

World Journal of *Clinical Cases*

World J Clin Cases 2021 November 26; 9(33): 10052-10391



REVIEW

- 10052** Effects of alcohol consumption on viral hepatitis B and C
Xu HQ, Wang CG, Zhou Q, Gao YH

MINIREVIEWS

- 10064** Effects of anti-diabetic drugs on sarcopenia: Best treatment options for elderly patients with type 2 diabetes mellitus and sarcopenia
Ma XY, Chen FQ

ORIGINAL ARTICLE**Retrospective Cohort Study**

- 10075** Utility of cooling patches to prevent hand-foot syndrome caused by pegylated liposomal doxorubicin in breast cancer patients
Zheng YF, Fu X, Wang XX, Sun XJ, He XD

Retrospective Study

- 10088** Clinicopathological features of small T1 colorectal cancers
Takashina Y, Kudo SE, Ichimasa K, Kouyama Y, Mochizuki K, Akimoto Y, Maeda Y, Mori Y, Misawa M, Ogata N, Kudo T, Hisayuki T, Hayashi T, Wakamura K, Sawada N, Baba T, Ishida F, Yokoyama K, Daita M, Nemoto T, Miyachi H
- 10098** Comparison of dental pulp periodontal therapy and conventional simple periodontal therapy as treatment modalities for severe periodontitis
Li L, Chen HJ, Lian Y, Wang T
- 10106** Tripartite intensive intervention for prevention of rebleeding in elderly patients with hypertensive cerebral hemorrhage
Li CX, Li L, Zhang JF, Zhang QH, Jin XH, Cai GJ
- 10116** Clinical and electroencephalogram characteristics and treatment outcomes in children with benign epilepsy and centrotemporal spikes
Chen RH, Li BF, Wen JH, Zhong CL, Ji MM
- 10126** Endoscopic ultrasonography diagnosis of gastric glomus tumors
Bai B, Mao CS, Li Z, Kuang SL
- 10134** Learning curves of robot-assisted pedicle screw fixations based on the cumulative sum test
Yu J, Zhang Q, Fan MX, Han XG, Liu B, Tian W
- 10143** Value of GRACE and SYNTAX scores for predicting the prognosis of patients with non-ST elevation acute coronary syndrome
Wang XF, Zhao M, Liu F, Sun GR

- 10151** Effectiveness of enhanced recovery after surgery in the perioperative management of patients with bone surgery in China

Zhao LY, Liu XT, Zhao ZL, Gu R, Ni XM, Deng R, Li XY, Gao MJ, Zhu WN

Clinical Trials Study

- 10161** Association between plasma dipeptidyl peptidase-4 levels and cognitive function in perinatal pregnant women with gestational diabetes mellitus

Sana SRGL, Li EY, Deng XJ, Guo L

- 10172** Paricalcitol in hemodialysis patients with secondary hyperparathyroidism and its potential benefits

Chen X, Zhao F, Pan WJ, Di JM, Xie WN, Yuan L, Liu Z

Observational Study

- 10180** Did the severe acute respiratory syndrome-coronavirus 2 pandemic cause an endemic *Clostridium difficile* infection?

Cojocariu C, Girleanu I, Trifan A, Olteanu A, Muzica CM, Huiban L, Chiriac S, Singeap AM, Cuciureanu T, Sfarti C, Stanciu C

- 10189** Effect of nursing intervention based on Maslow's hierarchy of needs in patients with coronary heart disease interventional surgery

Xu JX, Wu LX, Jiang W, Fan GH

- 10198** Impacts of statin and metformin on neuropathy in patients with type 2 diabetes mellitus: Korean Health Insurance data

Min HK, Kim SH, Choi JH, Choi K, Kim HR, Lee SH

META-ANALYSIS

- 10208** Is endoscopic retrograde appendicitis therapy a better modality for acute uncomplicated appendicitis? A systematic review and meta-analysis

Wang Y, Sun CY, Liu J, Chen Y, Bhan C, Tuason JPW, Misra S, Huang YT, Ma SD, Cheng XY, Zhou Q, Gu WC, Wu DD, Chen X

- 10222** Prognostic value of ground glass opacity on computed tomography in pathological stage I pulmonary adenocarcinoma: A meta-analysis

