

Current Epidemiology of Intracranial Metastases in Two University Teaching Reference Hospitals of the Town of Yaounde, Cameroon: Analysis of 35 Cases Recorded in the Neurosurgery Departments

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Abstract

Background: The incidence of intracranial metastases (ICMET) has been steadily rising, and its frequency with respect to primary brain tumours is relatively high. **Objective:** The objectives of this study were to elucidate the current epidemiology and describe the clinical, diagnostic and therapeutic features of ICMET in Yaounde. **Method and findings:** A descriptive cross-sectional study was done in the neurosurgery departments of the General and Central Hospitals of Yaounde during the period from January 2016 to December 2022. We included all medical booklets of patients admitted for a tumoral intracranial expansive process with our target population being patients with histological evidence of ICMET, and did a retrospective inclusion of data using a pre-established technical form aimed at collecting sociodemographic data, clinical data, paraclinical data, and the treatment procedures. Analysis was done using the SPSS statistical software. A total of 614 cases of intracranial tumors were included among whom 35 presented histological evidence of ICMET. This gives a frequency of 5.7%. The sex ratio was 0.94, the mean age was 55.68 +/- 14.4 years, extremes 28 and 86 years and the age range 50 - 59 was affected in 28.57% of cases. The clinical presentation in-

cluded signs of raised intracranial pressure (headache, blurred vision, vomiting) in 26 cases (74.3%), motor deficit 48.6%, seizures 17.1%. The mode of onset was metachronous in 71.4% and synchronous in 28.6%. The imaging techniques were cerebral CT scan in 82.9%, cerebral MRI in 40%, TAP scan in 22.9%. The metastatic lesions were supratentorial in 94.3% and single in 62.9%. The primary cancers found were breast cancer (31.4%), lung cancer (25.7%), prostate cancer (17.1%), thyroid cancer (5.7%), colon cancer (2.9%), and melanoma (2.9%). The therapeutic modalities were total resection (68.6%), radiotherapy (37.1%). **Conclusion:** Intracranial metastases are relatively frequent. There is a female sex predominance and the age group 50 - 59 years is the most affected. Brain metastases mostly occur in patients with a history of known primary tumor. The clinical signs mainly include signs of raised intracranial pressure, motor deficit, seizures and mental confusion. Cerebral CT Scan is the main imaging technique used. Most of the lesions are single and supratentorially located. The primary cancers most represented include breast cancer, lung cancer and prostate cancer. Surgery is the main treatment procedure. The adjuvant treatment (radiotherapy, chemotherapy) was limited.

Keywords

Intracranial Metastases, Epidemiology, Yaounde

1. Introduction

Intracranial metastases (ICMET) occur when cancer cells spread from their original site to the brain and its surrounding structures within the cranium. Any cancer can spread to the brain but this mostly occurs with lung cancer, breast cancer, and melanoma [1] [2] [3]. ICMET are mainly located in the brain parenchyma and may form one or many tumors.

The incidence of intracranial metastases has been steadily rising as new therapeutics, advanced imaging, and improved screening have led to lengthened survival after primary diagnosis for cancer patients. They are the most common malignant adult intracranial tumors with a 3 - 5 times higher incidence than newly diagnosed primary malignant brain tumors each year. They occur in approximately 10% - 30% of cancer patients and generally lead to a poor prognosis. Estimates of the frequency vary significantly [2] [4] [5]. In the United States and Europe, its reported incidence ranges from 7.0 to 15.7 per 100,000 person years. In Korea, the incidence is 5.0 per 1000 person years among patients with cancer [6]. In Senegal, Dakar a study conducted in 2017 found a frequency of 2.9% [7]. In Cameroon, a study published in 2019 on cerebral tumors in the Yaounde Central Hospital revealed a frequency of 3.1% for ICMET with respect to intracranial tumors [8]

