



# Primary central nervous system sarcomas. Clinical, radiological and pathological features in our institution

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## ABSTRACT

**Objective:** Primary CNS sarcomas are very rare tumours with no defined standard of care.

**Patients and methods:** This study was a retrospective review of seven patients diagnosed with a primary CNS sarcoma at neurosurgery department, Mansoura university hospital between 2006 and 2018. We reviewed the clinical, radiological, and pathological data of these patients. There were 2 female (28.6%) and 5 male (71.4%) with age ranged from 8 years to 73 years (mean age 25.4 years). Three patients (42.9%) had an intracranial sarcoma, and four (57.1%) had intraspinal tumours. All intracranial tumours located in supratentorial region.

**Results:** we have characteristic imaging findings inform of osteolytic bony erosion in 3 patients and marked enhancement of the tumour in 5 (71.4%) patients. We operated upon all patients to remove the tumour surgically with our aim is gross tumour resection. Tumour was totally resected in 5 patients (71.4%) and subtotal in another 2 patients (28.6%). Tumour has dural attachment in 5 cases (71.4%) and brain invasion was present in all intracranial 3 patients (42.9%). Postoperative radiotherapy was used in 5 patients and postoperative chemotherapy was used in all patients. We used immunohistochemical studies for all patients with the most consistent finding being strong Desmin positivity. The mean length of patients survival was 4.6 years (range from 3 month to 8 years).

**Conclusions:** Primary CNS sarcomas are very rare CNS tumours, total surgical resection and post-operative radio and chemotherapy provided encouraging outcomes.

## INTRODUCTION

Primary CNS sarcomas are rare tumours. There are many theories of the cell of origin of these tumour. Tumour may arise from pluripotential primitive mesenchymal cells which located in the dura, or originated from the leptomeningial cells or their extensions via the pia into the brain and the spinal cord along the stroma of the choroid plexus, the tela choroidea, or the periadventitial spaces and these considered as widely accepted theory.

We can defined sarcomas that have originated from metastases of soft tissue or bone sarcomas to the CNS as Secondary CNS sarcomas. These tumours result from direct extension of sarcoma located at places neighbouring the CNS.

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**Keywords**  
Primary CNS,  
sarcoma

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**PATIENTS AND METHODS**

We looking for all types of primary CNS sarcomas between 2006-2018 at Mansoura university hospital through retrospective analysis of our CNS tumor database which archived in our neurosurgery department in these period. The Research Ethical committee at Mansoura medical school give us permission to use these patients' data. In this study, we defined primary CNS sarcomas as tumours that originated primary in the CNS from non-neuronal, non-glial, and non-reticular elements, and we not include any previously diagnosed benign tumour with sarcomatous transformation.