Pan XL, Liao ZL, Yao H, Yan WJ, Wen DY, Wang Y, Li ZL

CASE REPORT

- 10233** Atrial fibrillation and concomitant left subclavian, axillary and brachial artery embolism after fiberoptic bronchoscopy: A case report

Yang CL, Zhou R, Jin ZX, Chen M, Zi BL, Li P, Zhou KH

- 10238** Streptococcal toxic shock syndrome after hemorrhoidectomy: A case report

Lee CY, Lee YJ, Chen CC, Kuo LJ

- 10244** Subsequent placenta accreta after previous mifepristone-induced abortion: A case report

Zhao P, Zhao Y, He J, Bai XX, Chen J

- 10249** Autosomal dominant tubulointerstitial kidney disease with a novel heterozygous missense mutation in the uromodulin gene: A case report
Zhang LL, Lin JR, Zhu TT, Liu Q, Zhang DM, Gan LW, Li Y, Ou ST
- 10257** Novel *KDM6A* mutation in a Chinese infant with Kabuki syndrome: A case report
Guo HX, Li BW, Hu M, Si SY, Feng K
- 10265** Pancreatic cancer with synchronous liver and colon metastases: A case report
Dong YM, Sun HN, Sun DC, Deng MH, Peng YG, Zhu YY
- 10273** Veno-venous-extracorporeal membrane oxygenation treatment for severe capillary leakage syndrome: A case report
Nong WX, Lv QJ, Lu YS
- 10279** Anticoagulant treatment for pulmonary embolism in patient with cerebral hemorrhage secondary to mechanical thrombectomy: A case report
Chen XT, Zhang Q, Zhou CQ, Han YF, Cao QQ
- 10286** Complete restoration of congenital conductive hearing loss by staged surgery: A case report
Yoo JS, Lee CM, Yang YN, Lee EJ
- 10293** Blastic plasmacytoid dendritic cell neoplasm with skin and bone marrow involvement: Report of three cases
Guo JH, Zhang HW, Wang L, Bai W, Wang JF
- 10300** Extracranial multiorgan metastasis from primary glioblastoma: A case report
Luan XZ, Wang HR, Xiang W, Li SJ, He H, Chen LG, Wang JM, Zhou J
- 10308** Transverse myelitis after infection with varicella zoster virus in patient with normal immunity: A case report
Yun D, Cho SY, Ju W, Seo EH
- 10315** Duodenal ulcer caused by coil wiggle after digital subtraction angiography-guided embolization: A case report
Xu S, Yang SX, Xue ZX, Xu CL, Cai ZZ, Xu CZ
- 10323** Crab lice infestation in unilateral eyelashes and adjacent eyelids: A case report
Tang W, Li QQ
- 10328** Local random flaps for cervical circumferential defect or tracheoesophageal fistula reconstruction after failed gastric pull-up: Two case reports
Zhang Y, Liu Y, Sun Y, Xu M, Wang XL
- 10337** Incurable and refractory spinal cystic echinococcosis: A case report
Zhang T, Ma LH, Liu H, Li SK
- 10345** Individualized treatment of breast cancer with chronic renal failure: A case report and review of literature
Cai JH, Zheng JH, Lin XQ, Lin WX, Zou J, Chen YK, Li ZY, Chen YX

- 10355** Persistent fibrinogen deficiency after snake bite: A case report
Xu MH, Li J, Han L, Chen C
- 10362** Successful prolonged cardiopulmonary resuscitation after intraoperative cardiac arrest due to povidone-iodine allergy: A case report
Xiang BB, Yao YT, Jiao SL
- 10369** Clinical algorithm for preventing missed diagnoses of occult cervical spine instability after acute trauma: A case report
Zhu C, Yang HL, Im GH, Liu LM, Zhou CG, Song YM
- 10374** Carbon ion radiotherapy for synchronous choroidal melanoma and lung cancer: A case report
Zhang YS, Hu TC, Ye YC, Han JH, Li XJ, Zhang YH, Chen WZ, Chai HY, Pan X, Wang X, Yang YL
- 10382** Heart failure as an adverse effect of infliximab for Crohn's disease: A case report and review of the literature
Grillo TG, Almeida LR, Beraldo RF, Marcondes MB, Queiróz DAR, da Silva DL, Quera R, Baima JP, Saad-Hossne R, Sasaki LY

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Carbon ion radiotherapy for synchronous choroidal melanoma and lung cancer: A case report

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Abstract

BACKGROUND

Despite being the most common intraocular malignancy among adults, choroidal melanoma is a rare cancer type, even more so when accompanied by lung cancer. We report a patient with synchronous choroid melanoma and lung cancer treated with carbon ion radiotherapy (CIRT).