Intracranial metastases are most frequently diagnosed in patients with an es-

established primary site of malignancy (metachronous presentation). Intracranial metastases are symptomatic in 60% - 70% of patients with neurologic symptoms including headache (40% - 50%), focal neurological deficits (40%), and seizures (15% - 20%). As a general rule, brain metastases should be suspected in any patient with known systemic cancer in whom new neurologic findings develop [9]. In both asymptomatic and symptomatic patients, imaging of the brain has a primary role in the diagnosis and is important for subsequent patient management. Magnetic resonance imaging (MRI) with intravenous contrast is preferable for the greater sensitivity than computed tomography (CT), particularly for lesions in the posterior fossa or multiple punctuate metastases [10]. Apart from morphological analysis, the most effective tool for characterizing ICMET is immunohistochemistry. The choice of therapeutic approaches, both in clinical trials and daily practice is guided by natural prognostic factors (performance status, age, primary/systemic tumor activity, number of lesions). These approaches include surgery, stereotactic radiosurgery, radiotherapy, chemotherapy and targeted therapies [9].

The diagnosis and management of intracranial metastases has improved with the amelioration of diagnostic tools (immunohistochemistry and molecular biology). In our settings, we observe an increase in technical facilities in the neurosurgical field, neuroimager, and anatomopathology making studies on ICMET feasible. We then opted to elucidate the current epidemiology and changing trends in clinical, diagnostic and therapeutic features of ICMET in two reference hospitals of the town of Yaounde.

2. Methods

2.1. Sites of Study

This study took place in the neurosurgery departments of two University Teaching Reference Hospitals of the Town of Yaounde: the Yaounde General Hospital (YGH) and the Yaounde Central Hospital (YCH). These hospitals receive the majority of the neurosurgery cases in the Centre Region and numerous referred neurosurgery cases from the other regions of Cameroon.

2.2. The Yaounde General Hospital (YGH)

The YGH is a public institution created in 1988 by presidential decree N° 1921. It is a first category and 4th reference hospital that provides the Cameroonian population with first-class health care in the fields of general surgery and specialties, internal medicine, gynecology and obstetrics, anesthesia and resuscitation, cancerology, and anatomopathology. It is the center of excellence for Neurosurgery and Oncology in Cameroon. The neurosurgery department is headed by a Full Professor in neurosurgery assisted by an Associate Professor in neurosurgery and a neurosurgeon. It is the main training site for interns and residents of neurosurgery and has annual surgical activity of about 200 interventions.

2.3. The Yaounde Central Hospital (YCH)

The YCH is a second category and 3th reference hospital created in 1933. It is the first neurosurgery center in Cameroon and has a Hemato-oncology reference center. It provides patients with quality care via its various departments among which a neurosurgery department. This department is headed by a neurosurgeon. It has an annual surgical activity of about 200 interventions.

2.4. Type of Study

We conducted a retrospective and descriptive cross-sectional study of patients diagnosed with brain tumors at the neurosurgery departments of the General and Central Hospitals of Yaounde during a 7-year period, from January 2016 to December 2022.

2.5. Population of Study

Our population of study was made of up of the medical booklets of patients in the neurosurgery departments of the YGH and the YCH with diagnosis of intracranial tumours during the study period. The target population is medical booklets of patients with histopathological results confirming the existence of intracranial metastases (ICMET). 614 medical records of patients with intracranial tumors were reviewed within the framework of our study period and 35 presented evidence of ICMET. A simple and consecutive recruitment was done. Therefore, no formal sample size calculation was performed.

2.6. Procedure of Data Collection and Analysis

With the aid of a pre-established technical sheet, the following data were collected from the medical records of our target population: demographic features (age, gender), clinical features (mode of onset and clinical signs), investigations (brain computed tomography scan, brain magnetic resonance imaging, thoraco-abdominopelvic computed tomography scan), histological features (microscopy, immunohistochemistry), therapeutic features (surgical extirpation, radiotherapy, hormonotherapy). The data collected were entered and analysed using the statistical softwares SPSS version 20 and Microsoft Excel 2010.

2.7. Results

In our study, 614 medical records of patients with intracranial tumors were reviewed. 35 showed histological evidence of intracranial metastases. This gives a frequency of 5.7%.

2.8. Socio-Demographic Features

The mean age was 55.68 +/- 14.41 years. The age distribution was as follows (**Figure 1**). The modal age range was 50 - 59 representing 28.57%. The extremes were 28 and 86 years. There was a slight female predominance with a sex ratio of 0.94. 18 cases were females (51%) and 17 were males (49%) (**Figure 2**).