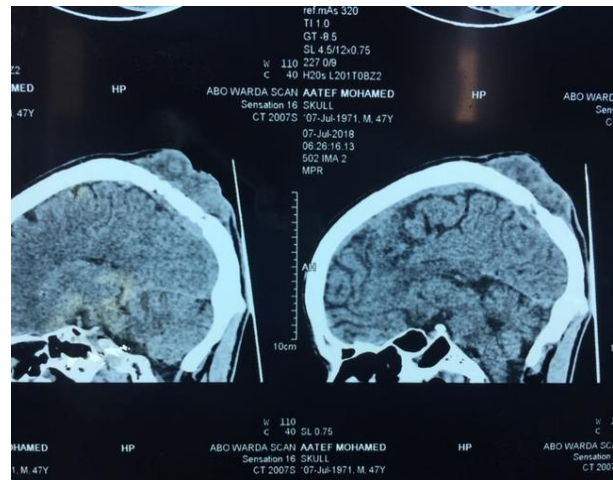
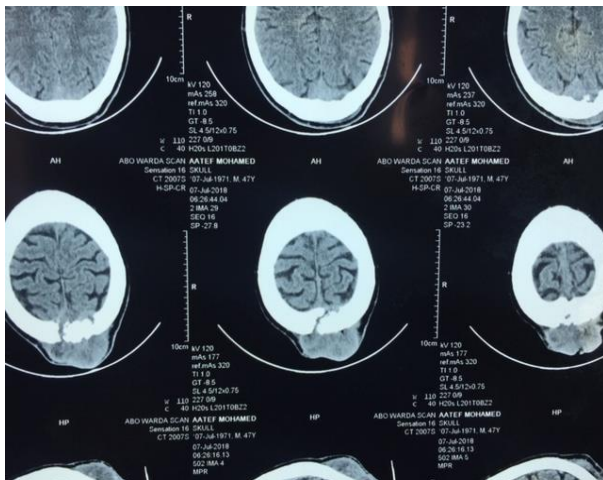
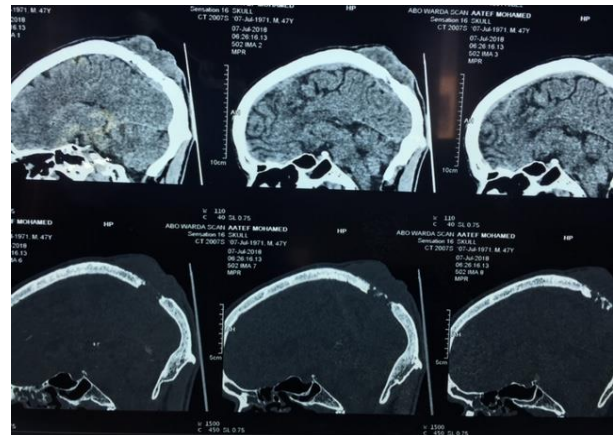
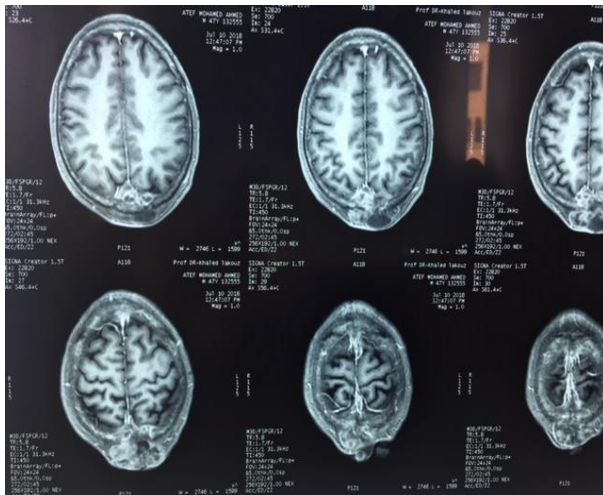
The medical data of these patients included in our definition of a primary CNS sarcoma were then