CASE SUMMARY

A 41-year-old woman was transferred to our center with a diagnosis of choroidal melanoma in her right eye. During the examination, we found a right lung tumor that was histologically diagnosed as lung cancer. The patient was treated with CIRT for both malignant neoplasms. The CIRT dose was 70 photon equivalent doses (GyE) in five fractions for the right eye choroidal melanoma and 72 GyE in 16 fractions for the right lung cancer. At 3 mo after CIRT, the choroidal melanoma completely disappeared, as did the right lung cancer 7 mo after; the patient was in complete remission.

CONCLUSION

CIRT may be an effective treatment for double primary lung cancer and choroid melanoma.

Key Words: Melanoma; Lung neoplasms; Heavy ion radiotherapy; Neoplasms; Choroid neoplasms; Case report

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Core Tip: Simultaneous choroidal melanoma and lung cancer are extremely rare. This report details a case of a 41-year-old woman with right-side choroidal melanoma and lung cancer treated with carbon ion radiotherapy. Seven months after treatment, the patient was in complete remission.

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INTRODUCTION

Uveal melanoma is the most common primary ocular malignancy among adults[1] and is treated with conventional surgery or various radiotherapy techniques[2,3]. The most common radiotherapy modalities are plaque brachytherapy and proton radiotherapy (PRT)[4-6]. However, carbon ion beams conform to the prescribed dose better than proton beams because of a sharper lateral falloff. Carbon ion beams are also biologically advantageous over PRT in treating relatively resistant tumors. Therefore, carbon ion radiotherapy (CIRT) was hypothesized to have similar or better clinical outcomes than PRT for choroidal melanoma. The National Institute of Radiological Sciences (NIRS) in Japan started using CIRT for uveal melanoma in 2001, and, as anticipated, CIRT was safe and effective[7]. CIRT is also effective with acceptable toxicity for early-stage and locally advanced non-small cell lung cancer. Moreover, it is equally safe and effective for elderly patients or patients with severe comorbidities who cannot receive surgery or chemoradiotherapy[8-10].

We present a case of concurrent choroidal melanoma and lung cancer that was successfully treated with CIRT. This report follows the CARE Guidelines: Consensus-based Clinical Case Reporting Guideline Development[11].

CASE PRESENTATION

Chief complaints

A 41-year-old woman was referred to the Wuwei Heavy Ion Center in June 2020 with choroidal melanoma of her right eye.

History of present illness

The right eye melanoma was histologically confirmed *via* fine-needle aspiration biopsy at an eye hospital. Written informed consent was obtained from the patient for publication.

Laboratory examinations

The immunohistochemical profile was C-erbB-2 (-), CK7 (+), Ki-67 (index = 25 %), Napsin A (+), P63 (-), and TTF-1 (+).

Imaging examinations

Computed tomography (CT) and magnetic resonance imaging (MRI) demonstrated that the tumor was located on the cranial side of the right eye. The patient presented with right eye malaise with gradual diminution of vision in the right eye over a period of 2 mo. After being transferred to our center, the patient's vision rapidly worsened, and she became completely blind in 15 d.

The patient underwent MRI at our hospital (3.0T; Siemens), which identified a lesion behind the right eye bulb from abnormal T1- and T2-weighted signals and high intensity on diffusion-weighted images (Figure 1). Ophthalmoscopy of the right eye showed a solid dark-gray mass in the posterior segment of the choroid with intense brown pigmentation occupying the posterior third of the vitreous chamber and mild retinal detachment at the peripheral choroidal mass rim. The mass was dome-shaped, 11.1 mm × 12.1 mm in size, and occupied a third of the posterior segment of the right

