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# Solitary Muscle Metastasis of Hepatocellular Carcinoma to the Biceps Femoris Muscle with Only Elevated Serum PIVKA-II: A Case Report

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Statistical Analysis C  
Data Interpretation D  
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**Conflict of interest:** None declared

**Patient:** Male, 81  
**Final Diagnosis:** Solitary muscle metastasis of hepatocellular carcinoma  
**Symptoms:** A growing mass in the proximal posterior thigh  
**Medication:** —  
**Clinical Procedure:** Operation  
**Specialty:** Orthopedics and Traumatology





**Objective:** Rare disease  
**Background:** Hepatocellular carcinoma (HCC) is a common primary hepatic cancer. Regardless of its metastatic potential, metastasis to skeletal muscle is rare, especially to one solitary muscle. The diagnostic efficiency of Protein induced by Vitamin K absence/antagonist-II (PIVKA-II) has been illustrated sufficiently and it has been proven that PIVKA-II is a potent biomarker and independent of alpha-fetoprotein (AFP). The present report describes a case of solitary muscle metastasis with PIVKA-II elevation.

**Case Report:** An 81-year-old man noticed a growing mass in the proximal posterior thigh, and it was found to be a solitary tumor in the biceps femoris muscle. He had undergone a medial segmentectomy for primary HCC and transcatheter arterial chemoembolization for an intrahepatic recurrence 7 and 4 years before, respectively. The level of PIVKA-II was elevated to 11 400 mAU/mL, but the alpha-fetoprotein (AFP) level was normal. Elevation of PIVKA-II to over 50 mAU/mL had been observed 7 months before the muscular lesion was first observed. When the solitary metastasis was diagnosed, a wide resection was performed in the same way as for primary sarcoma, and the PIVKA-II value decreased to 71 mAU/mL. No recurrence at the muscle was observed, but multiple lung metastases were seen and the PIVKA-II was elevated to 1410 mAU/mL 4 months after the resection.

**Conclusions:** Resection of the solitary muscle metastasis helped control the local metastatic lesion and helped with ability to perform daily activities, as well as possibly prolonging survival. PIVKA-II is an important biomarker for HCC surveillance in conjunction with alpha-fetoprotein (AFP). PIVKA-II can be independent of AFP. Examination of the whole body is still necessary in cases with elevated PIVKA-II in order to detect extrahepatic metastasis.

**MeSH Keywords:** Carcinoma, Hepatocellular • Magnetic Resonance Imaging • Neoplasm Metastasis

**Full-text PDF:** <https://www.amjcaserep.com/abstract/index/idArt/913730>

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## Background

Hepatocellular carcinoma (HCC) is a common primary hepatic cancer. The most frequent sites of hematogenous metastases include the lungs, the bones, and the adrenal glands [1]. HCC with hematogenous spread to the skeletal muscle is rare, with a reported incidence rate of 0–1.5% [2,3]. With HCC, a solitary metastasis to the skeletal muscle is extremely rare, and only 3 cases reported in the English language literature [4–6].

HCC is an aggressive cancer, and the prognosis for patients with extrahepatic metastasis is poor due to limited effective treatment options. It has been reported that the cumulative survival rates at 1 year, 3 years, and 5 years after the diagnosis of extrahepatic metastasis were 39.3%, 7.4%, and 4%, respectively [7]. Recently, it was reported that surgical resection of HCC metastases prolonged survival in selected patients. When only 1 or 2 extrahepatic tumors were present, surgical resection was beneficial for patients with HCC who had good hepatic reserve, good performance status, controlled intrahepatic disease, and no portal vein invasion [8].

Protein induced by Vitamin K absence/antagonist-II (PIVKA-II) and alpha-fetoprotein (AFP) are widely used as tumor markers for HCC. The diagnostic efficiency of (PIVKA-II) has been illustrated sufficiently and it has proven that it is a potent biomarker and independent of alpha-fetoprotein (AFP) [9].

The present case report describes a solitary HCC metastasis to the biceps femoris muscle. Before the metastatic lesion in the muscle was detected, the serum level of PIVKA-II was elevated, but the AFP level was normal. The value of PIVKA-II and AFP for a solitary metastasis to a single muscle is reviewed in reported cases.

## Case Report

A 74-year-old Asian male patient had been diagnosed with HCC associated with hepatitis C infection, and underwent medial segmentectomy. When the patient was 77 years old, he underwent transcatheter arterial chemoembolization (TACE) for intrahepatic recurrence of HCC.

The patient noticed a small palpable mass at the posterior side of his right proximal thigh. The size of the lesion increased gradually. Two months after the patient first detected the mass, he was referred to our institute with a working diagnosis of primary soft-tissue tumor; the mass was 7 cm in diameter. The tumor site had no tenderness or radiating pain. Magnetic resonance imaging showed a well-defined lesion in the biceps femoris muscle. The T1-weighted images of the tumor revealed heterogeneous signal intensity slightly higher than that of the

muscle, and the T2-weighted images revealed heterogeneous high signal intensity with iso to high in the muscle (Figure 1).

