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Case Report

Pure testicular choriocarcinoma Cannonball metastases as a presenting imaging feature: A case report and a review of literature

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ABSTRACT

Pure testicular choriocarcinoma is an extremely rare subtype of nonseminomatous germ cell tumor, accounting for less than 1% of all germ cell tumors and only 0.19% of all testicular tumors. It is a highly aggressive malignant tumor with early multiorgan metastasis and poor prognosis. We present a case of 23-year-old male presented to the hospital with mild hemoptysis which was thought as a sequela of his past COVID-19 pneumonia infection, however; chest radiograph showed multiple rounded cannonball opacities seen throughout both lungs raising the suspicion of metastatic deposits to the lungs. During physical examination, left testicular painless swelling was noted leading to an ultrasound of the scrotum which revealed a left intratesticular infiltrative, heterogeneous mass. Tumor markers, including beta-human chorionic gonadotropin, lactate dehydrogenase and alpha fetoprotein were extremely high. Computed tomography scan of the brain, chest, abdomen, and pelvis showed hemorrhagic metastatic deposits to the brain, chest, and left para-aortic lymph nodes. The patient underwent radical orchiectomy and histopathology reports confirmed the diagnosis of pure testicular choriocarcinoma.

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Introduction

The most common type of testicular tumor is germ cell tumors (GCTs) which account for approximately 95% of testicular tumor. They are further classified into seminoma and nonseminomatous germ cell tumors (NSGCT). The least common

type and the most aggressive type of NSGCT is choriocarcinoma, accounting for less than 1% of the cases [1]. It is characterized by the production of human chorionic gonadotropin (HCG) molecule and commonly presents with early hematogenous metastasis to different areas of the body including the lungs, liver, and brain. Average age of presentation is between the ages of 20–30 years old [2]. It is rare for choriocarcinoma of the testis to present in pure form (0.2%–0.6%); it is usually an element of mixed GCTs of the testis (7%–8%) [3,4]. We present a case of pure choriocarcinoma of a young man presenting with

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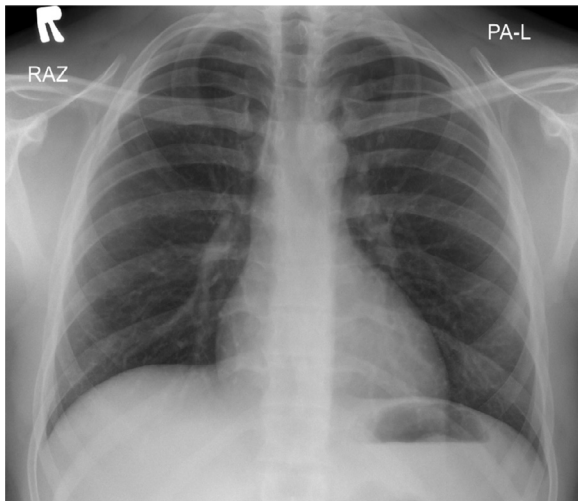


Fig. 1 – Posterior-anterior chest radiograph done 3 months back showing clear lung fields.

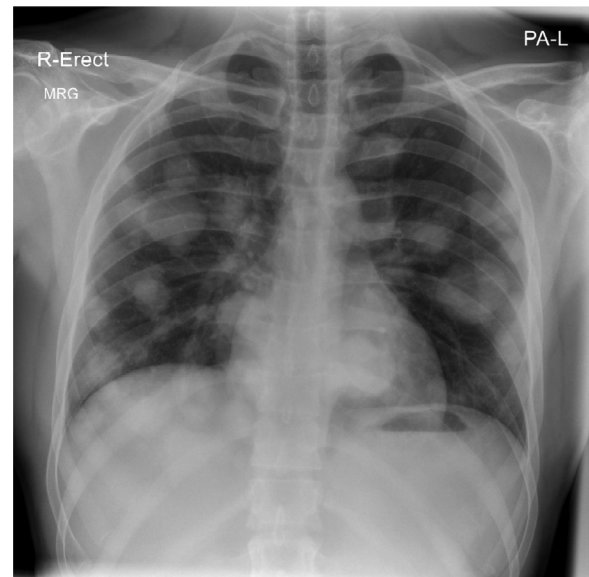


Fig. 2 – Posterior-anterior chest radiograph showing multiple rounded lung nodules of varying size involving both lung fields with no obvious central cavitation.

hemoptysis. Only few cases in literature were reported of the pure subtype of choriocarcinoma [5–8].