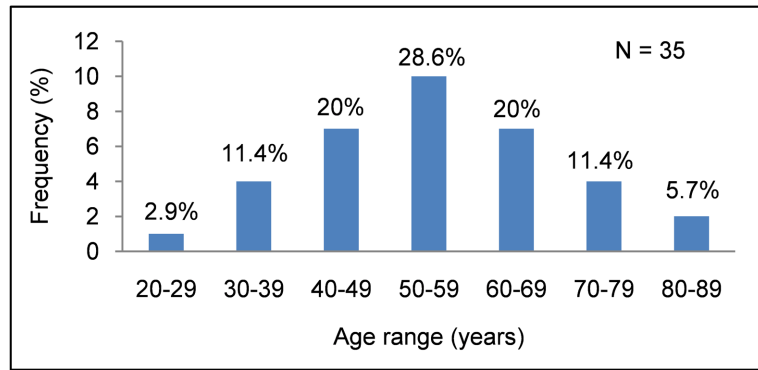


Figure 1. Age distribution of patients.

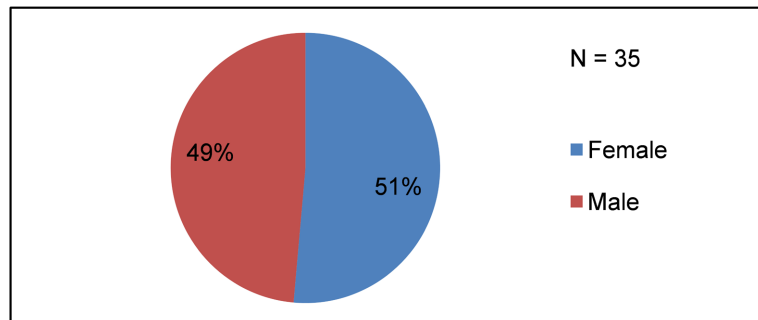


Figure 2. Sex distribution of patients.

2.9. Clinical Features

At the admission, 25 patients with intracranial metastases had a known primary cancer. These were breast cancer (9), lung cancer (7), prostate cancer (6), thyroid cancer (2) and melanoma (1) (**Table 1**). This onset was therefore metachronous in 25 cases (71.4%) and synchronous in 10 cases. Clinical signs got were: raised intracranial pressure (headache, blurred vision, vomiting) in 26 cases (74.3%), motor deficit in 17 (48.6%) of cases, seizures in 6 cases (17.1%), Mental confusion in 5 cases (14.3%), altered consciousness in 4 cases (11.4%), signs of meningeal irritation in 3 cases (8.6%), cognitive impairment in 3 cases (8.6%), difficulty speaking in 3 cases (8.6%), sleep disorders in 1 case (2.9%), cerebellar syndrome in 1 case (2.9%) (**Table 2**).

2.10. Paraclinical Features

Brain CT Scan alone was performed in 21 cases (60%), MRI alone in 6 cases (17.1%) and Brain CT + MRI in 8 (22.9%) of cases (**Figures 3-5**). In 33 cases, the lesions were located supratentorially (94.3%) and infratentorially in 2 cases (5.7%). The lesions were single in 22 cases (62.9%) and multiple in 13 cases (37.1%). The main associated lesions were perilesional oedema in 17 cases (48.6%), mass effect in 8 cases (22.9%) and herniation in 4 cases (11.4%) (**Table 3**). The investigations used for the extension analysis and the search of the primary cancer were TAP (Thoraco-abdomino-pelvic) Scan in 8 cases (22.9%), Chest X-ray 5 (14.3%), Prostate ultrasound 3 (8.6%) (**Table 4**).

Table 1. Distribution of patients according to history of known primary tumour at consultation.

Variable	Total number (N = 35)	Percentage (%)
Breast cancer	9	25.7
Lung cancer	7	20
Prostate cancer	6	17.1
Thyroid cancer	2	5.7
Melanoma	1	2.9
Unknown	10	28.6

Table 2. Distribution of patients according to the clinical signs.