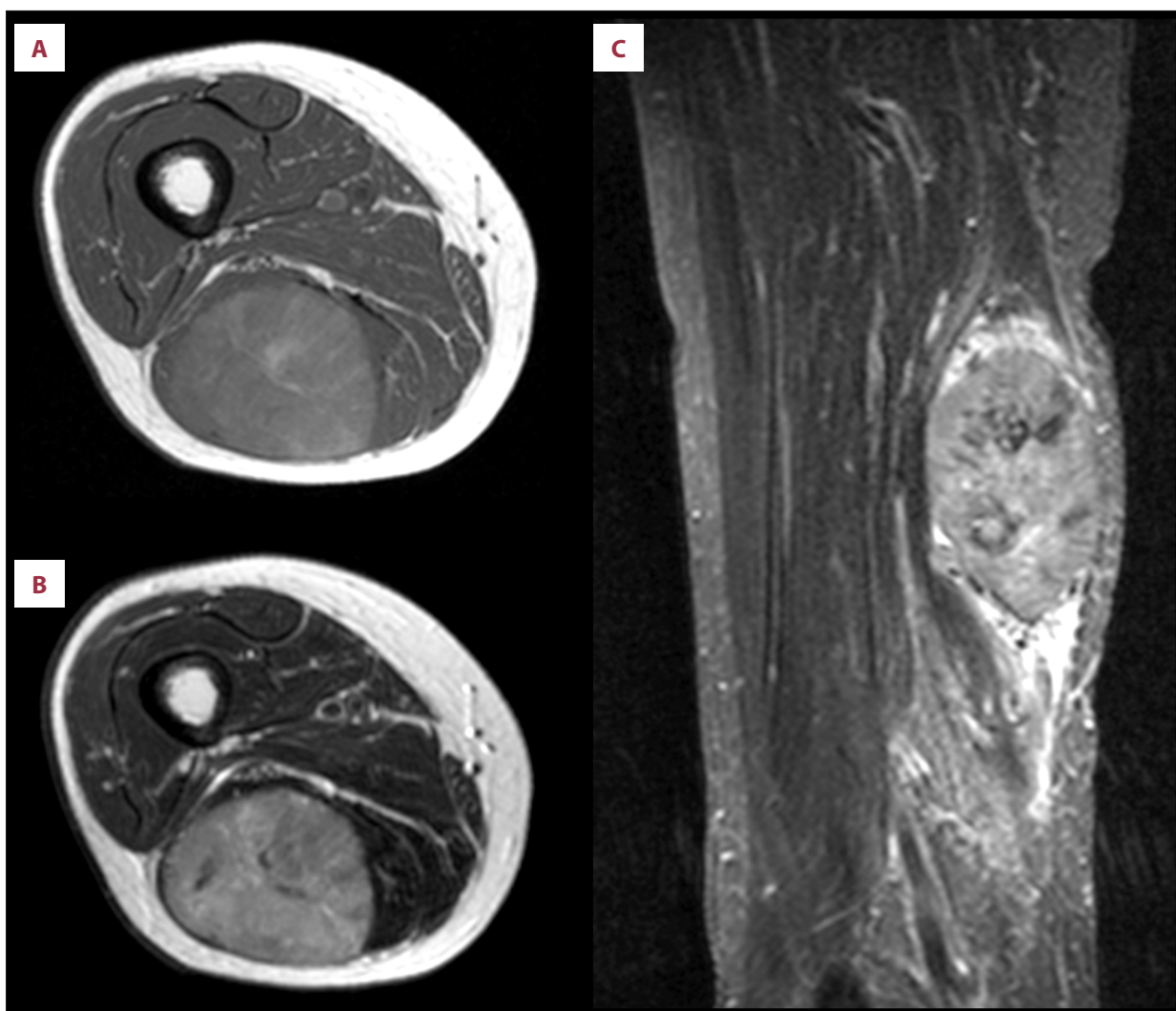
The laboratory investigations revealed a normal complete blood count, normal liver enzyme levels, and coagulation activity. The serum AFP level was normal at 6.1 ng/mL (normal range: less than 15 ng/mL), but the PIVKA-II level was 11 400 mAU/mL (normal range: less than 40 mAU/mL). After TACE, the PIVKA-II level had been less than 10 mAU/mL. Fourteen months before the muscular lesion was detected, the PIVKA-II level had increased to 29 mAU/mL. From 13 to 9 months before the lesion was detected, the levels ranged from 30 and 40 mAU/mL, which were still within the normal limits. At 7, 5, 4, and 2 months before, the levels had increased to 54, 69, 78, and 569 mAU/mL, respectively.