Common pulmonary manifestation of metastatic choriocarcinoma on imaging is cannonball metastases. They typically appear as multiple round well-defined pulmonary nodules representing hematological spread of the malignancy. Cannonball metastases classically present in cases with choriocarcinoma and renal cell carcinoma as well as endometrial and prostate cancer [9]. As presented in this case, cannonball metastases may be the initial presentation in cases with no history of primary malignancy. This specific imaging feature of metastasis suggests advanced stage of malignancy and poor prognosis. Nonmalignant causes of cannonball appearance may include fungal infections, tuberculosis, Wegener's granulomatosis, and sarcoidosis. Therefore, a broad diagnostic workup should be conducted [10].

Case report

A 23-year-old male presented to the accident and emergency department with chief complaint of mild hemoptysis (<30 mL/24 hours) and chest pain for the last 4 days. The patient also complained of headache, lower back pain, palpitation, fatigue, and loss of appetite for the last 2 weeks. He also gave a history of left testicular swelling for 1 week. He denied any history of fever, cough, shortness of breath, night sweats, abdominal pain, vomiting, or changing in bowel habits.

He is a heavy smoker with no significant past medical or surgical history. He has family history of hypertension and negative for history of cancer. On physical examination, the

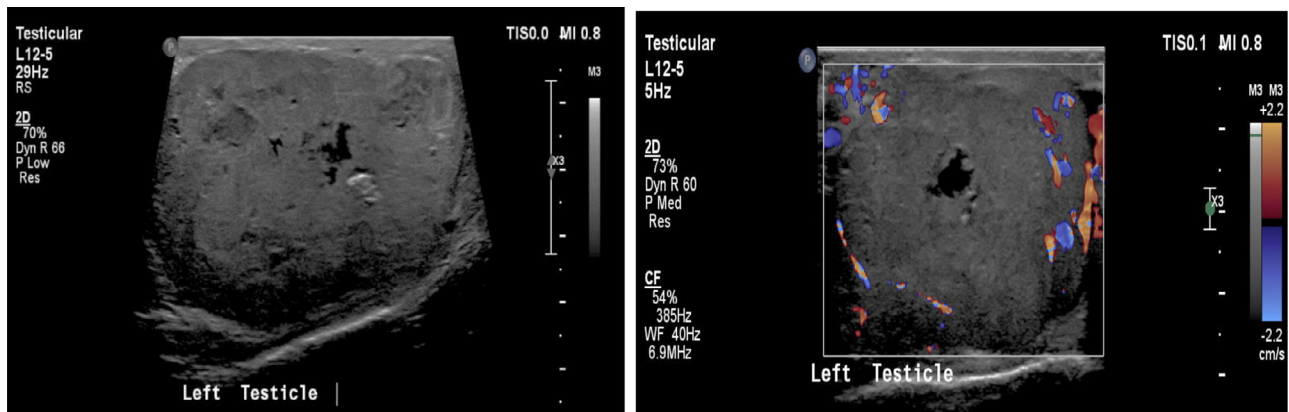


Fig. 3 – (A, B) Ultrasound of the left testicle showing (A) a large infiltrative, heterogeneous solid mass enlarging and distorting the left testicle parenchyma. (B) The mass shows faint peripheral vascularity with no internal vascularity noted on color Doppler image.