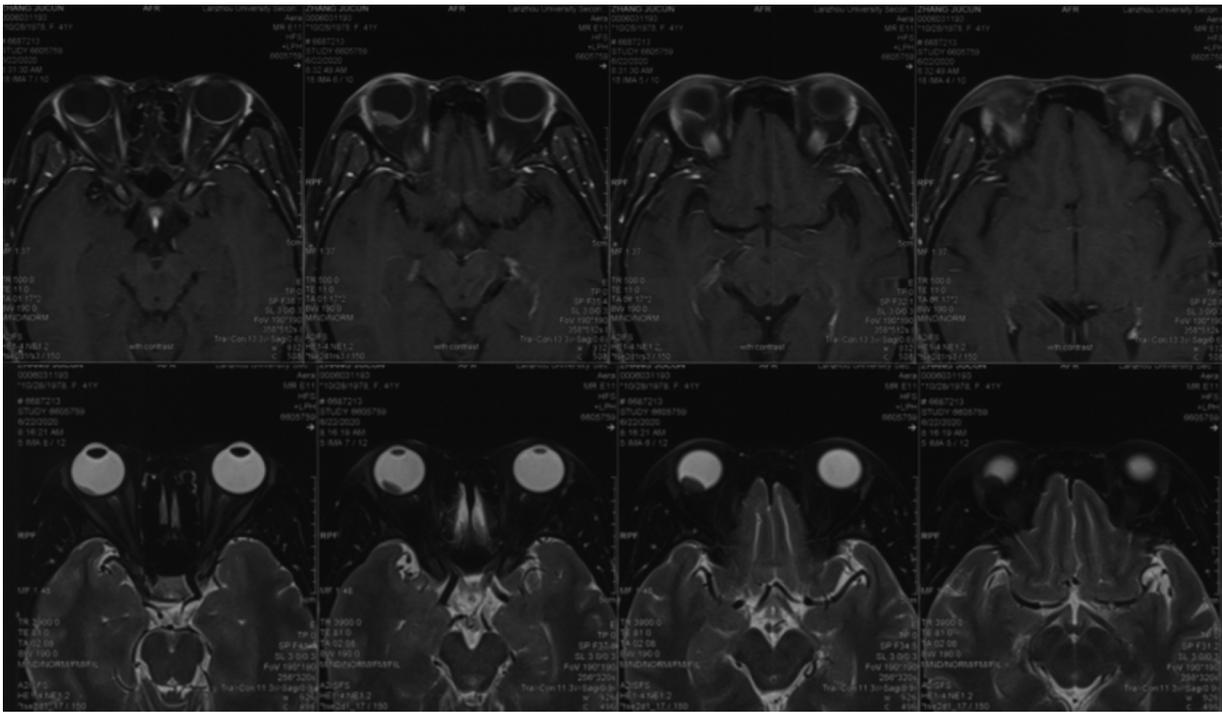


Figure 1 Magnetic resonance imaging of the right eye showed an abnormal signal shadow behind the right eye bulb, short T1 and T2 signals, and high diffusion-weighted imaging signals.

eye (Figure 2). During the examination, a tumor in the lower lobe of the right lung was also observed. A multidisciplinary team discussion concluded that double primary neoplasms, ocular metastasis of lung cancer, and ocular melanoma with lung metastasis were possibilities. Subsequently, the patient underwent a lung biopsy, which indicated infiltrating acinar adenocarcinoma.

FINAL DIAGNOSIS

The final histologically confirmed diagnoses were: (1) choroidal melanoma of the right eye, cT2N0M0 [per the American Joint Committee on Cancer (AJCC) 8th edition]; and (2) right-sided lung cancer, infiltrating acinar adenocarcinoma, cT3N0M0, IIb (per the AJCC 8th edition), KPS: 90. CIRT for lung and eye cancer was planned after discussion with the patient and family.

TREATMENT

First, we treated the right eye tumor. The patient was immobilized in a supine position with a bite block device (trUpoint ARCH; CIVCO, Orange City, IA, United States) (Figure 3). A set of 1-mm thick CT images was obtained using a CT simulator. Gross tumor volume (GTV) was determined using CT images and referencing the ophthalmoscopy and MRI findings. Clinical target volume (CTV) was the GTV plus 1 mm, and planning target volume (PTV) was the CTV plus a 1.0-mm margin. CIRT was performed with the anterior and right lateral portals. The total prescribed dose was 70.0 photon equivalent doses (GyE) in 5 fractions (Fx; 2 Fxs from the anterior portal and 3 Fxs from the right lateral portal) once daily, five times per week (Monday to Friday). Carbon ion doses were expressed in GyE, defined as the physical dose multiplied by the relative biological effectiveness (RBE) of the carbon ions, which was assumed to be 3.0[12].