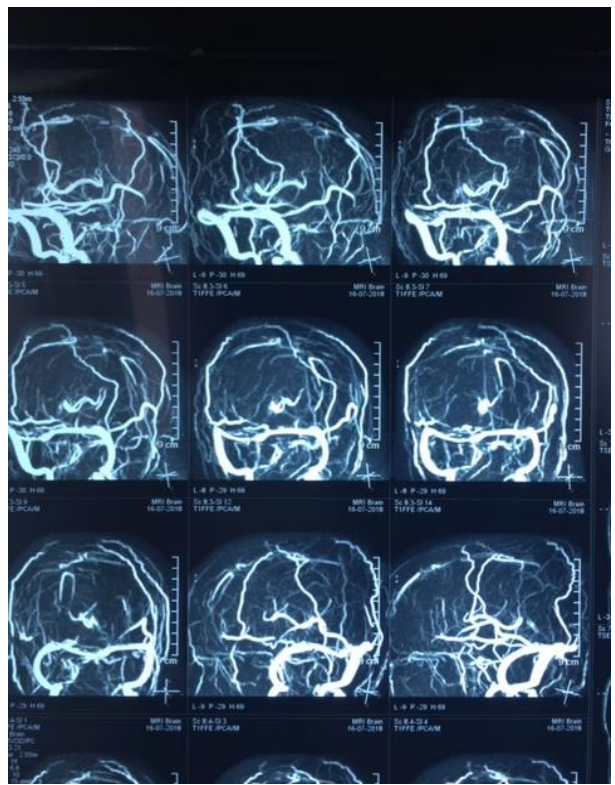
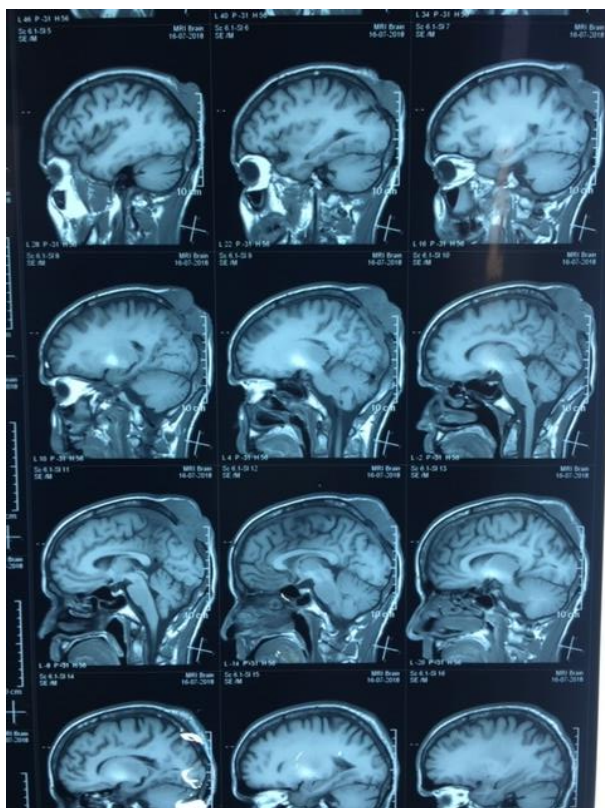
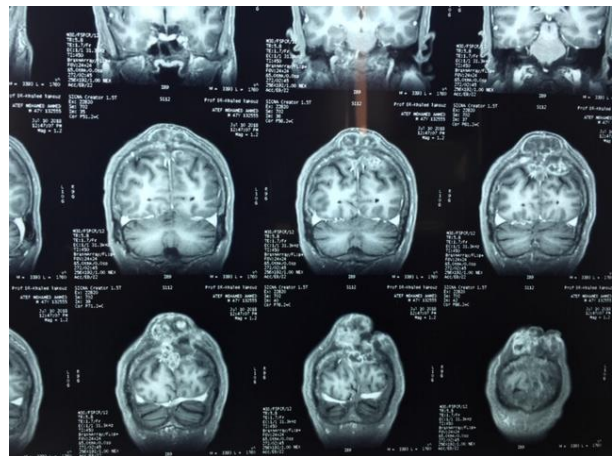
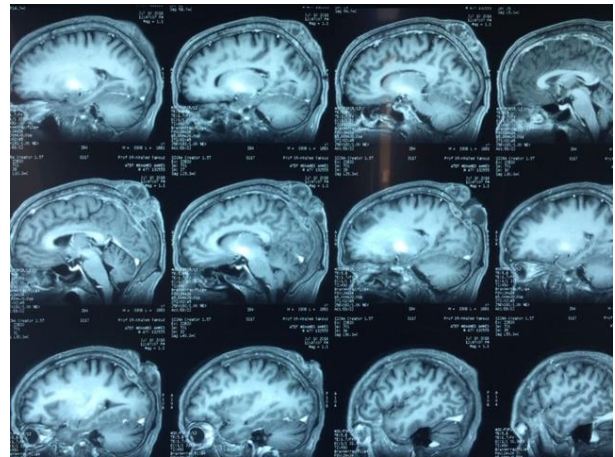
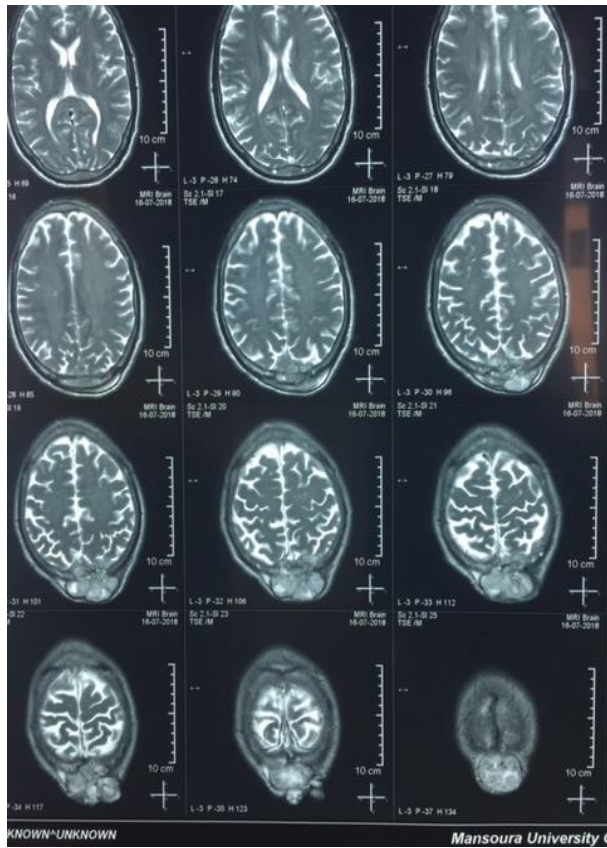
analysed for clinical, radiological and pathological features.

