A Case Study On Pulmonary and Right Atrial Cardiac Metastases Among Children with Hepatocellular Carcinoma

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Abstract: The occurrence of hepatocellular carcinoma (HpC) hepatoblastoma (HB) in children with metastases in both the right atrium and lungs is a rare occurrence. Overcoming these challenges in treatment is an intricate and demanding process. We present a rare clinical case involving a pediatric patient diagnosed with hepatoblastoma (HpC) that exhibited metastasis to both the lungs and the right atrium. In response to this complex condition, surgical intervention was undertaken, complemented by a carefully administered combination of chemotherapy. This dual-phase chemotherapy, administered both pre- and post-operation, served as an adjuvant treatment strategy. The primary objective of this comprehensive therapeutic approach was to attain full remission, eliminating any traces of the malignancy. The intricacies of managing metastatic HpC in pediatric cases underscore the importance of multidisciplinary interventions, emphasizing the critical role of surgery and adjuvant chemotherapy in the pursuit of a positive treatment outcome. Thus, individuals with HB that has spread to the lungs and right atrium may have a favorable outcome by undergoing proactive and multimodal therapy.

Keywords: Atrium, hepatoblastoma, lung, metastasis and prognosis

Funding: This case study did not receive any specific grant from any funding agencies in the public, commercial or not for profit sectors.

Citation: Dr.Sumalatha KR.,Dr.John Abraham.,Dr. Pachai Pandy. A Case study on Pulmonary and Right atrial cardiac metastases among children with hepatocellular carcinoma.(2024).Int. J. Trends in OncoSci.2(2), 41-44 http://dx.doi.org/10.22376/ijtos.2024.2.2.41-44

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1. INTRODUCTION

Despite being a relatively uncommon malignant solid tumor, HpC or HB is the predominant malignant liver tumor in children, with an annual incidence of 1.2-1.5 million persons. The general prediction of HpC is favorable, with a survival rate ranging from 71% to 80%. Though, the survival rate before receiving combination treatment is just 30%. The prognosis of HpC is primarily influenced by many key criteria, including the PRETEXT stage of illness before to therapy, the amount of serum alpha fetoprotein (AFP), the existence of numerous lesions and distant metastases, and the histological categorization of undistinguishable small cell tumor. Lung metastasis is often seen in the context of distant metastasis, occurring in 10%–20% of individuals with HpC. The overall survival rate for individuals with lung metastasis ranges from 25%–50%. Subsequent research have shown a correlation between lung metastasis and other organ involvement outcome. While vascular involvement is often linked to HpC, it does not significantly impact the prognosis. There is a scarcity of reports documenting instances of HpC that exhibit both lung and right atrial metastasis. Reports of a singular occurrence of HpC accompanied by an atrial tumor thrombus and metastases in many locations is a rare case. Effective management with a comprehensive and coordinated surgical approach was reported in a similar case of HpC with metastases in the lungs and right atrium that achieved total cure after six rounds of chemotherapy. There was a reported instance of complete remission of HpC after undergoing liver resection. The results specify that combining postoperative chemotherapy, including both preoperative and postoperative chemotherapy, with surgery is critical in the treatment of metastatic HpC. Treatment protocols for HpC vary depending on disease stage and risk stratification. High-risk individuals undergoing a more intensive cisplatin and doxorubicin regimen have shown improved survival rates, albeit with significant toxicity limitations on dosages. Conversely, a novel treatment strategy incorporating subsequent chemotherapeutic drugs like oncovin (vincristine) and camptosar (irinotecan) has proven highly effective against huge risk HpC. Our case study aims to address the the necessity and optimal duration of preoperative neoadjuvant chemotherapy for pediatric hepatic malignancies. This case study provides insights and therapeutic approaches from various medical groups and to provide a concise overview of medical, healing, and therapy of HpC with concurrent right cardiac metastases and lung.