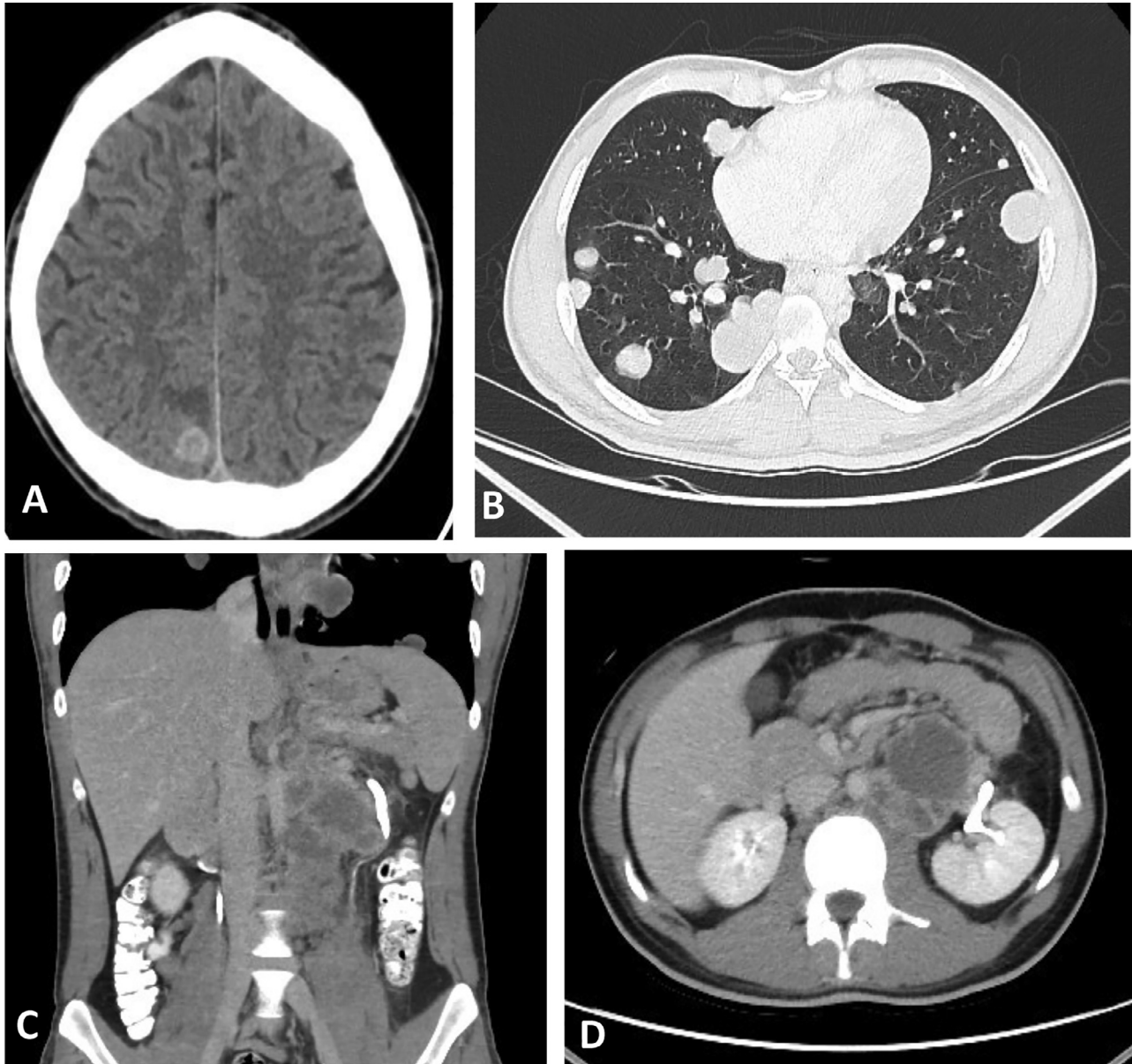


Fig. 4 – (A–D) Contrast enhanced CT of the brain, chest, abdomen, and pelvis. (A) Axial cut of the brain shows multiple hemorrhagic lesions (B) Axial cut of the chest in lung window shows hemorrhagic cannonball lesions in lungs, and (C, D) Coronal and axial cuts of the abdomen and pelvis in soft tissue window show large para-aortic necrotic lymph nodes along lymphatic drainage pathway of left testicle.

patient was conscious and orientated with no signs of acute distress. He was also vitally stable. Local scrotal examination showed left testicular painless swelling. Right testicle was normal. The rest of the physical examination was unremarkable, and the patient was vitally stable.