After completing CIRT for choroidal melanoma, we continued with treating the right-sided lung cancer. The patient was immobilized in the prone position using a customized vacuum cushion and chest thermoplastic mask. CT images were obtained using four-dimensional CT (4DCT) with 3-mm thick images. GTV was delineated based on the 4DCT images, CTV was defined as GTV plus 5 mm, ITV was defined as

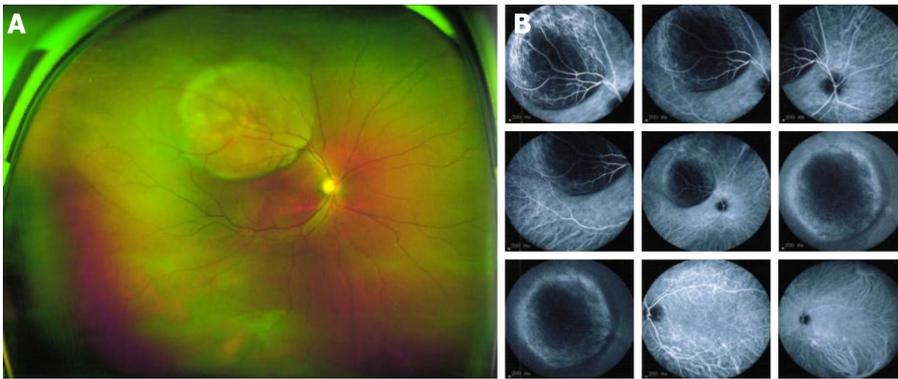


Figure 2 Ophthalmoscopy of the right eye. A, B: Solid dark gray mass in the posterior segment (choroid) with intense brown pigmentation, occupying posterior third of the vitreous chamber along with mild retinal detachment observed at the peripheral rim of the nodular choroidal mass. The mass size of 11.11 mm × 12.1 mm.

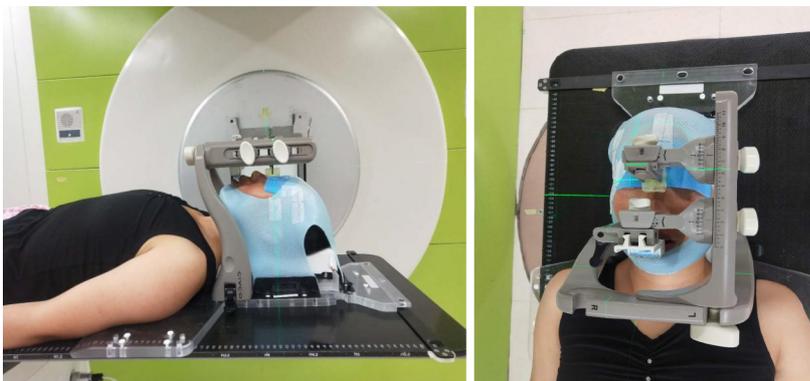


Figure 3 Head immobilization with trUpoint.

CTV plus the tumor motion on the 4DCT images, and PTV was expanded by 5 mm based on ITV. The CIRT plan delivered 72 GyE to the target volume in 16 Fx using the broad-beam method once daily, five times per week (Monday to Friday).

CIRT was planned using the carbon ion plan (ciPlan, version 1.0; IMP, Lanzhou, China). Treatment planning included a biologic treatment plan optimization procedure using the carbon ion Treat Plan (ciTreat) (version 1.0, IMP) treatment planning software system that considers local RBE values calculated by the ciPlan software based on the mixed beam model.

Efficacy evaluation was performed based on the Response Evaluation Criteria in Solid Tumours version 1.1 guidelines. The Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 guidelines were used to evaluate adverse events. The Radiation Therapy Oncology Group (RTOG) acute radiation injury classification criteria were used to evaluate radiation damage. During and after CIRT, there were only grade 1 adverse events and no grade ≥ 2 RTOG acute effects.