2. CASE PRESENTATION

A 5-year-old male child was taken to a nearby medical facility around 6 years ago due to experiencing discomfort in the stomach region. A hepatic mass was detected using abdominal ultrasonography. CT scans of the chest and abdomen, together with cardiac ultrasonography, have verified the existence of a substantial tumor in the liver obstructing the median, the right portal vein, left and right hepatic veins and the inferior vena cava (V. cava). Additionally, a tumor thrombus in the right atrium, pleural effusion in both lungs, and nodules in both lungs were identified. Upon diagnosis, his blood alpha-feto-protein (AFP) level was measured at 30,883 nanograms per milliliter (ng/mL). A comprehensive examination of his whole body revealed no more distant metastases. He has no notable medical background or familial medical background. A biopsy was declined due to parental refusal. Three days later, he underwent preoperative induction chemotherapy at the hospital. The chemotherapy regimen involved cisplatin at a dosage of 20 mg/m² administered from Day 1 to Day 5, pirarubicin at a dosage of 25 mg/m² administered from Day 1 to Day 3, and cyclo-phosphamide at a dosage of 810–1,100 mg/m² controlled on Day 1 (regimen 1). This protocol was then interchanged with a second regimen in which cyclophosphamide was swapped by etoposide at a dosage of 100 mg/m² controlled from Day 1 to Day 4 (regimen 2). After 2 cycles of preoperative neo-adjuvant chemotherapy, significant reductions in the size of the lung tumors and liver, as well as the atrial tumor thrombus, were observed. The individual's blood AFP level fell to 4,077 ng/mL. After a period of two months, he had a surgical procedure to remove a mass in his liver and to remove a blood clot in the vein connecting the inferior vena cava and the right atrium. The postoperative pathological examination showed the presence of HpC, namely of the embryonal and fetal subtypes. Following the surgery, he had ten rounds of postoperative chemotherapy at our institution. The first regimen included alternating treatment between cisplatin (90 mg/m²) and vincristine (1.5 mg/m²) on Day 1. The second regimen, known as regimen 3, consisted of administering 5 fluorouracil (300 mg/m²) on Day 2–3. After undergoing this therapy, the lung metastatic lesions disappeared entirely. After a period of six months, the administration of chemotherapy after surgery was discontinued. At this point, the individual's blood AFP level was measured to be 2.48 ng/mL, and not any cancers were seen in the lungs and liver. He was monitored for a period of 2 months using frequent CT imaging and serum AFP testing. At the end of this period, his AFP level rose to 526 ng/mL. The results of the chest and abdominal CT scan showed a reappearance of tumors in both the lungs and liver. Consequently, the individual had surgical removal of both lung and liver tumors 1.6 years after the first diagnosis. The pathological diagnosis once again confirmed the presence of HpC, namely the embryonal and fetal subtypes. Following the surgery, the postoperative serum AFP level reduced to 83.04 ng/mL. After the surgery, the individual received six cycles of chemotherapy following this specific protocol: irinotecan 50 mg/m² and cisplatin 20 mg/m² were administered from Day 1 to Day 5, vincristine 1.5 mg/m² was given on Day 1, and cyclophosphamide 250 mg/m² was administered from Day 2 to Day 4. It was interchanged with another treatment plan called regimen CSVD, which consisted of cisplatin 20 mg/m² and 5 fluorouracil 200 mg/m² from Day 1 to Day 5, vincristine 1.5 mg/m² on Day 1, and pirarubicin 25 mg/m² on Day 2 and Day 3 (regimen 5). After a period of two years, the administration of chemotherapy after surgery was stopped, and the serum AFP level was found to be 1.22 ng/mL. He had monthly follow-up examinations, which consistently showed no signs of the disease returning. He has been completely free of the disease for 5 years and 3 months. The presence of a liver tumor, as well as lung and right atrial metastases, was identified at the first diagnostic, as shown in Figure 1 A,C and E. A complete removal of the tumors was carried out, and no remaining tumors were seen following the second surgery with post-operative chemotherapy as illustrated in Figure 1 B, D and F.
3. DISCUSSION

