CASE REPORT

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Sorafenib as Salvage Therapy after Radioembolization in a Patient with Huge Hepatocellular Carcinoma in a Geriatric Patient with Normal Alfa-Feta Protein Levels: A Case Report

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Abstract

Hepatocellular carcinoma (HCC) is a common type of liver cancer and is a widespread cause of death from malignancy worldwide. The diagnosis of HCC is made by radiological liver imaging and the presence of serum alfa-fetoprotein. Our patient, a 75-year-old man, had a mass (14x17 cm) in the right liver lobe. Serum AFP was normal. There were no signs of metastasis except for several suspicious subcentimetric lymph nodes. Diagnosis of HCC confirmed by liver biopsy. He was evaluated by a multidisciplinaryteam. The team favored the Yttrium-90 radioembolization treatment. The tumor showed slight regression. However, a new subcentimetric nodule was detected in the posterior segment of the left lower lobe of the lung. Sorafenib was initiated as a salvage drug by medical oncology.

In conclusion, this case shows that with HCC can present with normal AFP levels even in advanced diseases. Biomarkers other than AFP are believed to contribute to HCC tumor growth. Moreover, we can infer from this case that the tumor shows less aggression in HCC patients with normal AFP levels. The treatment of HCC should be based on the patient's age and comorbidities.

Keywords: Hepatocellular carcinoma, serum alfa-fetoprotein, geriatric oncology, cancer management, older patient

Introduction

Hepatocellular carcinoma (HCC) is a common type of liver cancer and is a widespread cause of mortality worldwide. Although it is highly prevalent in Asia and Africa, it is the leading cause of death in Europe and America (1,2).

HCC is also one of the most aggressive tumors, causing frequent intrahepatic metastasis and common recurrence after surgery. Cirrhosis represents the greatest risk factor for this malignancy and is the main indicator for screening and surveillance. Extrahepatic metastases to the lungs, brain, bone, and adrenal glands are observed in patients with advanced-stage intrahepatic tumors (3). Vascular invasion and tumor thrombosis are usually detected in most advanced HCC cases (4). In general, the diagnosis of HCC is identified by radiological liver imaging and the presence of serum alfa-fetoprotein (AFP), without the need for biopsy. The management of HCC requires a multidisciplinary approach including surgeons, radiation oncologists, radiologists, pathologists, hepatologists, and medical oncologists. With the advantage of having more than one treatment option for patients with HCC, there is a decision-making approach according to the patient's clinic. Systemic pharmacological therapy options are frequently preferred for older patients with HCC. In recent years, immune checkpoint inhibitors have played an essential role in HCC management. Sorafenib was the first multikinase inhibitor used as a treatment option for HCC for more than ten years. Sorafenib or lenvatinib as first-line therapy and cabozantinib, regorafenib, or ramucirumab as second-line therapy are approved for most patients with HCC receiving current systemic treatment (5).

Here we report a patient diagnosed with a massive mass of HCC with imaging and tissue sampling whose serum AFP level was

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normal and hepatitis markers were negative. He had no prior history of alcohol consumption. Imaging revealed no signs of cirrhosis or metastasis. With this rare case, we aimed to contribute to the diagnosis and treatment management of HCC in older patients in light of current guidelines.

Case Report

A 75-year-old man with a history of pacemaker implantation due to sick sinus syndrome and Parkinson's disease local hospital with difficulty starting urination. An abdominal ultrasound was performed because of his complaints regarding urination. Ultrasound revealed a mass in the right liver lobe of approximately 15.8x12.8 cm with a clear boundary and uneven internal echo mass in the liver. Serum AFP was 1.65 µg/L (normal value <13 µg/L). His routine biochemistry showed no abnormalities. Hepatitis B virus surface antigen was negative. Then, he was referred to our hospital for further investigation and treatment.

Abdominal MRI revealed a 14 16.5 13 cm lesion in the posterior right lobe of the liver with satellite lesions and a 17x14 mm lesion with significant contrast enhancement and diffusion restriction. Wash-out pattern was not reported. Repeat serum α-fetoprotein (AFP) level was 1.84 µg/L (normal value <13 µg/L). Ultrasound-guided liver biopsy was performed, which confirmed a diagnosis of HCC. Because AFP negative, a pathology revision was ordered to exclude the fibrolamellar variant of HCC However, there were no significant features for the particular variant, and genetic testing was negative for both DNAJB1-PRKACA oncogenic driver fusion gene and PRKAR1A abnormalities. Immunophenotype analysis revealed that CK7 and CD68 levels were negative.

