Management of Brain Metastases: Distinctive Features in the Elderly

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12.1 Generalities

Metastases represent the majority of brain tumors in the elderly. Up to 25 % of elderly patients dying of cancer harbor one or more brain metastases at autopsy. Despite recent advances in chemotherapy, targeted treatments, and radiotherapy including radiosurgery, median survival remains poor usually ranging from 3 to 6 months in average as does the functional outcome. The most frequent sources of brain metastases in the elderly are the respiratory tract cancer, particularly small-cell cancer, and breast cancer. Melanoma is also a common provider of brain metastasis in the elderly, representing 10 % of all brain metastases. Almost 40 % of patients with melanoma have brain metastases at autopsy (Figs 12.1 – 12.6) [1, 2].

Obviously, the incidence of brain metastases in the elderly is increasing secondary to several factors. Firstly the widespread use of brain imaging either CT scan or MRI allows precocious diagnosis even in asymptomatic patients. Secondly, a longer survival of patients with cancer in general provides enough time to develop brain dissemination. Finally, the absence of chemotherapy drugs that penetrates efficiently the blood–brain barrier which still leaves the brain as a therapeutic sanctuary for chemotherapy [3].

In about 10 % of elderly patients presenting with brain metastases, the primary neoplasm remains untraceable despite exhaustive explorations. The preferential location is the cortico–subcortical junction with a clear majority of supratentorial locations (90 %) versus infratentorial ones (10 %).

In contrast with younger patients whom usually present with intracranial hypertension signs and/or seizures, elderly patients with brain metastases commonly

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suffer from more insidious symptoms such as cognitive changes and progressive focal deficits [4, 5]. In some cases, the clinical presentation can even be acute pseudovascular either secondary to intra-tumoral hemorrhage or to post-seizure motor deficit, leading to misdiagnoses of stroke. About one third of elderly patients with brain metastases will suffer from seizures during the course of their disease, particularly those harboring hemorrhagic metastases (melanoma, kidney, and thyroid).

12.2 Management in the Elderly

In the majority of cases, there is a relatively large amount of peri-tumoral edema that can be more threatening than the metastasis itself. The benefic role of corticosteroids has been clearly proven, reducing the signs of intracranial hypertension and usually improving neurological deficits. In the elderly, the use of high doses of corticosteroids should be closely monitored to prevent and timely detect specific complications such as diabetes mellitus, gastroduodenal ulcerations, and venous thrombosis. Roughly one third of elderly patients with brain metastases will have seizures during the course of their disease, reaching even 50% in hemorrhagic lesions or melanoma metastases, and therefore may require anticonvulsant therapy. This latter should not be systematic and prescribed only in cases of proven seizures because of the risk of interference with chemotherapy agents and may even cause complications (psychiatric morbidity, allergy, etc.). The doses should be rigorously adapted to the renal function.

12.3 Role of Neurosurgery

Neurosurgery can be useful in life-threatening solitary brain metastases (temporal lobe and cerebellar locations) or in hemorrhagic cases. Surgery can be helpful as well if a histopathological proof is needed particularly when the primary cancer site is not known or when there is a doubt with different brain expansive lesions (glioma, lymphoma, granuloma, etc.). Besides, the surgical resection can be very effective in large cerebellar metastases obstructing the cerebrospinal fluid flow and causing tonsillar herniation as it offers the possibility to the patient to better tolerate radiation therapy. Obviously, the surgical option should be considered only after a multidisciplinary discussion with the oncologist, the radiotherapist, the neurosurgeon, and the patient with his family as well taking into account the systemic control of the cancer and the estimated global survival. In these cases, a complete surgical resection appears to prolong survival and enhance the neurological functional outcome even in the era of radiosurgery [6]. The main keyword remains the appropriate multidisciplinary selection of the patients. In very selected cases, there is even a place to surgical resection in multiple brain metastases when one of these is life-threatening (especially for posterior fossa).

All adjuncts usually used in young adults can be used in the surgical treatment of brain metastases in the elderly: neuronavigation, cortical and subcortical stimulations, and awake surgery. The preoperative anesthetic preparation should mandatorily include cardiovascular and pulmonary assessments.

12.4 Role of Radiotherapy and Radiosurgery

Whole brain radiotherapy (WBRT) has been widely used during decades, prolonging survival but does not appear to be superior to surgical resection. Commonly 20–30 grays are delivered to the whole brain (with or without hippocampus sparing [7]) in 10–15 fractions. The number of fractions can be tailored to the status of the elderly patient, with an accelerated schema allowing very fragile old patients to better endure the radiation [8].