Variable	Total number (N = 35)	Percentage (%)
Raised intracranial pressure	26	74.3
Motor deficit	17	48.6
Seizures	6	17.1
Mental confusion	5	14.3
Altered consciousness	4	11.4
Signs of meningeal irritation	3	8.6
Difficulty speaking	3	8.6
Cognitive impairment	3	8.6
Sleep disorders	1	2.9
Cerebellar syndrome	1	2.9

Table 3. Distribution of patients according to the associated lesions

Variable	Total number (N = 35)	Percentage (%)
Perilesional oedema	17	48.6
Mass effect	8	22.9
Herniation	4	11.4
Subdural hematoma	2	5.7
Subacute cerebral hematoma	2	5.7

Table 4. Distribution according to investigations for the extension and search of primary cancer.

Variable	Number (N = 35)	Percentage (%)
TAP Scan	8	22.9
Chest X-ray	5	14.3
Prostate ultrasound	3	8.6
PSA	3	8.6
Breast ultrasound	2	5.7

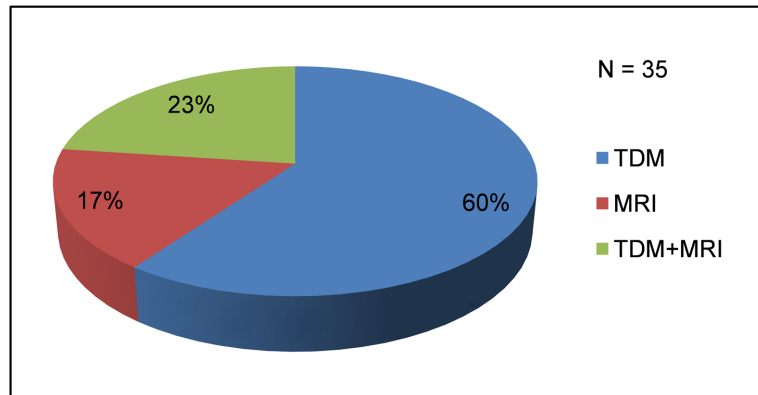


Figure 3. Distribution of patients according to the cerebral imaging technique used.

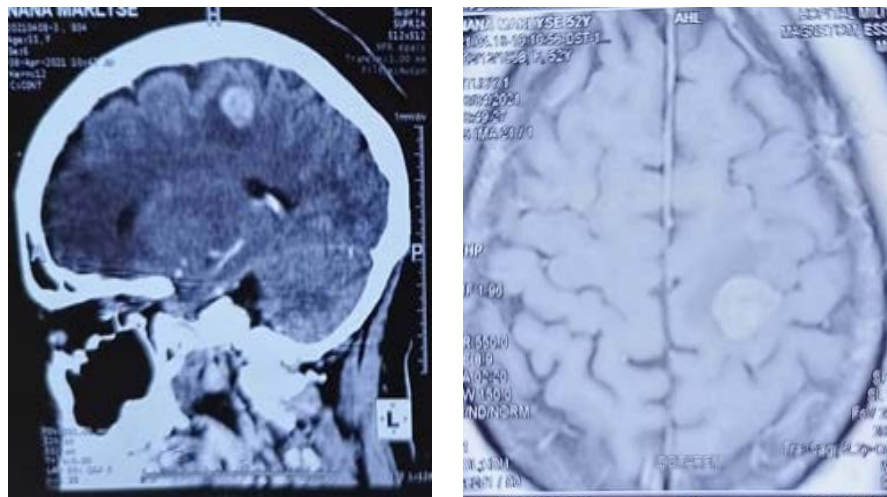


Figure 4. Single brain metastases of a breast cancer of 49 years old woman in our study (MRI, T1). Archive of the neurosurgery department of Yaounde General Hospital.