Positron emission tomography-computed tomography revealed a 15-cm right hepatic mass with high 2-fluoro-2-deoxy-D-glucose (FDG) metabolism (SUV_{max} =9.69). There was also a 14x18 mm nodular lesion in segment 4A of the liver with no abnormal FDG metabolism, suggesting a benign liver lesion. There were no signs of pathological FDG metabolism apart from several subcentimetric paraacealiac lymph nodes suspicious for primary tumor metastasis. The patient was evaluated by a multidisciplinary hepatobiliary surgery team in cooperation with the Department of Diagnostic Radiology, Department of Medical Oncology, and Nuclear Medicine. The team favored Yttrium-90 radioembolization treatment over surgery because of his co-morbidities. Positron emission tomography/computed tomography scan was ordered to assess treatment response. The tumor volume showed slight regression. However, a new subcentimetric nodule with minimal metabolism was detected in the posterior segment of the lung's left lower lobe, which raised suspicion for metastasis. Based on this evaluation, the patient was transferred to medical oncology for further treatment options. Sorafenib was initiated as a salvage therapy, and the patient is currently followed up at frequent intervals by the medical oncology department.

Discussion

HCC is a common leading cause of cancer-related death, and its prevalence is increasing worldwide. The age at diagnosis is increasing in adults. Thus, HCC is a rising issue in these vulnerable patients. Therefore, reliable management strategies are required for older patients with HCC.

The major risk factors for developing HCC are viral hepatitis, cirrhosis, obesity, diabetes mellitus, and non-alcoholic steatohepatitis (NASH) (6). It is based on the typical radiological signs in dynamic contrast imaging for diagnosing HCC and uses AFP as a standalone tool.

AFP is routinely used as a tumor marker for screening, diagnosis, and treatment follow-up of HCC. AFP-positive HCC can be easily diagnosed based on typical imaging features and high serum AFP levels. Some studies have shown that AFP is a predictor of tumor development (7).

Most AFP-normal HCCs are also associated with small and early-stage tumors. However, some patients with HCC have normal AFP levels, even in advanced diseases. Some studies have shown that most of these HCC patients with normal AFP levels are associated (NASH) (8,9). A study found that HCC patients with normal AFP levels were significantly older (10).

It has also been suggested that AFP, as a diagnostic serum tumor marker, has functional roles in HCC and is associated with aggressive HCC behavior, metastasis, and poor prognosis (11). This information shows that our patient with a large liver mass had a normal AFP value and significant metastases. It is also unknown whether large tumors show more significant invasion. In another study, HCC patients with higher serum AFP levels had a larger tumor size, more frequent hepatic cirrhosis, portal vein thrombosis and metastasis, high Child-Pugh score, and advanced clinical stage (12).

Studies show that many factors other than AFP contribute to increased HCC size. Inflammatory cytokines are hypothesized to be important in HCC growth. Therefore, new biomarkers are required (13). Some studies have focused on DNA, RNA, and protein biomarkers in addition to AFP for HCC diagnosis (14).

Successful HCC management requires a multidisciplinary approach, including surgeons, radiation oncologists, radiologists, pathologists, hepatologists, and medical oncologists (15,16). Geriatric patients with moderate-to-advanced HCC at diagnosis are poorer candidates for surgical resection or transplantation because of comorbid conditions and compromised liver regeneration. In an older patient with multimorbidities, as preferred in our patient, Yttrium-90 radioembolization therapy was the main treatment for HCC. Systemic therapy is considered when extrahepatic nodal or distant metastatic disease is present or if the patient has a tumor burden or other comorbid conditions (17).

The patient profile impacts decision-making regarding the use of different pharmacological options against HCC. Systemic therapy is a part of the standard disease management for patients with advanced HCC. Systemic treatments are frequently preferred for patients with HCC, especially for patients for whom surgery is not possible. Nowadays, immune checkpoint inhibitors have been used to treat HCC Traditionally, the multikinase inhibitor sorafenib has been one of the most frequently approved agents for over a decade (18). There are studies evaluating immunotherapies in all stages of HCC that could change the management of disease (19).

We demonstrated that many treatment options for older HCC patients, especially pharmacological treatments, are preferred over surgical treatment because of comorbidities and vulnerability.

Conclusion

HCC is a common liver malignancy worldwide, with a high mortality rate. AFP is routinely used as a tumor marker for the diagnosis and follow-up of cancer. However, some patients with HCC have normal AFP levels, even in advanced diseases. Therefore, AFP is not an ideal reliable biomarker, and the diagnosis of HCC relies mainly on imaging. New biomarkers are needed. In addition, in HCC patients with normal AFP, the tumor shows less aggression, as in this case. There are multiple treatment options for patients with HCC. To select the best treatment options for each patient, a multifactorial and multidisciplinary approach must be shaped by the patients' characteristics and the availability of treatment. Radioembolization and systemic pharmacological treatments are appropriate treatment options for patients with liver cancer in older adults.

Considering this case, we aim to contribute to the literature by attracting attention to the diagnostic and therapeutic management of HCC, the latest evidence, and the recommendations in the guidelines for accurate HCC management.

Ethics

Informed Consent: Informed consent was obtained.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: G.U.A., Data Collection or Processing: G.U.A., B.B.K., R.B.D., Analysis or Interpretation: G.U.A., R.B.D., Writing: G.U.A., B.B.K., R.B.D., A.D.

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