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CASE REPORT

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Indocyanine green navigation in minimally invasive resection of multiple metachronous pulmonary metastases of hepatoblastoma

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Abstract

Pulmonary metastases from hepatoblastoma (HB) have traditionally been identified by preoperative computed tomography scan image evaluation, and intraoperative visual and palpatory examinations through thoracotomy have been generally recommended. However, the safety and accuracy of surgery can be problematic in patients with small multiple lung metastases due to postoperative respiratory dysfunction risk secondary to decreased residual lung capacity in wedge resections. We present an 8-month-old patient with metastatic HB with multiple metachronous pulmonary lesions in whom thoracoscopic lung resections were performed guided by indocyanine green (ICG) administered intravenously 24 h earlier (0.5 mg/kg). ICG fluorescence allowed identification and limited resection of lung parenchyma, avoiding postoperative respiratory dysfunction. A total of 16 lung lesions were resected during four operations (two bilateral and two right thoracoscopies), with no postoperative complications. ICG-guided thoracoscopic surgery allowed identification and resection of metastatic nodules in both lungs during the same procedure, achieving a hospital stay of less than 3 days for each intervention. The patient is currently 24 months old and remains asymptomatic, with no distant disease at the last imaging control. ICG-guided resection via a thoracoscopic approach is particularly useful in patients with multiple and/or metachronous metastases requiring multiple surgical interventions.

KEYWORDS

fluorescence, hepatoblastoma, indocyanine green, pulmonary metastasectomy

INTRODUCTION

Preoperative computed tomography (CT) scan image evaluation and intraoperative visual and palpatory examinations have been traditionally performed for pulmonary hepatoblastoma (HB) metastases, therefore exploration through thoracotomy has been generally recommended.[1] However, the safety and accuracy of surgery can be problematic in patients with small multiple lung metastases due to postoperative respiratory dysfunction risk secondary to decreased residual lung capacity in wedge resections.

Indocyanine green (ICG) is a fluorescent dye that is well absorbed by hepatocyte-derived neoplastic cells and is excited by infrared radiation at 760 nm, emitting fluorescence at 830 nm.[2] Based on these unique characteristics, it has been applied to detect both liver and metastatic site lesions in HB,[3,4] although its utility in minimally invasive surgery has been rarely reported. We present the utility of ICG navigation in thoracoscopic resection of multiple metachronous pulmonary metastasis of HB.

CASE PRESENTATION

A 8-month-old girl was diagnosed as having PRETEXT III HB (segments 2, 3, 4, 5, and 8 affected) with bilateral lung

metastasis (5-mm nodule in the right upper lobe and two nodules in the left lower lobe, 8 and 6 mm in diameter), with alpha-fetoprotein values of 701 591 ng/ml (refrerence range 14–2300 ng/ml). Ultrasound-guided biopsy confirmed histological diagnosis of fetal/embryonal mixed epithelial HB, and intensive cisplatin chemotherapy was started with a 12% reduction in tumor volume achieved after two cycles (POSTTEXT III) and persistence of pulmonary nodules resistant to chemotherapy. Therefore, lung metastases resection followed by living-donor liver transplantation was decided, given the tumor unresectability.

Elective surgery with ICG-guided near-infrared (NIR) fluorescence was conducted. Preoperative intravenous ICG (0.5 mg/kg) was injected 24 h before surgery. A bilateral thoracoscopic approach was performed, with metastases nodules resection guided with ICG fluorescence using the Voyant Maryland Fusion® 5 mm device (Applied Medical), which allowed limited pulmonary

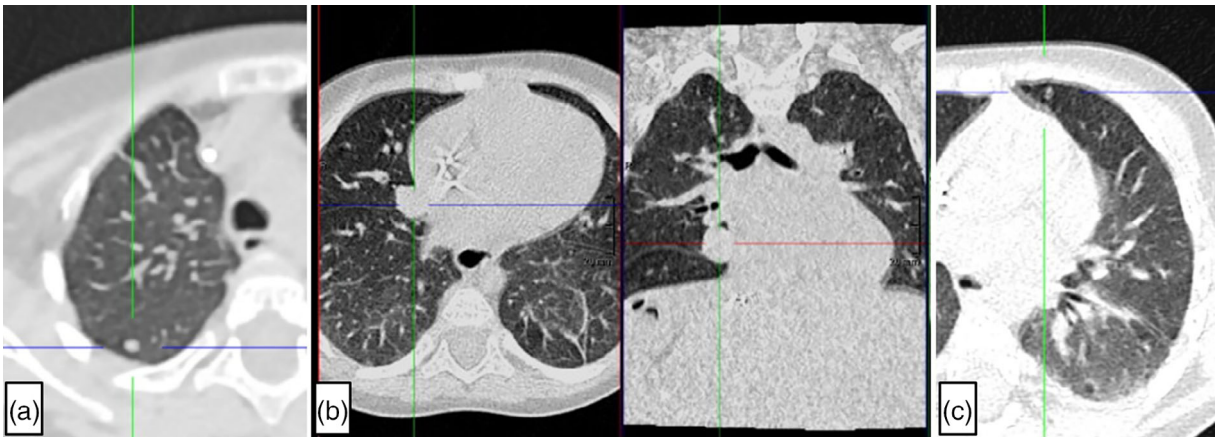

FIGURE 1 Thoracic CT scan showing several new solid nodular lesions. (a) Subpleural nodule in the upper segment of the right lower lobe. (b) Right paramediastinal nodule in the middle lobe, in contact with the pericardium and the minor cisura. (c) Subpleural nodule located in the area of the lingula in the right lung