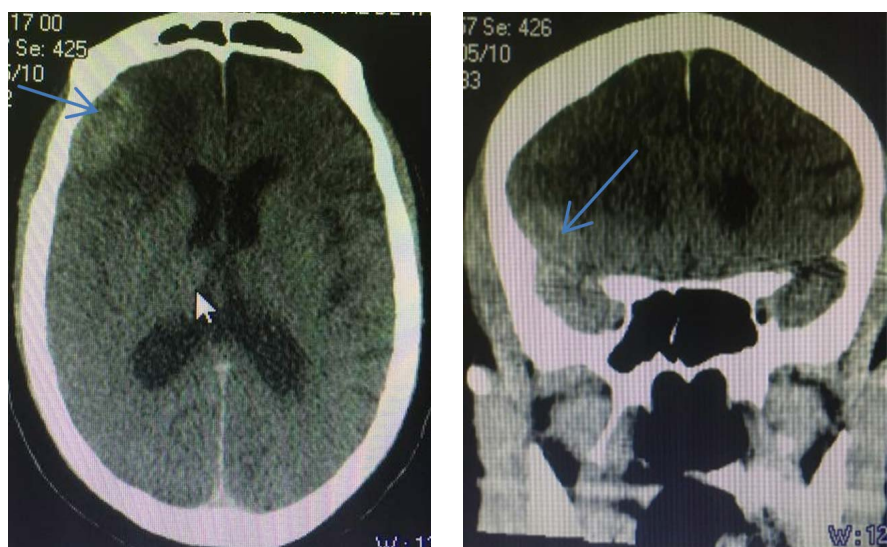


Figure 5. Single brain metastases of a prostate cancer of 84 years old man in our study (CT scan). Archive of the neurosurgery department of Yaounde Central Hospital.

The histological types of intracranial metastases were adenocarcinoma (48.6%), poorly differentiated carcinoma (20.0%), well differentiated follicular carcinoma (5.7%), and melanoma (2.9%). 7 types of primary cancers were identified: breast cancer (31.4%), lung cancer (25.7%), prostate cancer (17.1%), undetermined cancer (14.3%), Thyroid cancer (5.7%), colon cancer (2.9%), melanoma (2.9%), and (Figure 6).

The surgical modalities used were total resection in 24 cases (68.6%), sub-total resection in 6 cases (17.1%), and partial resection in 5 cases (14.3%) (Figure 7). The adjuvant treatment was WBRT in 13 cases (37.1%), hormonotherapy in 10 cases (28.6%), and chemotherapy in 3 cases (8.6%).

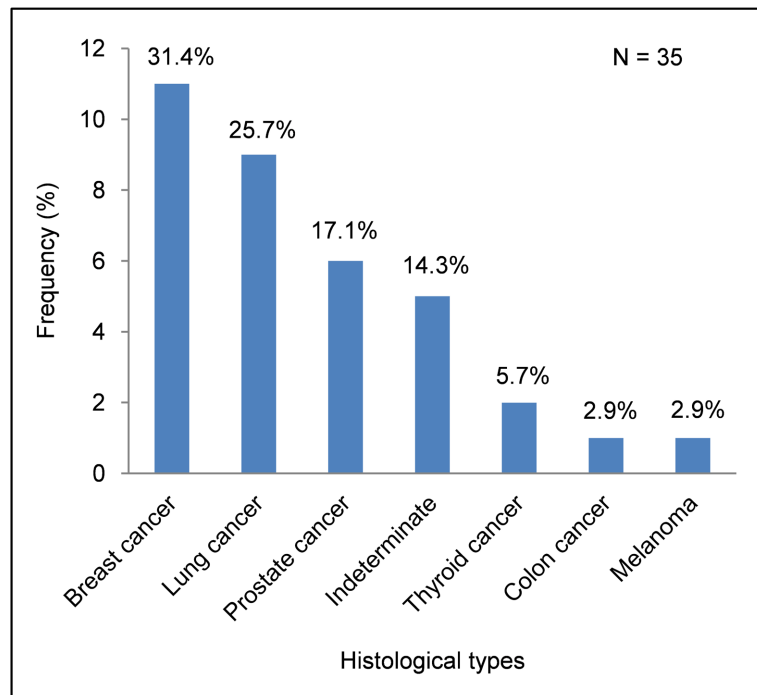


Figure 6. Distribution of patients according to the primary tumors.

