“Case Report” A case of successful surgical resection and chemotherapy for unresectable hepatoblastoma with pulmonary metastases and for lung recurrence after liver transplantation

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Abbreviations: AFP alpha-fetoprotein, CT computed tomography, CTX chemotherapy, HB hepatoblastoma, ICG indocyanine green, LDLT living donor liver transplantation, LTx liver transplantation, OS overall survival, THP-ADR tetrahydropyranyladriamycin, US ultrasonography

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TRANSPLANTATION PROCEEDINGS

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Abstract

Background

Liver transplantation (LTx) is indicated for unresectable hepatoblastoma (HB) without distal metastasis. However, there is no consensus on the management of unresectable HB with pulmonary metastases, or on the treatment of recurrent HB. We report a successful case of metastatic HB treated with repeated lung resection, chemotherapy, and LTx. This study strictly complied with the Helsinki Congress and the Istanbul Declaration regarding donor source.

Case Report

Our case was a 1-year-old boy who developed PRETEXT III HB with multiple pulmonary metastases. The liver tumor was unresectable because it involved all hepatic veins. After three cycles of chemotherapy (cisplatin/carboplatin plus doxorubicin), the remaining two pulmonary metastases were resected and living-donor liver transplantation (LDLT) was performed. Five months after LDLT, a tumor recurrence was detected in the right lung. Repeat lung resection was performed followed by one cycle of chemotherapy (carboplatin plus doxorubicin). There has been no recurrence for 18 months since the last lung resection.

Discussion

Previous reports revealed that 14 patients, including the present case, underwent LTx after resection of metastatic HB pulmonary lesions. Of these patients, the 2-year survival rate after LTx was 91%.

Recurrence was reported in five patients, two of whom were successfully treated with repeated resection of the metastatic lesions. LTx after resection of lung recurrence may be a potential treatment for unresectable HB with pulmonary metastases.

1. Introduction

Hepatoblastoma (HB) is the most common liver tumor in childhood, typically occurring in children younger than 5 years old and accounting for 1% of all pediatric malignant tumors[1]. The overall survival rate in HB has improved with advances in chemotherapy (CTX), with a 5-year survival rate of 80%[2,3]. Liver transplantation (LTx) is a standard treatment option for HB if the tumor is still unresectable after preoperative CTX[3].

Pulmonary metastases are the most common metastatic lesion, and HB patients with pulmonary metastases have a worse prognosis than those without[3]. Patients with metastatic HB are treated with CTX followed by surgical resection of the primary lesion. LTx is performed if the metastatic lesions have been eradicated by CTX or surgical resection and if the primary lesions remain unresectable after CTX[3]. However, there is still minimal experience with LTx for metastatic HB and with pulmonary recurrence of HB after LTx. We report a case of recurrent pulmonary metastases after resection of metastatic pulmonary lesions and LTx for unresectable HB. This study strictly complied with the Helsinki Congress and the Istanbul Declaration regarding donor source.

2. Case report

A previously healthy 1-year-old boy presented to his primary care physician with complaints of fever and abdominal distention. An intrahepatic tumor was detected on abdominal ultrasound, and the patient was transferred to the pediatric institute. Abdominal computed tomography (CT) confirmed the presence of a

single large hepatic tumor of approximately 11 cm × 10 cm involving the right lobe and left medial lobe. The alpha fetoprotein (AFP) level was elevated, with a value of 816,975 ng/ml at diagnosis (Fig. 1). Chest CT detected multiple nodules in the bilateral lungs that were diagnosed as multiple pulmonary metastases. No biopsy was performed because HB was diagnosed by imaging and blood tests.

The tumor was classified as PRETEXT III and was unresectable because it involved all hepatic veins. CTX was performed as the modified SIOPEL-4 regimen[4], consisting of two cycles of cisplatin and THP-ADR (tetrahydropyranyl–adriamycin), and one cycle of carboplatin and THP-ADR. After CTX, the tumor shrank to 6.6 cm in diameter, but all hepatic veins were still involved and the tumor was determined to be unresectable. While most pulmonary nodules disappeared, chest CT detected two nodules of 3 mm in diameter in the right lung. Living donor liver transplantation (LDLT) was planned after eradication of the pulmonary lesions. Partial resection of the two lesions was conducted using CT-guided dye staining and indocyanine green (ICG) immunofluorescence. LDLT was performed 2 months after pulmonary resection, followed by two cycles of CTX with carboplatin and THP-ADR. The graft was a left lateral segment graft from the patient's mother and the ABO blood type was incompatible. The AFP level before LDLT was 1,089 ng/ml (Fig. 1). Immunosuppressant treatment was initiated with tacrolimus and prednisolone, with everolimus added later. Although there was no acute cellular rejection or vascular complications after LDLT, strangulated ileus occurred 3 weeks after LDLT, and an ileostomy was created. The ileostomy was closed 1 month later, and the patient returned home 3 months after LDLT.

Five months after LDLT, the AFP level rose again, to 77 ng/ml (Fig. 1), and chest CT detected a recurrence in the right lung. Repeat lung resection was performed with ICG immunofluorescence guidance, followed by one cycle of chemotherapy with carboplatin and THP-ADR. There have been no other recurrences for 18 months since the last lung resection.