OUTCOME AND FOLLOW-UP

Ophthalmic examination before CIRT revealed complete loss of vision in the right eye. One month after CIRT, the patient's right eye began to perceive light and continued to gradually improve. [Table 1](#) presents findings of the ophthalmic examination. After 3 CIRT Fxs, mild right eye edema occurred. Upon CIRT completion, MRI demonstrated that the melanoma increased, with obvious retinal detachment ([Figure 4A](#)). One month after CIRT, the choroid tumor was smaller, and the retinal detachment was resolved ([Figure 4B](#)). Three months after CIRT, the right eye choroid tumor disappeared completely, achieving complete remission (CR) ([Figure 5](#)). The patient's right eye vision slowly returned ([Table 1](#)).

Table 1 Ophthalmic examination

	Right		Left	
	VOD	IOP, mmHg	VOS	IOP, mmHg
Before CIRT	HM/30 cm	9.8	1.0	16.4
1 mo after CIRT	Light perception	13.9	1.0	18.8
2 mo after CIRT	Hand motions	11.0	0.8	18.2
4 mo after CIRT	0.02	14.0	1.0	15.2
6 mo after CIRT	0.04	13.0	1.0	16.0

CIRT: Carbon ion radiotherapy; VOD: Vision right eye; VOS: Vision left eye; IOP: Intraocular pressure.

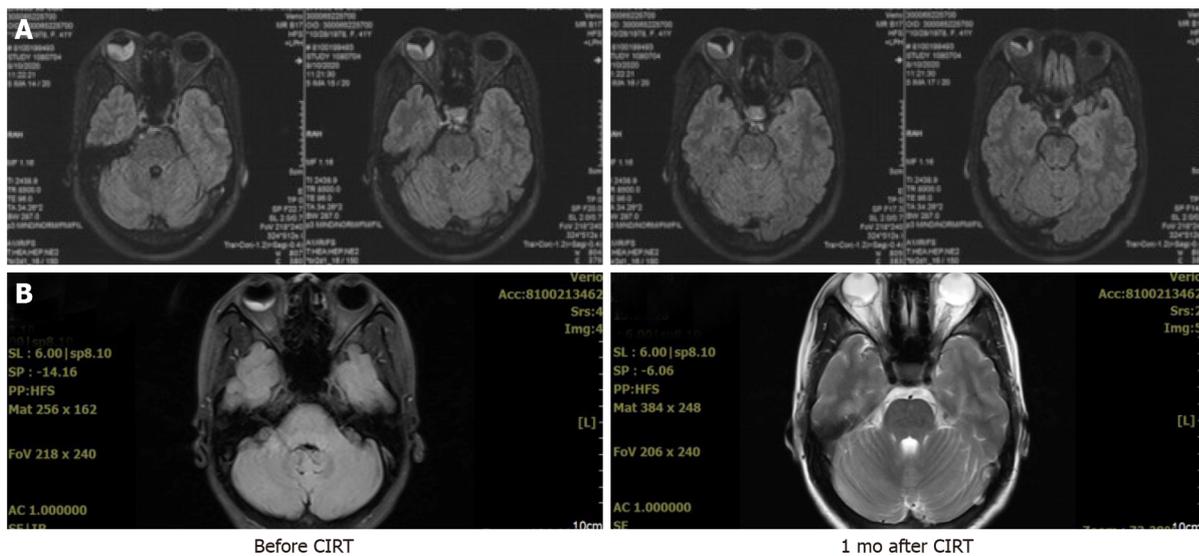


Figure 4 Images after 5 fractions of carbon ion radiotherapy, and 1 mo after carbon ion radiotherapy. A: The tumor is bigger, retinal detachment was obvious; B: The choroidal tumor of right eye was smaller and retinal detachment was improved. CIRT: Carbon ion radiotherapy.

Before CIRT, the lung cancer size was 4.7 cm × 5.2 cm. After CIRT, it regressed to 4.2 cm × 3.5 cm after 1 mo, 3.6 cm × 2.5 cm after 3 mo, and completely disappeared after 7 mo, with only a small area of pulmonary fibrosis, also achieving CR (Figure 6). The CTCAE evaluation showed grade 1 radiation dermatitis and right eye edema.