A needle biopsy was performed. The diagnosis was metastatic HCC, with a typical HCC finding of a rich blood vessel network. A computed tomography (CT) examination failed to detect any recurrence in the liver or any metastatic lesions in the thorax or the abdomen. With a diagnosis of solitary metastasis to the biceps femoris muscle, wide resection with the surrounding normal tissue was performed, which is the same procedure as is used for primary sarcoma. The patient was able to walk without a crutch, and he had no difficulties in his daily life activities after the operation.

At the follow-up visit 1.5 months after the operation, the serum PIVKA-II level had decreased to 71 mAU/mL. By 4 months after the operation, it was elevated to 1410 mAU/mL, and multiple lung metastases were detected on a CT scan. The patient began treatment with oral sorafenib, and he was alive with disease 1 year after the operation. No recurrence of the muscle lesion was observed at 1 year after the operation.

## Discussion

Among the 3 previously reported cases with a solitary metastasis to the skeletal muscle [4–6], no recurrence was seen by 5 months after the resection in one case [4], metastasis to the sacrum was seen 2 months after the resection in another case [5], and intrahepatic metastasis was seen 10 months after the resection [6]. In the third case, TACE was performed to treat the intrahepatic metastasis and no other extrahepatic recurrence has been observed [6]. No local recurrence was seen in any of these cases. In the present case, the metastatic solitary lesion in the muscle was resected using the same treatment strategy as for primary soft-tissue sarcoma. No local recurrence was found by 1 year after the resection, and the patient's walking ability was not impaired. These results suggest that resection of solitary muscle metastasis is beneficial to preserve the patient's ability to perform activities



**Figure 1.** An 81-year-old man with HCC metastasis to a muscle. In magnetic resonance imaging, a T1-weighted image (A), a T2-weighted image (B), and STIR (short inversion time inversion recovery) (C) depict an intramuscular metastatic lesion in the biceps femoris muscle.

of daily living. It is not conclusive whether resection of the muscle lesion contributes to a favorable prognosis. However, it was reported that surgical resection of extrahepatic metastases of HCC prolonged survival when only 1 or 2 metastases were present [8]. Moreover, resection of the rapidly growing solitary muscle metastasis helped with local control and ability to perform activities of daily living.

In the 3 reports of a solitary metastasis to a single muscle, the metastatic sites were the psoas, the humerus, and the intercostal muscle [4–6], and in this report, it was in the biceps femoris muscle. Among all cases of metastases to the muscles, the most commonly affected muscles seen in post-mortem studies were the iliopsoas (27.5%) and the gluteal muscle (16.3%) [9]; both muscles are near the hip. The biceps femoris muscle is also near the hip, and the location is thought to be typical.

Skeletal muscle metastasis in cancer, including HCC, is rare despite the abundant blood supply, but the reason is unclear. This rarity may be attributed to the “seed and soil” hypothesis, in which it is proposed that metastasis depends on cross-talk between selected cancer cells (the “seeds”) and specific organ microenvironments (the “soil”) [10]. The contractile properties of skeletal muscle, the local acidic environment resulting from the accumulation of lactic acid and other metabolites, and the presence of tumor suppressors or lymphocytes may create an unfavorable environment for metastasis [11].

In the present case, an elevated PIVKA-II level was seen before the solitary metastasis to the muscle was detected, while AFP was at a normal level. Then, after the resection of the metastasis, PIVKA-II significantly decreased. Among the previous 3 reports of solitary muscle metastases of HCC [4–6], serum AFP

was elevated in 2 of the cases [4,6]. PIVKA-II was elevated in one case [6], PIVKA-II was not measured in the other 2 cases [4,5]. It is important to measure both AFP and PIVKA-II for early diagnosis of recurrence and metastasis. The diagnostic efficiency of PIVKA-II has been illustrated sufficiently and it has proven that PIVKA-II is a potent biomarker and is independent of alpha-fetoprotein (AFP) [9]. In the present case, muscle metastasis had not been noticed until the size became large. When no recurrence was detected in cases with elevated PIVKA-II, examination of the whole body, such as fluorodeoxyglucose-positron emission tomography (FDG-PET), is still necessary.

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## Conclusions

In summary, we report a rare case of solitary metastasis to the biceps femoris muscle from the primary HCC. A wide resection of the solitary metastasis to the muscle was beneficial for local control to help preserve the ability to perform activities of daily living. It is important to measure both AFP and PIVKA-II for early diagnosis. PIVKA-II can be independent of AFP. Examination of the whole body is still necessary in cases with elevated PIVKA-II in order to detect extrahepatic metastasis, when no recurrence is detected.

## Conflict of interest

None.