The patient had previous admission 3 months back when he presented with dry cough, mild shortness of breath on exertion, and generalized body pain. Given the current COVID-19 pandemic, the patient had COVID-19 workup done, including PCR-RT COVID-19 nasal swab test and frontal chest radiograph. Two consecutive nasal swabs were positive for COVID-19 viral infection. However, the chest radiograph was normal (Fig. 1). He was treated as per local guidelines that involved a

stay of 14 days in an isolation facility and symptomatic treatment with Ambroxol cough syrup, Otrivin spray, paracetamol, and oral Vitamins, including Vitamin C and Vitamin D. The patient's initial symptoms eventually resolved throughout his stay. He also had 2 COVID-19 PCR nasal swabs with negative results upon which the patient was seen fit for discharge.

Initial laboratory results of the tumor markers showed high beta-HCG (513,389 mIU/mL, normal range is <2 mIU/mL), elevated lactate dehydrogenase level (992 U/L, normal range is 105–222 U/L), and elevated alpha fetoprotein (AFP) level (518 IU/mL, normal range is <5.8 IU/mL). Laboratory investigation also revealed abnormal thyroid functions with high free T4 and low thyroid stimulating hormone.



Fig. 5 – Postoperative image of the excised testicle sent for histopathological examination revealing hemorrhagic tumor with central necrosis.

Upon the recent presentation of hemoptysis, the emergency physician ordered another chest radiograph and it showed multiple rounded lung opacities of varying size seen throughout both lungs with no obvious cavitation. No hilar lymphadenopathy or pleural effusion noted. No pneumothorax (Fig. 2).

Suspicion of metastatic disease to the lungs (Cannonball metastases) was raised and the patient was admitted to the hospital for further evaluation.

Scrotal ultrasonography (Fig. 3) was done using linear array probe and it showed a large, infiltrative, hypovascular, heterogeneous solid mass with indistinct borders occupying the left testicle with associated left hydrocele and varicocele suggestive of testicular neoplastic lesion.

Further brain, chest, abdomen, and pelvic CT scan with intravenous contrast was done and it showed multiple bilateral intracerebral supratentorial rounded hemorrhagic lesions seen at gray-white matter junction with perifocal edema suggestive of metastatic deposits (Fig. 4A). It showed also multiple rounded nodules of variable size surrounded by ground glass halo in both lung fields suggestive of hemorrhagic Cannon-ball lung metastasis (Fig. 4B). Furthermore, left para-aortic large matted necrotic lymph nodes (along the left testicular drainage pathway) with no solid abdominal organ primary mass lesion or metastasis (Figs. 4C and D).

Following multidisciplinary team discussion, radical orchidectomy through transinguinal approach was done and specimen underwent pathological examination (Fig. 5). He

was also managed medically with propranolol 120 mg and carbimazole 30 mg a day in view of thyrotoxicosis.

Microscopic histopathology confirmed the diagnosis of NSGCT—pure choriocarcinoma type with primary tumor limited to testis. It showed sheets of syncytio-trophoblasts and cytotrophoblasts and arranged in solid nests/sheets. This tumor was positive for HCG, CK (AE1/AE3), CAM 5.2 and Inhibin immune markers, and negative for other immune-markers like AFP, OCT3/4, CD30, and PLAP which ultimately ruled out the possibility of mixed germ cell tumor. Final staging of the tumor is T2N0M1 S3 staged III-C High Risk according to American Joint Committee of Cancer TNMS classification (Fig. 6)

Patient was discharged in a stable condition. He was also scheduled for follow up with oncology and advised to start first line chemotherapy with VIP regimen (Vinblastine, Ifosfamide with mesna and Cisplatin).