3. Discussion

We reviewed all studies in which resection of pulmonary metastases was performed prior to LTx for the treatment of unresectable HB with metastasis to the lungs[1,5-13]. In 11 studies, including ours, 27 patients were treated for unresectable HB and pulmonary metastases. Of these patients, 13 demonstrated resolution of metastatic lesions with CTX and subsequently underwent LTx, while the other 14 had residual metastatic lesions after CTX and underwent resection of the pulmonary lesions followed by primary LTx (Table 1) [1,5-13]. The intervals between lung resection and LTx were 2 weeks[13], 3 months[1], 4 months[7], and in our case, 2 months. Of the 14 patients who underwent LTx after resection of metastatic pulmonary lesions, 10 (91%, three patients not stated) survived more than 2 years after LTx. Thus, the short-term outcome of LTx for unresectable HB after resection of metastatic pulmonary lesions was good. Five patients had tumor recurrence after LTx; their survival rate was 40%, and tumor recurrence was the cause of death in the three patients who died[5,9,12]. Of the five patients, three underwent repeat resection of metastatic lesions. One had multiple recurrent lesions in the lungs, brain, and bone after LTx and underwent multiple resections of metastatic lesions but died 28 months after LTx[12]. The other two

patients, including the present case, had recurrent lesions only in the lungs. They underwent repeat resection of metastatic pulmonary lesions after LTx, and survived for more than 2 years after LTx[13]. The remaining two patients who did not undergo resection of recurrent lesions died at 10 and 15 months after LTx, respectively[9,12].

In our experience, CT-guided dye staining and ICG immunofluorescence were useful for detecting small lesions during the resection of pulmonary metastases before and after LTx. Several studies on the efficacy of image-guided surgery using ICG immunofluorescence and CT-guided dye staining have been reported, and Yamamichi et al. reported the efficacy of CT-guided dye staining for the resection of lung metastatic lesions of approximately 3 mm in diameter in pediatric patients[13,14].

In conclusion, we experienced a successful case of unresectable HB with pulmonary metastases in which recurrences were treated with lung resection, CTX, and LDLT. In our literature review, both patients who had only pulmonary recurrence and whose lesions could be resected survived. We believe that LTx following resection of pulmonary metastases and resection of recurrent pulmonary lesions after LTx is a feasible option when lesions are located only in the lung. However, there is limited evidence and experience regarding both LTx for unresectable HB with metastases and pulmonary recurrence of HB after LTx, and more data are needed.

4. References

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5. Table

	Year	N with cleared lung metastases	N who received lung resection and LTx	N who had recurrence after LTx	Location of recurrence	Follow up years from LTx	Outcome
Suh MY et al.[13]	2008	1	1	1	Lung, brain, bone	2.3	**Repeated metastasectomy,** death by recurrence
Kosola S et al.[6]	2010	6	1	0	-	15.9	Death by cardiomyositis
Miyamura T et al.[12]	2010	2	1	0	-	2.0	Alive
Zsiros J et al.[7]	2013	1	1	0	-	NA.	Alive
Sakamoto S et al.[1]	2014	NA.	1	0	-	3.6	Alive
Samuk I et al.[8]	2016	1	1	1	NA.	0.8	Death by recurrence
Busweiler L et al.[9]	2017	0	2	NA.	-	NA.	NA.
Isono K et al.[10]	2018	2	1	0	-	4.4	Alive
Ramos GG et al.[11]	2018	0	3	1	Lung, brain, forearm	2.4	Death by recurrence
Uchida H et al.[5]	2018	0	1	1	Lung	4.8	**Repeated metastasectomy,** Alive
Our case	2021	0	1	1	Lung	1.9	**Repeated metastasectomy,** Alive
Total	-	13	14	5	-	-	-

LTx: liver transplantation, N: number of patients, NA.: not available

Table 1. Review of all studies in which resection of pulmonary metastases was performed prior to liver transplantation for the treatment of unresectable hepatoblastoma with metastasis to the lungs

6. Figure

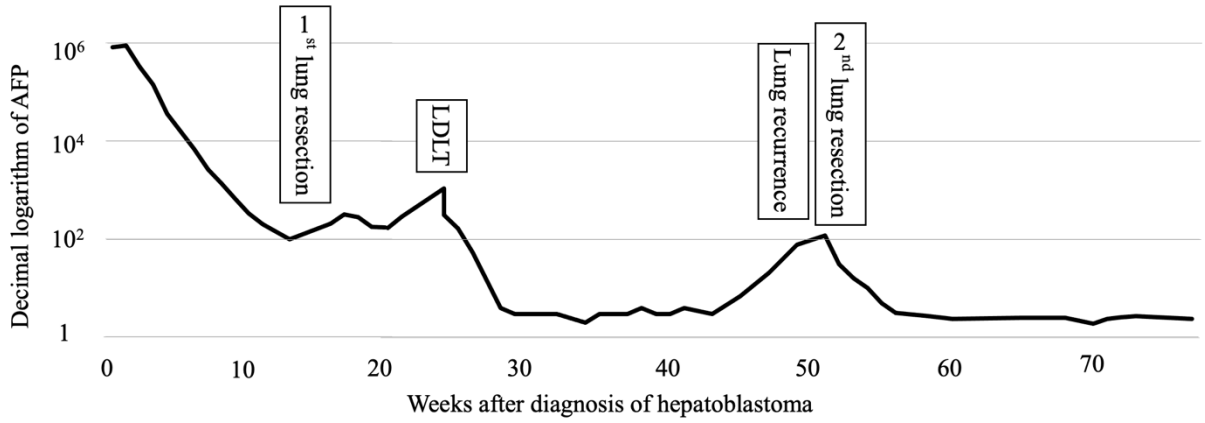

Fig.1 Changes in AFP (decimal logarithm of AFP) and surgical events of the case after the diagnosis of hepatoblastoma

AFP alpha-fetoprotein, LDLT living-donor liver transplantation