All primary CNS sarcoma were investigated for any possibility of the presence of extra CNS sarcomas at the time of study. The work-up study were chest X-ray, chest CT, abdominal and pelvic CT, and abdominal ultrasound.

All cases surgical specimens were examined in pathology department by light microscopy using eosin and hematoxylin stain, periodic acid-Schiff, and reticulin. We used immune histochemical studies in all cases.

The range of follow up varied from 3 month to 8 years (mean 2.9 years). We calculated the length of survival from the date of diagnosis of the disease and the end points were the patient death day or the last follow-up visit.





PATIENT	Age/sex	location	CT	MRI	Extent of resection	Radio-therapy	Chemo-therapy	Dural attachment	Brain invasion	survival
1	73/f	D10	Enhancement ++, bone destruction		Total	Yes	Yes	No	No	Alive 1 years then absent
2	8/f	D11-12	Enhancement +++, cystic		Near total	No	Yes	Yes	No	Alive 1years 6 months
3	8/m	Frontal lobe	Enhancement +++, bone destruction		Total	Yes	Yes	Yes	No	Alive 8years
4	47/m	Occipital lobe	Cystic, enhancement ++, bone destruction		Total	Yes	Yes	Yes	Yes	Alive 3months
5	8/m	L2-5	Enhancement +++, bone destruction, cystic		Total	No	Yes	No	No	Alive 7years
6	18/m	Bifrontal lobe	Cystic, enhancement ++,		Near total	Yes	Yes	Yes	Yes	Alive 7months
7	16/m	D4-6	Enhancement +++, bone destruction		Total	Yes	Yes	Yes	No	Alive 2years

## RESULTS

### Clinical pictures

We summarized the clinical pictures in this study in Table 1. There were 2 female (28.6%) and 5 male (71.4%) ranged in age from 8 years to 47 years (mean age 19.4 years). Three patients in this study (42.9%) were in the first decade of life. Three sarcoma patients (42,9%) were intracranial and 4 patients (57.1%) were intraspinal. All intracranial sarcomas in this series were supratentorial in location, two of them presented bilaterally either in frontal or occipital lobes. Three of intraspinal tumours (75%) were located in the dorsal area and the remaining presented in the lumbar region.

The clinical presentation of these patients varied from symptoms and signs of ICP as vomiting, headache and papilloedema and other presentation as focal neurological deficit such as dysphasia, fits, hemiparesis for intra cranial tumours and paraparesis for the intra spinal tumours.

### Radiological features

We summarized the radiological data in Table 1. CT

and MRI used for investigation (Fig. 1). CT was performed in all patients, tumour enhancement with contrast had been obtained. All intracranial tumours patients in this study showing osteolytic bony destruction. 5 patients (71.4%) showed marked humoral enhancement. Magnetic resonance imaging in selected cases revealed increased signal on T2 images on these lesions, and irregularly enhancement after contrast study (Fig. 2).

### Surgery

All patients in these series underwent at least one surgical procedure with the aim of surgery is gross tumoural resection; only 2 cases underwent another surgical operation due to recurrence of the tumour. Surgical tumoural resection was total in 5 cases (71.4%) and subtotal in the remaining 2 patients (28.6%). We performed true cut needle biopsy in just a patient of intracranial tumour with extra cranial extension prior to surgical excision. Postoperative radiotherapy was used in 5 patients (71.4%) and postoperative chemotherapeutic agents were used in all patients (100%).