Discussion

Choriocarcinoma is a rare type of testicular neoplasm, accounting for 1% of all neoplasms [1]. It is classified as pure choriocarcinoma, composed of only syncytio-trophoblastic and cytotrophoblastic components, or as mixed GCT, which contains choriocarcinoma as one of the components. Pure choriocarcinoma is considered the rarest yet the most aggressive type of testicular carcinoma [1].

Average age of incidence in young males is between 25 and 30 years old [2]. They typically present with high levels of serum HCG and rapid hematological metastases with symptoms of hemorrhage at metastatic sites rather than palpable testicular mass. Most common sites of metastasis are lungs and brain, leading to have hemoptysis as an initial presentation (exactly like in our case), seizures, and/or confusion [1]. More often, the disease is not diagnosed until in advanced stages.

Laboratory investigation involves tumor markers such as beta-HCG and AFP. Beta-HCG is significantly high in pure choriocarcinoma (>1000 IU/L, normal range is <2 mIU/mL) and choriocarcinoma does not produce AFP.

Choriocarcinoma syndrome is a rare life-threatening complication that tends to develop in metastatic choriocarcinoma. It consists of hemorrhagic manifestations at the sites of metastasis, most seen in the lungs, leading to alveolar hemorrhage and acute respiratory failure. While the exact pathophysiology behind choriocarcinoma syndrome is unknown, it has been generally attributed to the extremely high beta-HCG levels. It is frequently seen after induction of chemotherapy; some cases were reported as choriocarcinoma syndrome being the initial presentation of testicular choriocarcinoma [11].

Hyperthyroidism is seen in up to 50% of patients with beta-HCG levels over 50,000 IU/L diagnosed with NSGCT [12]. The structural similarity of the alpha subunits of TSH and HCG may attribute to incidence of thyrotoxicosis.

Standard radiological investigation of testicular choriocarcinoma is with ultrasonography. Choriocarcinoma typically shows well-defined hypoechoic lesion with areas of hemorrhage and necrosis and may show more in-homogenous cys-