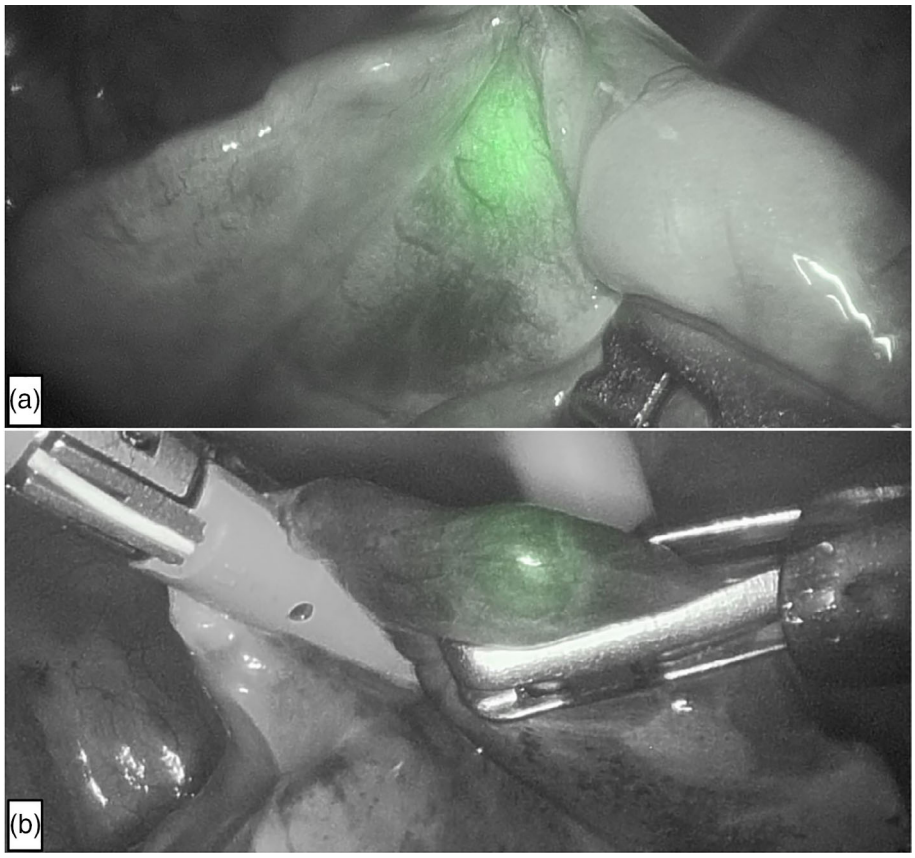

FIGURE 2 Thoracoscopic images with indocyanine green (ICG) fluorescence. (a) Right lower lobe metastatic lesion before resection. (b) Left lower lobe metastatic nodule resection guided with ICG fluorescence using the Voyant Maryland Fusion® 5 mm device

TABLE 1 Intraoperative features and histological findings of each intervention

Metastases location	ICG vision (Yes/No)	Resected segment size (mm)	Resected nodule size (mm)	Free-surgical margins (Yes/No)	Histological study
First intervention (8 months)					
Right lung					
Right upper lobe	Yes	17 × 13 × 8	6 × 6 × 5	Yes	FEME HB No necrosis
Left lung					
Left lower lobe (fissure)	Yes	15 × 10 × 12	8 × 6 × 5	Yes	FEME HB No necrosis
Left lower lobe (anterior)	Yes	30 × 11 × 10	6 × 5 × 5	Yes	FEME HB Necrosis
Second intervention (13 months)					
Right lung					
Right hilium adenopathy	Yes	15 × 15 × 12	15 × 15 × 12	Yes	FEME HB No necrosis
Right lower lobe (anterior)	Yes	10 × 7 × 5	5 × 5 × 5	Yes	FEME HB No necrosis
Right lower lobe (posterior)	Yes	20 × 10 × 7	3 × 3 × 2	Yes	FEME HB No necrosis
Right middle lobe	Yes	12 × 10 × 5	1.5 × 1.5	Yes	FEME HB No necrosis
Left lung					
Left lower lobe (upper)	Yes	17 × 10 × 4	5 × 2 × 2	Yes	Fetal HB No necrosis
Third intervention (15 months)					
Right lung					
Right lower lobe (anterior)	Yes	20 × 10 × 10	5 × 2 × 2	YES	FEME HB No necrosis
Right lower lobe (upper)	Yes	14 × 7 × 2	2 × 2 × 1	Yes	FEME HB No necrosis
Right lower lobe (posterior)	Yes	5 × 5 × 3	2 × 2 × 2	Yes	FEME HB No necrosis
Right apex adenopathy	Yes	6 × 4 × 4	2 × 2 × 2	Yes	FEME HB No necrosis
Fourth intervention (17 months)					
Right lung					
Right upper lobe (apex)	Yes	3 × 3 × 2	2 × 2 × 2	Yes	FEME HB No necrosis
Right middle lobe (upper)	Yes	15 × 7 × 5	5 × 5 × 4	Yes	FEME HB No necrosis
Right middle lobe (lower)	Yes	10 × 7 × 4	6 × 5 × 5	Yes	FEME HB No necrosis
Paratracheal adenopathy	Yes	2 × 2 × 1	2 × 2 × 1	Yes	FEME HB No necrosis