TABLE 1 showed the operative details of the patients included in this series. At surgery, we found dural attachment of the tumour in 5 patients (71.4%) and parenchymal invasion of the tumour in 2 patients (28.6%). We found a well-defined demarcation plane of dissection around the lesion in four patients, two of them were intracranial sarcoma and the other were intra spinal.

### Pathological features

In this series, we found similar histological characters of the different intracranial and extra cranial sarcomas. We did immunohistochemical studies for all cases (Table 2). The most consistent data in immunohistochemical studies were strong positive results of vimentin and general negative results for both neuronal and glial markers. All patients showed positive Desmin with more rhabdomyoblastic differentiation.

All patients tumour examined by Electron microscopic studies. There are many feature as the spindle shape of the cells, lack of well-developed junctions, dilated rough endoplasmic reticulum, and absence of microvilli and neurosecretory granules.

The final pathological diagnosis in these series was a ewing's sarcoma in 2 (28.6%) patients, a embryonal rhabdomyosarcoma in 2 (28.6%), an otherwise low grade chodrosarcoma (14.3%), synovial sarcoma and an undifferentiated sarcoma in the remaining three patients alternatively.

Patient No	desmin	neurone specific enolase	BDL-2	LCA,CD3,CD99
1	negative	positive	negative	NA
2	negative	negative	positive	NA
3	positive	negative	NA	NA
4	negative	negative	NA	negative
5	negative	positive	NA	NA
6	NA	NA	NA	NA
7	positive	NA	NA	negative

### Survival

We calculate the length of survival from the day of the diagnosis of the disease (Table 1). We have data

on survival for 6 patients and lack information in just one patient.

The longest survival time in these study was eight years and the shortest survival time was three month (mean 3.2 years).

The durations of patient survival in intracranial tumours ranged from three months to eight years (mean 2.9 years), while the intraspinal tumours ranged from 18 months to 7 years (mean 3.5 years).

Three months to 8 years (mean 4 years) was the length of survival in the cases with gross surgical resection of the lesion; and the range of length of survival in cases with subtotal tumour resection was 18 months to 2 years (mean 1, 8 years).

### Adjuvant therapy

We used Postoperative radiation in 5 patients; with a radiation dose ranged from 4,500–5,900 Gy.

On the other hand we used Postoperative chemotherapy in all patients. The most used chemotherapeutic agents were ifosfamide, carboplatin, vincristine and cyclophosphamide.

### DISCUSSION

The occurrence of a primary CNS sarcoma described firstly by Bailey in 1929.2 CNS sarcoma with all forms considered as rare tumours.<sup>6-14-30</sup>the survival in sarcoma patients increased than in the past due to advances technique in chemotherapy.<sup>6-26-45</sup>In different studies, we found variation in the incidence of primary CNS sarcomas which ranged from 0.1% to 4.3%.<sup>3-19-27-31-33-36</sup>

This variation happened due to the term of a primary CNS sarcoma were inconsistent in different series. Previous reported studies included different forms such as giant cell sarcoma, circumscribed sarcoma of the posterior fossa, reticulum cell sarcoma, and hemangiopericytoma, and this gave a false result in high incidence of these tumour type.<sup>7-20-21-25-35</sup> In other series, they considered cases of primary glial, neuronal, neuroectodermal, and/or previously diagnosed benign meningeal tumours with sarcomatous features as sarcomas and this lead to falsely high incidence of these tumour type.<sup>23-31</sup>finally, many studies not used immunohistochemistry that could be helpful to resolve diagnostic issues for many examined sarcomatous tumors.<sup>23-33-36-43</sup>

The origin of sarcoma have many theories, the most accepted theory assumed the origin of these

tumour to pluripotential primitive mesenchymal cells, the leptomeninges or their extension into the brain and the spinal cord via the pia along the periadventitial spaces, the stroma of the choroid plexus and the tela choroidea.<sup>2-4-1-24-25-31-3-35-45</sup>

The causes for occurrence of the primary CNS sarcoma is not known yet well accepted inciting agent of sarcoma in the literature is radiation therapy<sup>19-23-27-34-5-38-44</sup>. There are another predisposing factor as trauma<sup>17-19-27-28-29-31</sup>, genetic and familial factors<sup>19-31</sup> and viruses such as RSV.<sup>8-21-27-31</sup>

Primary CNS sarcomas may happen at any life decade, with high incidence in children <sup>23-31-44</sup>. In these series sarcomas were exist in the age range 8-73 years, with the youngest case was 8 years old.