Stereotactic radiosurgery (SRS) is being increasingly used as an alternative to whole brain radiotherapy as it is supposed to have less toxicity particularly in elderly patients [2–4, 9] while it provides a local control of the disease. The neurotoxicity of radiation therapy may impact significantly the quality of life and the cognitive status in this elderly group of patients while their survival is prolonged with chemotherapies. Indeed, after 6–12 months following radiotherapy, elderly patients are exposed to radiation encephalopathy with subsequently subcortical dementia, gait disturbances, and urinary dysfunction mimicking chronic hydrocephalus and considerably altering the quality of life [10]. Recent randomized studies comparing WBRT plus SRS and SRS alone in patients harboring one to four brain metastases did not show significant differences in terms of survival, frequency of neurological deaths, and preservation of neurological status [11]. However, SRS appears to provide a local control while preserving the performance status and limiting the risk of radiation encephalopathy [12]. In fine, SRS alone may be considered in elderly patients having less than three to four metastases inferior to 3 cm of diameter either as an alternative or as an adjunct to WBRT.

Key Points

- The prognosis of elderly patients with brain metastases depends upon their performance status (Karnofsky Performance Score superior to 60) and the control of the extracranial cancer disease
- SRS should be considered in oligometastatic patients (one to four metastases) as an alternative or as an adjunct to classical WBRT. SRS alone is susceptible to preserve learning and memory functions when compared to SRS plus WBRT [13].
- Neurosurgical resection should be systematically discussed in cases of a unique large metastasis amenable to resection without significant neurological risk.
- The management of elderly patients with brain metastases should consider the local control of the disease, the systemic one, and their performance status scale at mid- and long term as the global survival is being prolonged with the use of systemic targeted therapies and new chemotherapies (Figs. 12.1, 12.2, 12.3, 12.4, 12.5, and 12.6).

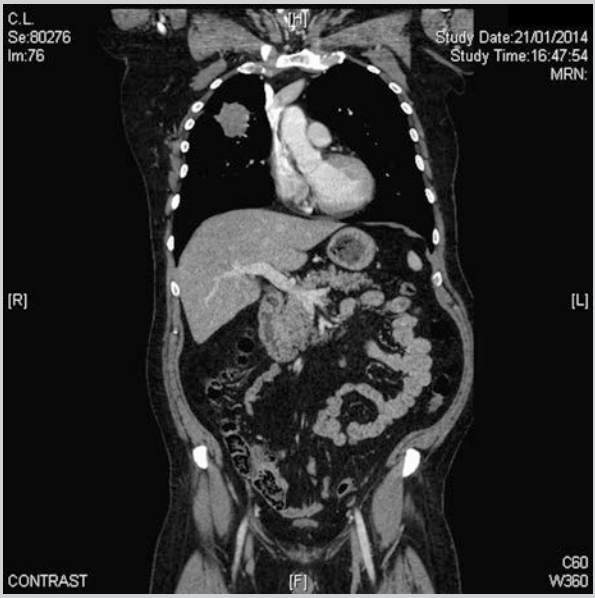

Fig. 12.1 Lung cancer is one of the most common provider of brain metastases particularly the small-cell cancer

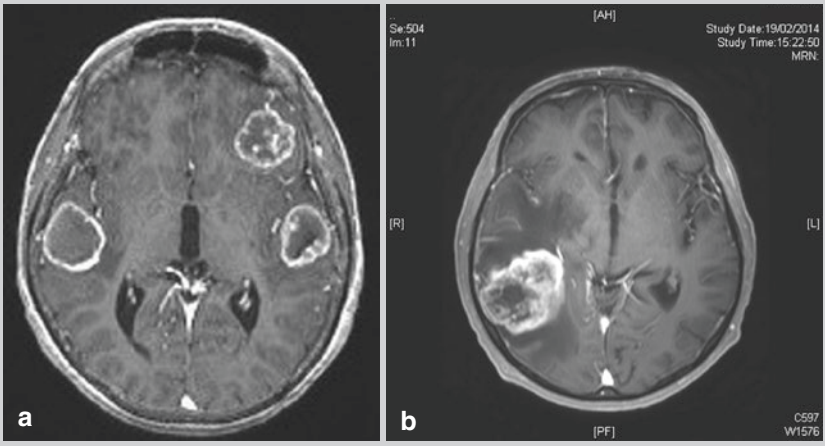

Fig. 12.2 Multiple brain metastases are not amenable to surgery except if there is a need for histological proof (**a**), while neurosurgical resection remains a good option for large unique metastasis (**b**)

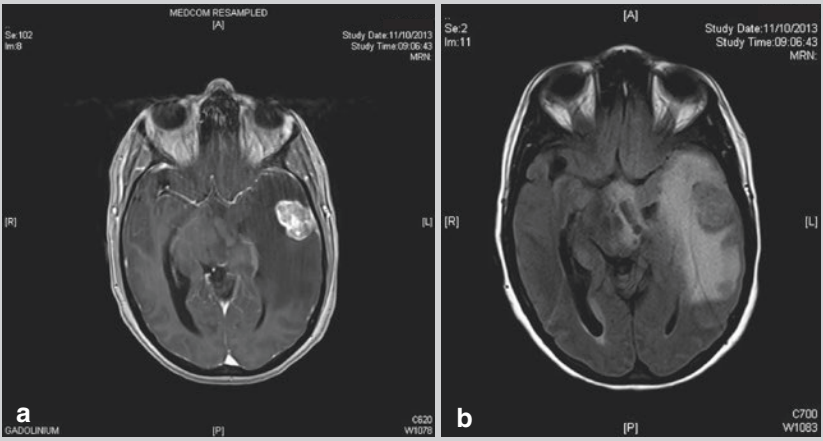

Fig. 12.3 Left temporal lobe unique metastasis (kidney cancer) (**a**) with a very extensive life-threatening edema (**b**)