Abbreviations: FEME HB, fetal/embryonal mixed epithelial hepatoblastoma; ICG, indocyanine green.

parenchymal resection adjacent to the nodules, with free tumor margins in the histological study (Figure 1). A chest tube was placed in both hemithoraxes, which were removed after 24 h. The patient was discharged after 48 h without complications.

Two months later, tumor resection was performed by complete hepatectomy and living-donor liver transplantation, after verifying the absence of distant disease in a control CT scan, and immunosuppression with tacrolimus was started. However, 3 months later, bilateral lung metastasis was observed, and ICG-fluorescence guided bilateral thoracoscopy was performed, with identification and limited lung resection (Supporting Information Video S1 and Figure 2).

Two further operations were required for suspected metachronous pulmonary metastases in the following CT scans, right thoracoscopy at 15 and 17 months of age. ICG fluorescent imaging was applied during the resection of lung metastatic lesions, with the same protocol as previous interventions. A total of 16 lesions were resected over the four interventions, with no postoperative complications. Table 1 lists the intraoperative and histological findings of each intervention. All operations were performed using the same laparoscopic system (Stryker Endoscopy). The patient is currently 24 months old and remains asymptomatic, with no distant disease at the last imaging control.

DISCUSSION

Pulmonary metastatic lesions are easily detected by ICG fluorescence due to the lack of ICG accumulation in normal lung tissue, which results in a clear contrast generated in pulmonary metastases of hepatocyte neoplasic cell such as HBs or hepatocarcinomas.[3] In addition, one of the limitations of ICG fluorescence imaging is its inability to probe deep tissue, as the fluorescence emitted by ICG can only penetrate 5–10 mm of tissue.[2] However, typical HB metastatic lesion location in peripheral pulmonary areas reduces the impact of this drawback.[5] Moreover, intraoperative lung collapse by one-lung ventilation may facilitate detection of the metastatic lesion if it is not near the surface of the lung once the lung has been collapsed.[5]

ICG has been previously used in the resection of pulmonary HB metastases by an open approach.[3,4] Nevertheless, ICG-guided thoracoscopic resection of multiple metachronous pulmonary metastases of HB has not been reported to date. From our point of view, it has numerous advantages over the open approach, mainly due to the lower surgical impact compared to thoracotomy, with smaller incisions, less postoperative pain, and therefore shorter length of hospital stay. Due to this lower surgical aggressiveness, in cases with bilateral lesions it is feasible to resect lesions of both lungs during the same surgical procedure, without requiring resection of the contralateral side 3–4 weeks after the first intervention. In our patient, three bilateral and one unilateral thoracoscopies were performed, and in all cases the patient was discharged 48–72 h after surgery.

An additional advantage of pulmonary metastases resection by a minimally invasive approach in patients with HB is the easier and more accessible approach in case of recurrences or new metachronous lesions as in our patient, since the formation of adhesions to the chest wall is minimal with thoracoscopy compared to thoracotomy. In our case, it allowed us to perform four thoracic interventions using the same incisions and entry routes in both hemithoraxes without any incidence or complication, achieving adequate visualization of all the pulmonary lesions by ICG fluorescence. In this case, although the fluorescent lesions were all resected during the first bilateral thoracoscopy, metachronous metastases emerged 5 months after this operation (3 months after living donor liver transplantation). A possible reason is that there were extremely small lesions that were not detectable and grew rapidly. These metastases may have increased in size after the onset of the immunosuppression required to prevent rejection after liver transplantation. This involves an unstable balance between achieving an adequate level of immunosuppression to avoid immunological complications of liver transplantation and an adequate functioning of the immune system to detect HB cancer cells in the pulmonary lymph nodes, which may spread to the lung parenchyma. The smallest lesion detectable by the ICG fluorescent imaging in our patient was 1.5 mm in diameter, so lesions smaller than this size might not be detected.

In conclusion, ICG fluorescent imaging is relatively simple and complementary to conventional techniques, while providing additional information for the intraoperative localization of pulmonary metastasis in HB. ICG-guided resection via a thoracoscopic approach is particularly useful in patients with multiple and/or metachronous metastases requiring multiple surgical interventions.

AUTHOR CONTRIBUTIONS

CDM designed, conceptualised and wrote the initial draft of the manuscript. KE and MS edited graphics and tables. FHO critically revised the manuscript. All authors approved the final version of the manuscript.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study obtained the approval of the institutional ethics committee. The child's parents signed a written informed consent form, which included the publication of the images of this case.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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