1 : Primary sites of brain metastases

Primary systemic cancer	Percentage of patients
lung	66.6
breast	4.7
haematological	19
Renal	4.7
oesophagus	4.7

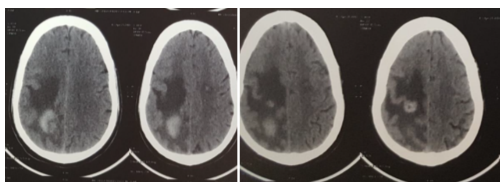

Figure 1 CT brain(plain) showing haemorrhagic cerebral metastases in a patient with denovo detected Renal Cell Carcinoma

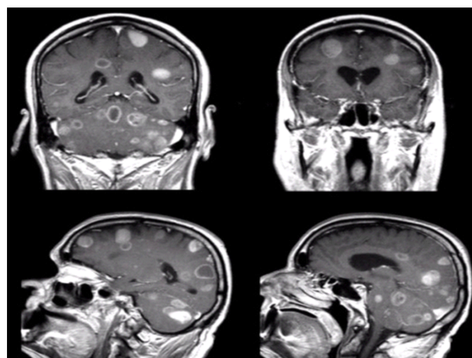

Figure 2 MRI brain gadolinium enhanced T1W images showing cerebral metastases in a patient with carcinoma lung.

Of the spinal cord metastasis (Table 2), most of them were from carcinoma lung (23%). Metastasis from breast, stomach and prostate accounted for 18% each. Less common systemic cancers which gave rise to vertebral metatstases included Multiple Myeloma, Acute Lymphoblastic Leukemia(ALL), pancreatic and cervical cancers. Most of the metastasis involved dorsal vertebrae (55%), followed by lumbar (32%) and cervical (13%). Dorsal vetrbrae were the most commonly involved ones in metastatic spinal cord disease, similar to previous studies14. Back pain was the commonest presenting symptom, occuring in 86% of the patients. Most patients had localised back pain with spine tenderness. According to previous studies, in 95% of the adults and 83% of children, initial symptom of metastatic epidural compression was progressive axial, radicular pain15. Only 6 patients(26%) had either paraparesis or quadriparesis. All patients had vertebral metastasis on MRI spine. In previous studies also, contrast enhanced MRI was superior to other diagnostic modalities for diagnosis of spinal cord metastasis 16. Therefore, all cancer patients with back pain should undergo imaging, which can lead to early detection of spinal metastasis.

Table 2 : Primary sites of spinal cord metastases

Primary systemic cancer	Percentage of patients
lung	21.7%
breast	17.4%
prostate	17.4%
gastric	17.4%
haematological	4.3%
renal	4.3%
pancreas	4.3%
cervix	4.3%
Multiple myeloma	4.3%

Of the 54 patients, 6 patients presented with cerebrovascular complications, which accounted for 11% of the neurological complications of systemic cancer in our series. Cerebrovascular lesions constitute approximately 15 percent of all cancer patients17.Of the 6 patients, 4 had Acute Lymphoblastic Leukemia(ALL), of which 2 patients had coagulopathy, resulting in cerebral venous thrombosis in one patient and subarachnoid haemorrhage (SAH) in another. Cerebrovascular disease in cancer patients can be caused by a tumor directly compressing or invading blood vessels, tumor-induced coagulation disorders (hemorrhagic and thrombotic) or treatment-related injury to blood vessels18. One patient with ALL presented with headache, blurring of vision and seizures and multiple T2 flair posterior subcortical hyperintensities on MRI brain and was diagnosed as posterior reversible leucoencephalopathy (PRES). PRES in a child with leukaemia is usually secondary to intrathecal chemotherapeutic agents19. One patient with lung cancer and another with breast cancer presented with acute strokes.

Other uncommon manifestations in this series included cough syncope causing seizures in a patient with lung cancer, episodic dystonic seizures secondary to basal ganglia metastasis in a lung cancer patient and paraneoplastic cerebellar ataxia in two patients with ovarian cancer. Cough syncope as a manifestation of lung cancer is well described20, but cough syncope causing seizures is rarely described.

Neurologic complications occur frequently in patients with cancer. Manifestations are diverse, ranging from to simple headache to complex encephalopathy or myelopathy. Central nervous system complications are more common compared to peripheral nervous system complications. Most brain and spinal cord metastasis result from carcinoma lung, breast, prostate, haematological malignancies and gastric carcinoma. Direct involvement of the central nervous system includes brain metastases, epidural spinal cord compression and leptomeningeal metastases. Indirect effects of systemic cancer include vascular disorders, infections, metabolic abnormalities and paraneoplastic syndromes. The index of suspicion should be high and the aim is early diagnosis which can lead to better treatment and prolonged survival.

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