We recommended that the patient receive chemotherapy and immunotherapy because of the high risk of metastasis from the two lesions. However, out of economic consideration, the patient refused further treatment and expressed that they and their family were content with the results, which already exceeded their expectations. The patient felt very satisfied with the CIRT treatment. Seven months after completing CIRT, the patient's right eye vision was still weak, but no other treatment-related side effects were observed, and the patient felt good.

DISCUSSION

A middle vascular pigmented layer, including the iris, ciliary body, and choroid, comprises the uvea of the eye[13], and uveal tract melanomas are anterior or posterior tract lesions. Anterior tract melanomas involve the iris, and posterior tract melanomas involve the ciliary body and the choroid layer. Malignant uvea melanomas are more common in the choroid and ciliary body than in the iris.

Melanomas are highly malignant cancers[14]. There are several histological subgroups with various degrees of aggressive behavior and systemic metastases risk. Cytogenetic features, such as chromosome 3 monosomy and the mutations in the *GNAQ* and *BAP1* genes, are also related to higher aggressiveness and systemic spread.

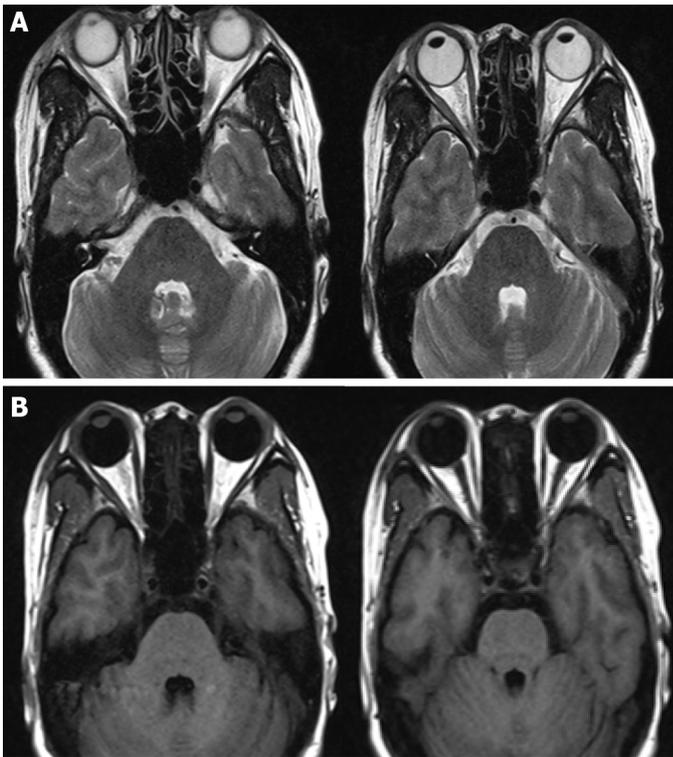


Figure 5 Choroidal tumor of the right eye disappeared completely 3 mo after carbon ion radiotherapy. A: T2W magnetic resonance imaging (MRI); B: T1W MRI.