This case of HpC with the presence of pulmonary metastases and the formation of a tumor thrombus in the right atrium. The 3-year survival rate without disease recurrence for children with lung and liver lesions is 56%. However, it decreases to 37% when total liver resection is carried out, and residual lung lesions persist. This corresponds with the finding that the prognosis of HpC is predominantly influenced by the presence of lung metastasis. The individual detailed in this article underwent liver tumor excision following preoperative neoadjuvant chemotherapy. In instances of high-risk HpC, such preoperative therapy is considered indispensable. This case study demonstrated the effectiveness of a more intense treatment regimen using cisplatin before surgery for the management of metastatic HpC. Based on our prior experiences with HpC chemotherapy, we provided therapies that varied between cisplatin established regimens 1 and 2. Following the comprehensive treatment of HpC, our primary approach for managing metastatic individuals was the administration of the C5VD adjuvant chemotherapy regimen, which includes cisplatin. Neoadjuvant chemotherapy administered prior to surgery for metastatic hepatoblastoma may successfully decrease the mass of liver cancers, facilitating their total removal, and may also result in a drop or elimination of metastatic lung lesions. Hence, in this case study,
patient received neoadjuvant chemotherapy before undergoing liver resection, which led to complete elimination or notable improvement of the lung lesions. Therefore, it is critical to provide neoadjuvant chemotherapy in individuals with HpC. Hence, the presence of metastases in the right atrium did not seem to have a substantial impact on the scenario of HpC. In addition, it is important to closely monitor children with HpC and pulmonary metastases within the first 6 months after discontinuing treatment. This is necessary to detect any recurrence, particularly in the liver and lungs, even if lung lesions may have disappeared following neoadjuvant and postoperative chemotherapy. For achieving full remission in instances of lung recurrence, it is necessary to surgically remove the metastases and provide postoperative chemotherapy. Instances of hepatoblastoma with tumor infiltration into the lower vena cava and subsequent extension into the right atrium are classified as huge risk instances. Nevertheless, due to their infrequency, no associated consequences have been documented. The metastases in the right atrium may have less impact on the function of the heart and lungs. Additional research with more extensive sample numbers is required to verify if relapse may impact the prognosis of HpC in these instances. Elevated levels of Serum AFP are often seen in the majority of cases of HpC, providing valuable assistance in the diagnosis, monitoring of therapy efficacy, and assessment of individual prognosis. After analyzing the changes before and after surgery, and throughout chemotherapy, we have determined that the serum AFP level may serve as a useful signal for detecting tumor recurrence. It is also an essential marker for HpC. Utilizing second-line chemotherapeutic medicines in the treatment of HpC is anticipated to enhance the prognosis. The concurrent administration of vincristine and irinotecan has shown to be efficacious in treating high-risk or relapsed hepatoblastoma, while also exhibiting manageable side effects. As a result, the tumors significantly decreased in size, allowing for the surgical removal of the tumors and the blood clots in the right atrium. Subsequent administration of chemotherapy after surgery led to the total eradication of the lung abnormalities and restoration of serum AFP levels to a normal state. Instances of relapse resulted in complete remission, indicating the effectiveness of the second-line medication irinotecan when used in the chemotherapeutic treatment plan for the recurrence of HpC or the spread of cancer to the lungs. Overall, the occurrence of HpC with pulmonic metastases and perfused right atrial tumor thrombosis is few and frequently linked to later stages of the illness. The primary treatments for these instances include a combination of many medical disciplines, such as surgical intervention, as well as the administration of neoadjuvant chemotherapy before surgery and postoperative chemotherapy. Administering neoadjuvant chemotherapy might decrease the size of the atrial thrombus, facilitating its complete removal, whereas postoperative chemotherapy can help prevent the reappearance of atrial tumor thrombus. The likelihood of liver and lung cancer recurrence influences the importance of vigilant monitoring to swiftly detect any relapse. When faced with such situations, the combination of irinotecan and conventional chemotherapy medications can be used to achieve a favorable overall prognosis.

4. FINANCIAL SUPPORT AND SPONSORSHIP

Nil.

5. AUTHORS CONTRIBUTION STATEMENT

Dr. Sumalatha KR wrote the initial draft. Dr. John Abraham, Dr. Pachai Pandy contributed to critical revision and supervision. All authors reviewed the manuscript.

6. CONFLICTS OF INTEREST

There are no conflicts of interest.

7. REFERENCES