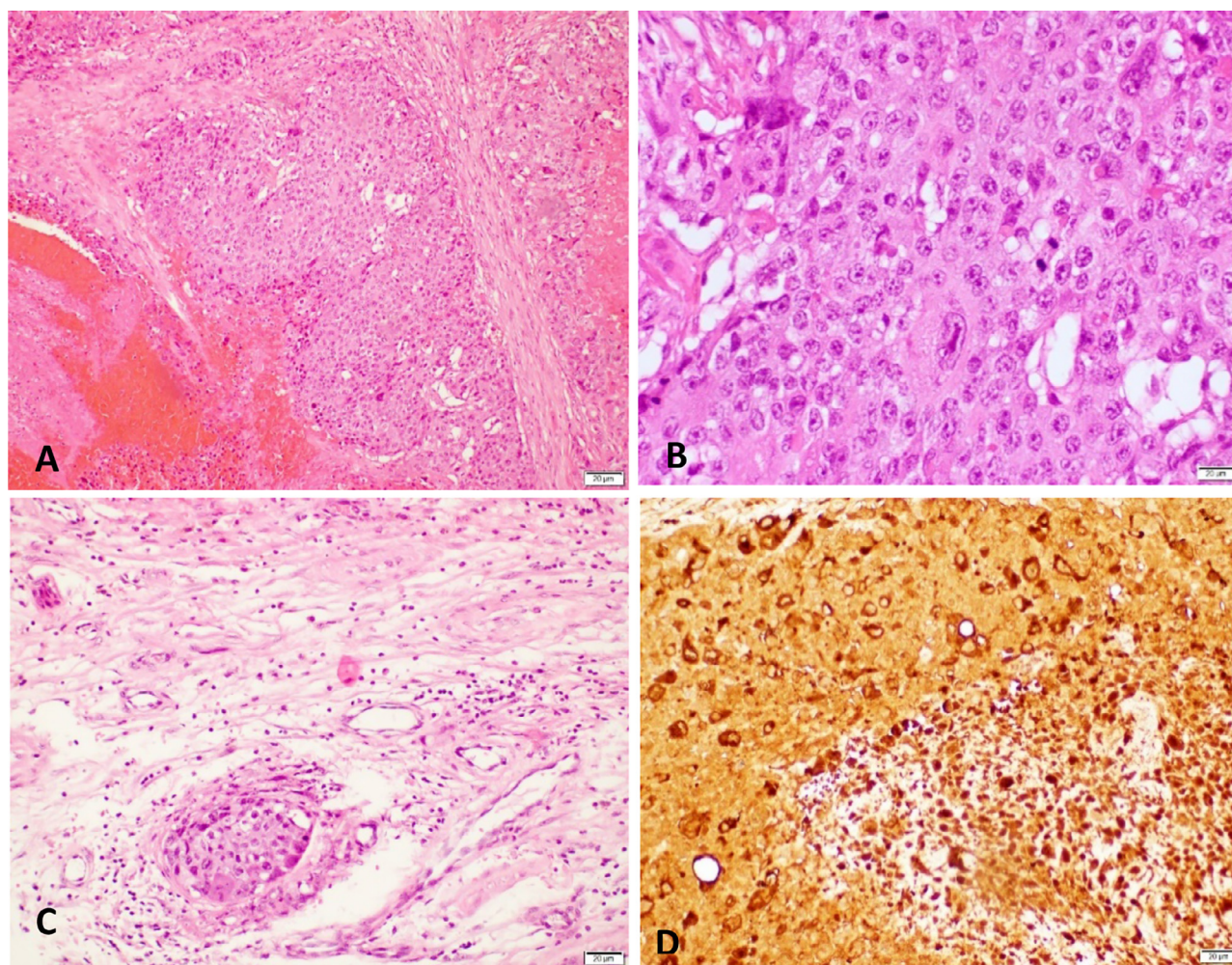


Fig. 6 – (A–D) Histopathology images showing typical microscopic appearance of choriocarcinoma. (A) $\times 100$ magnification with hematoxylin and eosin staining shows extensive areas of hemorrhage and necrosis. (B) Higher power image of the tumor shows sheets of syncytiotrophoblasts and cytotrophoblasts (H&E stain $200\times$). (C) choriocarcinoma with tumor emboli (H&E stain $100\times$). (D) HCG immunohistochemistry marker shows diffuse positive in syncytiotrophoblasts and cytotrophoblasts ($100\times$).

tic appearance than other types of testicular cancers. Combined with physical examination, ultrasound sensitivity can reach 100% [13]. Computed tomography (CT) is essential in identifying the extent of metastasis for staging purpose. The commonly used staging system is the American Joint Committee of Cancer that is TNMS-based classification (T = tumor, N = node, M = metastases, S = serum markers of AFP, HCG, and lactate dehydrogenase). Standard CT with intravenous and oral contrast administration is used in identifying metastatic lymphadenopathy. Given the lymphatic and venous drainage pathway of the testes (right testicular vein into the inferior vena cava and left testicular vein drains into left renal vein), para-aortic and paracaval lymph nodes at the level of the kidneys are the initial location of metastasis for testicular cancers [4]. CT also provides excellent anatomical identification and evaluation of solid organ metastasis. Most commonly prone organs to testicular choriocarcinoma are the lungs, liver, and brain [4,13]. The presence of brain metastasis from choriocarcinoma has poor prognosis [8,14].

Conclusions

Pure testicular choriocarcinoma is a rare entity and usually presents for the first time with early hematological metastasis. Imaging plays essential role in tumor localization and characterization and determine the extent of distant metastasis. Ultrasound is used for standard method of diagnosis and CT is the modality of choice for staging. Ultimately, correlation with tumor markers and histopathological examination would provide the final diagnosis.

Patient consent statement

A written consent was obtained from the patient for publication of this case and any accompanying images.

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