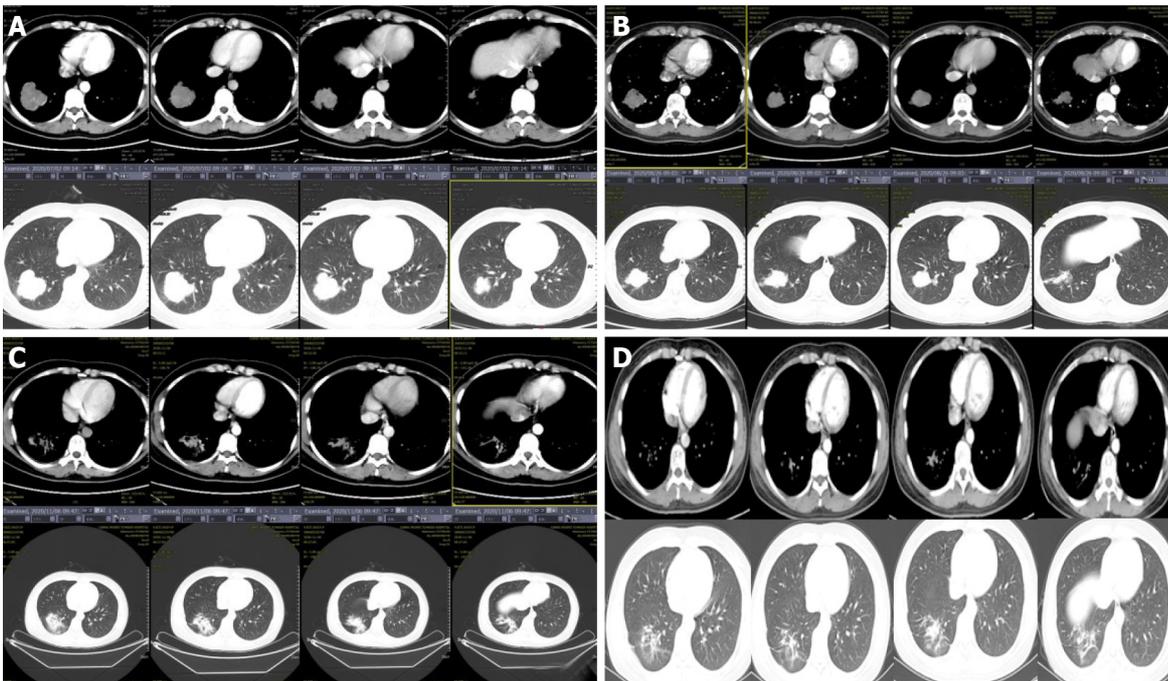


Figure 6 Images of lung tumor. A: Size of the lung tumor before carbon ion radiotherapy (CIRT) was 4.7 cm × 5.2 cm; B: Size of the lung tumor 1 mo after CIRT was 4.2 cm × 3.5 cm; C: At 3 mo after CIRT, the right lung tumor size was 3.6 cm × 2.5 cm; D: At 7 mo, the lung tumor disappeared completely, only showing a little pulmonary fibrosis.

Recently, *PALB2* and *MLH1* germline mutations were associated with a hereditary predisposition to the risk of uveal melanoma, and several other genes also have potential associations with uveal melanomas[15]. The clinical presentation of uveal melanoma relies on the mass location within the uveal tissue, size, pigmentation, associated bleeding, retinal detachment, inflammation, and extrascleral extension.

Most patients experience decreased visual acuity and blurred vision[1]. Although there are many cutting-edge treatment techniques, visual prognosis is usually poor, and many patients develop functional blindness in the affected eye. Further, metastasis to the liver and other organs is a primary cause of death despite recent advances in medical therapy[16].

Most patients with uveal melanoma undergo enucleation. Globally, a relatively small population of patients receive some form of radiotherapy. The most common radiotherapy modalities for uveal melanoma are plaque brachytherapy and PRT. Brachytherapy is effective for small-to-medium-sized uveal melanomas with thicknesses of less than 7 mm, whereas PRT is used when the uveal melanoma is larger or closer to the optic disc or fovea, taking advantage of the Bragg peak and biological profile. Newer techniques, such as stereotactic radiosurgery with CyberKnife, achieve similar local control rates with eye retention to PRT but have a poorer post-treatment visual prognosis[17]. Carbon ion beams have unique physical and biological properties that make high-precision, high linear energy transfer (LET) radiotherapy [12]. For choroidal melanoma, high-dose radiation with excellent dose conformity is necessary for optimal results, similar to PRT and plaque brachytherapy. Therefore, we expected that CIRT was suitable for treating this tumor. Moreover, the high LET characteristics of carbon ions make it an effective treatment that is likely to achieve comparable tumor control with a lower dose than PRT. NIRS results have demonstrated that for choroidal melanoma, CIRT is at least comparable to PRT[18,19].

Multiple primary malignant neoplasms indicate the simultaneous presence of two or more primary malignancies of different histological types in the same patient, which can affect multiple tissues and organs[20]. Currently, the most accepted criteria for diagnosing primary malignant tumors are that each tumor should be histologically confirmed as malignant, occur in different parts or organs, differ regarding the histological, cytological, and morphological features and immunohistochemical phenotypes, and the possibility that one tumor is the metastasis of another must be completely excluded clinically, radiologically, and pathologically[21].

CONCLUSION

We report a case of synchronous lung cancer and choroid melanoma. Both lesions were treated with CIRT, resulting in their complete resolution. The patient is currently experiencing relapse-free survival 7 mo after completing CIRT. The treatment outcome suggests that CIRT is an effective option for synchronous double primary lung cancer and choroid melanoma, and favorable results are likely.

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