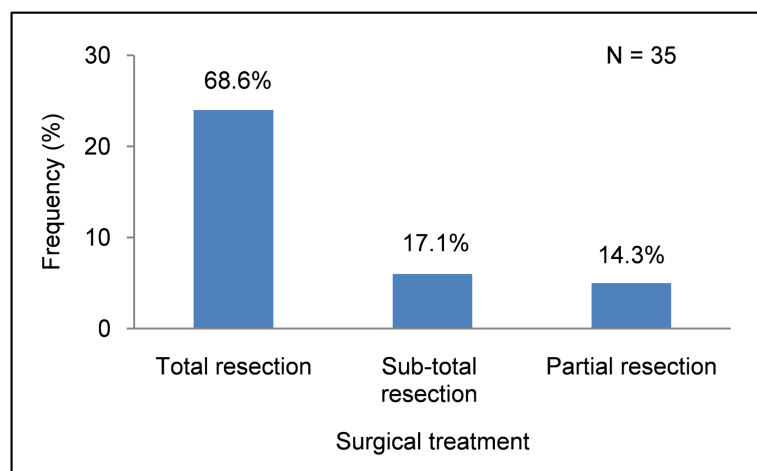


Figure 7. Distribution of patients according to the surgical modalities used.

3. Discussion

3.1. Frequency

The frequency of intracranial metastases in our settings was got to be 5.7% with respect to intracranial tumors. This finding is approximately double the frequency of 3.1% that was got from a study conducted in the YCH during the period from December 2011 to May 2017 [8] and of 2.9% in Dakar from 2010 to 2017 [7]. This increase can be explained by the improvements in primary disease therapeutics conferring greater systemic control, advancements in neuroimaging techniques and availability. This frequency is however lower compared to that obtained in Madagascar (16.95%) [11] and in the developed countries. This may be explained by the fact that many patients with brain metastases remain undiagnosed until death especially patients with cancer who do not present neurologic symptoms.

3.2. Age and Sex

The mean age of patients with ICMET in our series is 55.68 years. This is similar to the result obtained by Thiam *et al.* [7] but lower to that obtained in many countries in Europe where the mean age is about 60 years [12]. This result can be attributed to the increased life expectancy in these countries.

The sex ratio got was 0.94 with a female predominance. This finding is similar to that obtained in other studies that showed a female predominance [7] [13]. This similarity could be explained by the higher incidence of breast cancer in these countries. Moreso, breast cancer is the most common cancer in females [12] [14].

3.3. Clinical Features

Intracranial metastases are most frequently diagnosed in patients with an established primary site (metachronous presentation). To a lesser extent, the metastases are discovered at the same time as the primary tumor (synchronous presentation) [9] [10]. This is the case in our series where 25 patients (71.4%) had a known primary tumor on admission compared to those who had a synchronous or a precocious presentation in 28.6% of cases. The clinical presentation in our series is dominated by signs of raised intracranial pressure (headache, blurred vision, vomiting) which is present in 26 cases (74.3%). The common association of the metastatic lesions with perilesional oedema can explain the high frequency of raised intracranial pressure.

3.4. Paraclinical Features

Imaging of the brain has a primary role in the detection of brain metastases and is important for subsequent patient management and treatment [10]. In our study, CT scan alone was used as diagnostic tool in 21 cases (60%), MRI alone in 6 (17.1%) of cases and CT scan + MRI in 8 (22.9%) of cases. This is close to the

results obtained in a similar study in Dakar [7]. Despite the greater sensitivity of MRI particularly for lesions in the posterior fossa or multiple punctuate metastases over CT, the greater use of CT can be explained by the higher accessibility and availability of CT to MRI in our context.

The majority of the lesions (94.3%) were located supratentorially. With 28 (80%) in the cerebral hemispheres and 5 (14.3%) in the meninges. This can be due to the fact that metastases preferentially affect the cortex and subcortical white matter of large arteries' terminal supply areas and this can serve as a topographic reference for surgery and radiotherapy [15].