Primary intracranial sarcoma clinically presented as other intracranial tumours. However, it can present with intracranial hemorrhage due to their extreme vascularity<sup>1-15-27-30</sup>. The clinical presentation of primary intraspinal sarcoma had the same clinical presentation of other intraspinal tumours.

There are nonspecific image of primary CNS sarcomas on radiology as CT or MRI. In our series, tumour was large and with different heterogeneous density, cystic (hypodense), or solid and in one patient presented bilaterally in intracranial. Two of the 7 tumours had both solid and cystic components.

MRI of sarcoma was available with an inhomogeneous signal. Solid parts of the tumour usually enhanced after administration of intravenous contrast. Enhancement of the tumour after contrast in the MRI has been a feature of sarcomas in the many series in literature <sup>34-35</sup>. An important characteristic feature of sarcoma is the location near to the surface of the brain or the meninges, and it existed in four patients in our studies. CNS sarcoma have high incidence of leptomeningeal spread <sup>11-13-45</sup>. There are many differential diagnosis of primary CNS sarcoma on radiology as CT and MRI includes glioma, medulloblastoma in posterior fossa, cranial and spinal meningioma, and ependymoma <sup>19-27-32-36</sup>.

In current study, our patients tumor are located in supratentorial region with the most common sites of origin is the frontal lobes which is not match with other studies in literature <sup>13-22-23-32-36-45</sup>. None of our patients presented with their tumour in intraventricular region, although in many series

reported intraventricular sarcomas which originated from the choroid plexus<sup>23-26-28-40-4145</sup>. A common feature of primary CNS sarcoma is dural involvement<sup>5-17-36-44-45-47</sup>. We have dural involvement of the tumour in 3 patients which considered as a half of the cases in our study. We did not report any malignant glial tumour within or adjacent to the primary sarcoma on our series. Although some series document that reactive glioma can be happened in a primary CNS sarcoma <sup>16-23-29-46</sup>.

Primary sarcomas of CNS has the ability to send metastasis outside the central nervous system, as the liver, bone, and lung with a poor prognosis<sup>3-12-13-2</sup>. It is difficult to determine the incidence of the different histological subtypes of these tumour. This is due rare incidence of the lesion, and the deficient criteria for including specific subtypes in the patients who documented in study <sup>3-40</sup>. We have frequent changes happened in the classification system for primary CNS sarcomas due to appearance of new histological subtypes such as malignant fibrous histiocytoma, and in the literature its considered as most common soft tissue sarcoma<sup>4-5-16-27-38</sup>.

Undifferentiated sarcoma considered as the most common pathological type in our study, and this not matched with others series <sup>7-45</sup>. Other series reported fibrosarcomas and MFH as the most pathological tumoural subtype <sup>1-2-9-36</sup>.

Primary CNS sarcomas characteristic with a bad prognosis, although the long duration of postoperative survival is well reported in many series in literature<sup>13-31-32-34-40-45</sup>.

Many studies in the literature reported that gross surgical resection is considered as the best treatment of choice. We can use postoperative radiation or chemotherapy for prolonged the patient survival <sup>1-3-11-13-17-16-36-40-45-46</sup>.

In Our study, we found that maximal surgical resection of the tumour followed by post-operative radiotherapy help the patient to receive his best choice of management. Although, There are many side effects of radiation on young patient category. The aim of postoperative chemotherapy could not be exactly reported in our study.

## CONCLUSION

The primary central nervous system sarcoma is a rare tumour that mainly originated in the

supratentorial region with ability to be exist in the intraspinal region. CSF dissemination and dural attachment of the tumour are frequently exist. Metastases outside the CNS associated with bad prognosis. For long term survival we advised gross surgical resection followed by postoperative radiotherapy. Chemotherapy regimens may be considered as one of the factor that prolong the survival if they are tolerated by the patient. Future studies should be focused to understand the histopathological subtypes of primary CNS sarcoma to use different chemotherapeutic agents which be helpful to give patients long survival and best choice of treatment.

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