

the symptoms are non-specific with headache being the most common presenting symptom, but brain metastases should be suspected in all melanoma patients with new neurological findings.⁷ Mean time interval between the initial diagnosis of melanoma and development of first symptoms of CNS metastases is 3.5 years.⁸ Relentless progression of clinical signs and symptoms is seen in most patients once they present with evidence of CNS disease.

Metastases reach CNS via hematogenous spread of tumor cells. Tumor cells are released into the circulation, arrest in end arteries, penetrate the blood-brain barrier, enter CNS, and establish growth in the new tissue. Neurotrophins can facilitate invasion by upregulating enzymes such as heparanase (HPSE), which destroy the extracellular matrix and basement membrane of the blood-brain barrier. Although initial metastatic foci involve the gray-white matter junction, any part of the brain can be involved, including the pituitary gland, cerebellum, and cerebral hemispheres.⁹ The tumors most often are multifocal and have a unique tendency to hemorrhage. Metastases from melanomas can be classified based on size in order to assess the clinical course of the disease and predict response to treatment: smaller than 1cm (group A), between 1 and 4cm (group B), and bigger than 4cm (group C). Group B lesions are the most common, independent of the site of primary tumor, except for patients with rectal melanoma. Group C metastases are the least common and are usually solitary. Asymptomatic patients usually have group A metastases, whereas those with nonspecific complaints or behavioural changes usually have group B metastases. Solitary lesions usually belong to groups B or C, whereas multiple lesions belong mainly to groups A or B.¹⁰

Although primary diagnosis may rely on computed tomography scan, magnetic resonance images are usually used in order to study the characteristics of the lesions more precisely. Despite of advances in therapeutic options, prognosis for patients with melanoma brain metastases remains poor with a median survival time of six months after diagnosis.⁶ Patients with suspected brain metastases should not only undergo imaging studies of CNS but also of other systems to determine whether other organ involvement exists, as this will influence management. The poor prognostic factors for CNS melanoma are more tumor thickness, ulceration, increased tumor vascularity, lymphovascular invasion, presence of micrometastases, and concomitant visceral disease. High mitotic index and lack of tumor-infiltrating lymphocytes may also portend a poor prognosis. Depending on the clinical presentation, treatment options include surgical resection, whole-brain radiation therapy, stereotactic radiosurgery and systemic therapy.¹¹ Metastatic melanoma to the CNS is incurable. Treatment is aimed at tumor debulking, symptom relief, and palliation. Patients with solitary brain metastases, no lung or visceral metastases, and patients whose brain metastases