In our series, the majority of the lesions are single. This was the case in 22 patients (62.9%). This can be accounted for by the low admission of patients with multiple ICMET in the neurosurgery department. In addition, a surgical treatment is rarely offered to patients with multiple BM, who receive more a palliative treatment in other structures. This can equally be explained by the low use of MRI in favour CT, which may not visualize multiple punctuate metastases.

Tumor-associated vasogenic edema in brain metastasis is a significant cause of morbidity and mortality [16]. The major associated lesion in our series is perilesional oedema which is present in 17 (48.6%) of cases. This can be explained by the tumor mass effect and vessel density.

The investigations for the extension assessment were limited to the standard recommended investigations. This can be due to the poor financial status of our patients and to the fact that after brain imaging, the surgical procedure is given priority to the extension assessment or the search for the primary focus. The most used investigation in our series is thoraco-abdominopelvic CT with a frequency of 22.9%.

3.5. Therapeutic Features

The choice of therapeutic approaches, both in clinical trials and daily practice, is guided by the knowledge of the natural prognostic factors. Karnofsky performance status (KPS), age, primary/systemic tumor activity, neurocognitive function, number of brain metastases, primary tumor type, and time from primary tumor diagnosis to the brain lesion all have shown an individual prognostic significance in patients with BMs [17].

Surgery was the main treatment procedure used in our study. 24 (68.6%) of patients had total resection of the tumor. This is similar to the study done by Thiam *et al.* in Dakar where surgery was the mainstay of treatment for metastatic brain lesions [7]. Total resection eventually leads to a lower rate of local relapses and a longer time of functional independence and has shown a survival advantage for patients receiving total resection followed by WBRT (median survival 9 - 10 vs 3 - 6 months) [18] not neglecting the relatively higher risk of leptomeningeal disease especially for patients with posterior fossa metastases [19]. Even though in our study not all patients who received surgery equally received WBRT which was done in 13 cases (37.1%). The surgical indications frequently

encountered in our series include symptomatic lesions, mass effect, large single lesions or two to three surgically accessible lesions, good karnofsky performance status and controlled systemic disease and these join those stated in literature [20].

3.6. Histological Features

As in our study, adenocarcinoma which is the cancer type found on histological analysis in 17 cases (48.6%) is the most frequent histological type found in literature [7] [21]. IHC analysis revealed the primary tumor types in order of decreasing frequency to be breast cancer 11 (31.4%), lung cancer 9 (25.7%), prostate cancer 6 (17.1%), indeterminate 5 (14.3%), thyroid cancer 2 (5.7%), colon cancer 1 (2.9%), melanoma 1 (2.9%), These cancers especially for the first two are the most common risk factors of metastases to the brain and leptomeningeal structures as found in literature [7] [22].

The limitations in this study were principally due to its retrospective nature and the sample size which was relatively low.

4. Conclusion

This retrospective, descriptive and cross-sectional study on 35 cases of intracranial metastases, managed in the neurosurgery departments of the General and Central Hospitals of Yaounde from January 2016 to December 2022 permitted us to elucidate the current epidemiology and describe the clinical, diagnostic and therapeutic features of ICMET in Yaounde. Following our statistical results, we can conclude that intracranial metastases are relatively frequent. There is a slight female predominance and the age group 50 - 59 years is the most affected. The onset is mostly metachronous. The clinical presentation is dominated by signs of raised intracranial pressure (headache, blurred vision, vomiting). Cerebral CT Scan is the main imaging technique used. Most of the lesions are single and supratentorially located. The most frequent histological type is adenocarcinoma and the primary cancers most represented include breast cancer, lung cancer and prostate cancer. Surgery is the main treatment procedure for patients with good performance status, limited number of lesions and controlled systemic disease. The adjuvant treatment (radiotherapy, chemotherapy) was limited.

Conflicts of Interest

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

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Abbreviations

BMs: brain metastasis
CT scan: computed tomography
ICMET: incidence of intracranial metastases
IHC: immuno-histochemical
KPS: Karnofsky performance status
MRI: magnetic resonance imaging
TAP scan: thoraco-abdomino-pelvic scan
TDM: tomodensitometry
WBRT: whole brain radiotherapy
YCH: Yaounde Central Hospital
YGH: Yaounde General Hospital