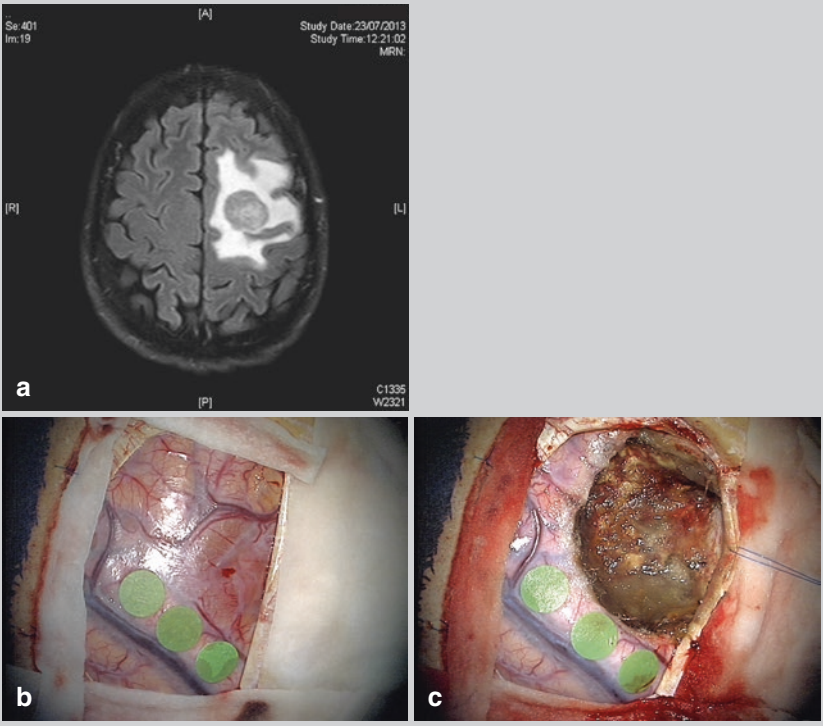

Fig. 12.4 Rolandic left metastasis with extensive edema without primitive cancer identified (**a**), requiring therefore surgical resection with an awake technique and cortical stimulation to identify the motor cortex (*green pastilles*) (**b**) allowing total removal without neurological deficit (**c**)

Fig. 12.5 Cerebellar life-threatening unique metastasis optimal for surgical resection because of tonsillar herniation

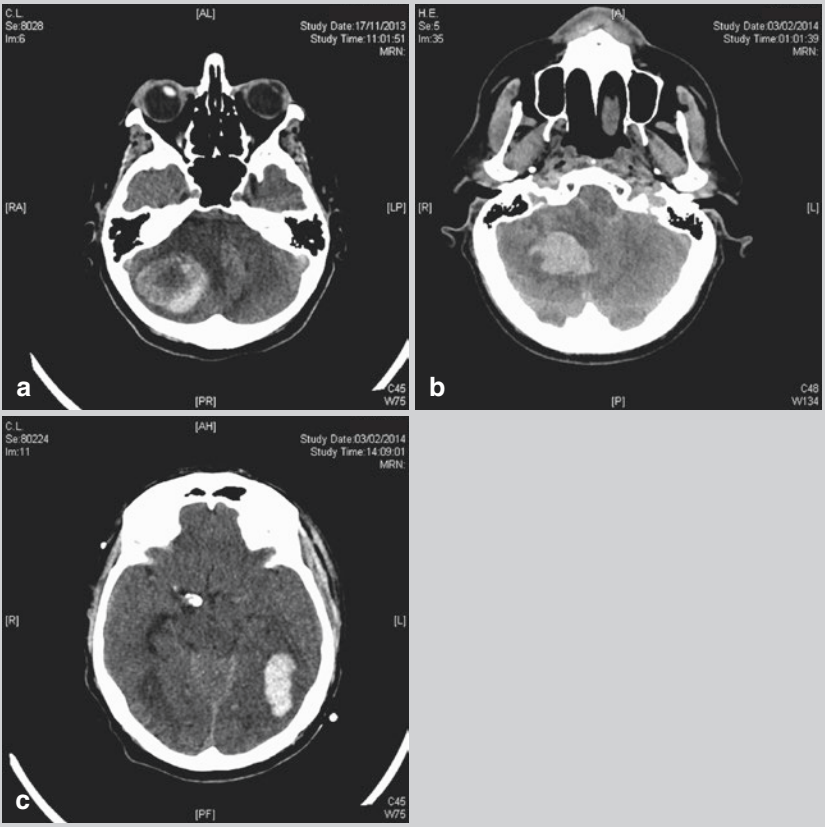

Fig. 12.6 Examples of brain metastases revealed in an acute pseudo-stroke presentation revealing melanoma (**a**), kidney (**b**), and thyroid (**c**) cancers

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