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WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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Malignant fibrous histiocytoma of the bone in a traumatic amputation stump: A case report and review of the literature

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Abstract

BACKGROUND

Malignant fibrous histiocytoma (MFH) is one of the most common soft tissue sarcomas among adults. It is characterized by large size, high grade, and biological aggressiveness. There are many reports of MFH after local stimulation, such as bone fracture, implants, and chronic osteomyelitis. In this paper, we report a patient who developed MFH 6 years after amputation, suggesting that wound healing and mechanical force play a role in the local stimulation of this disease.

CASE SUMMARY

A 66-year-old man complained of persistent pain in his residual mid-thigh. He had undergone amputation surgery due to a traffic accident 6 years prior. Physical examination showed tenderness but no abnormalities in appearance. X-ray radiographs and magnetic resonance imaging supported the diagnosis of a tumor, and a biopsy confirmed that the lesion was MFH. The patient received neoadjuvant chemotherapy and left hip disarticulation. During the 6-mo follow-up, there were no symptoms of recurrence.

CONCLUSION

Postsurgery MFH has been reported before, and many studies have attributed it to the biological effects of implants. Our case report shows that this disease can develop without an implant and thus highlights the importance of local stimulation. The wound-healing process and mechanical force can both promote this tumor, but whether they directly cause MFH needs further investigation.

Key Words: Malignant fibrous histiocytoma; Postamputation pain; Traumatic amputation; Case report

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Core Tip: In this paper, we report a patient who developed malignant fibrous histiocytoma 6 years after amputation, suggesting the role of wound-healing and mechanical force as local stimulation in this disease.

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INTRODUCTION

Malignant fibrous histiocytoma (MFH), also referred to as undifferentiated pleomorphic sarcoma, is one of the most common soft tissue sarcomas among adults and has a peak incidence between 60 and 70 years of age[1]. Most MFHs occur in extremities (49% in lower and 19% in upper extremities), followed by the trunk and retroperitoneum[2].

The relationship between MFH and local stimulation has been discussed for a long time. There are many studies attributing postsurgery MFH to the biological effect of the implants[3-6]. Keel *et al*[7] diagnosed four patients with MFH in their case series, all of whom had previously undergone surgery with implants. Reports of MFH occurring from 10 mo to 12 years after femoral fracture suggest that this tumor can be promoted by trauma[8,9]. In addition to implants and injury, MFH occurring at the site of chronic osteomyelitis is seen in the course of treatment[10-13]. The role of amputation was also mentioned by Inoshita *et al*[14] in their case report. In this paper, we present an MFH arising from the stump 6 years after amputation and discuss how local stimulation could induce MFH.

CASE PRESENTATION

Chief complaints

A 66-year-old man presented at the orthopedics clinic with a history of persistent pain in his amputation stump.

History of present illness

The patient's pain started 3 mo ago and was not relieved spontaneously.

History of past illness

Six years ago, the patient underwent a traumatic amputation at his mid-thigh after a traffic accident.

Personal and family history

None of the patient's family members developed tumors before.

Physical examination

On physical examination, there was tenderness of the patient's residual limb, and the appearance of his amputation stump was normal.

Laboratory examinations

Routine laboratory tests, including routine blood examination, erythrocyte sedimentation rate, alkaline phosphatase, lactate dehydrogenase, serum protein electrophoresis, *etc.*, were within the normal range.

Imaging examinations

X-ray radiography showed a soft tissue mass and bone lesions in the femoral greater

trochanter and residual femoral shaft without clear boundaries or periosteal reactions (Figure 1). Magnetic resonance imaging (MRI) also showed a soft tissue mass, supporting the diagnosis of a tumor (Figure 2). To obtain a definitive diagnosis, the patient underwent biopsy, which confirmed the diagnosis of MFH (Figure 3). Whole-body emission computed tomography did not reveal metastasis.

FINAL DIAGNOSIS

Malignant fibrous histiocytoma.

TREATMENT

The patient underwent neoadjuvant chemotherapy and left hip disarticulation.

OUTCOME AND FOLLOW-UP

At the 6-mo follow-up, the patient remained asymptomatic with no recurrence of MFH.

DISCUSSION

MFH is a pleomorphic sarcoma that was originally described by Ozzello *et al*[15] in 1963 and O'Brien and Stout[16] in 1964. It is characterized by large size, high grade, and biological aggressiveness. Tumors involving extremities frequently present as painless masses that grow over a period of months[17].

The factors possibly related to MFH have been discussed for a long time. Some investigators reported postsurgery MFH, and most of them tended to attribute the tumor to implants rather than surgery[3-6] because the components of the implants might be carcinogenic. Keel *et al*[7] considered the biological effects of metal components (*e.g.*, cobalt, chromium, stainless steel, nickel, iron, and manganese) and organic components (*e.g.*, polymethylmethacrylate, polyethylene, silicone, and aliphatic polyurethane). Another commonly used component, titanium, though regarded as a relatively safe material, has been reported to induce genomic instability *in vitro*[18]. However, in this case, the patient did not receive any implants, necessitating other explanations.

Another theory is that it is a coincidence. MFH usually occurs in males in the femur, and patients with MFH arising in preexisting bone abnormalities were older than those with MFH in normal bone[19], and all of these features were demographic features of this patient. This patient might have developed MFH spontaneously after amputation.

However, reports of MFH after amputation are rare but exist[14], indicating the possible role of amputation in tumorigenesis. After amputation surgery, the stump undergoes a wound-healing process and is then subject to mechanical force from the prosthesis. First, during wound healing, cell proliferation is promoted by certain growth factors (*e.g.*, epidermal growth factor, hepatocyte growth factor, vascular endothelial growth factor, insulin-like growth factor, fibroblast growth factor, and neuregulin) and signaling pathways (*e.g.*, mTOR, Hippo, Wnt, Bmp, and Notch signaling)[20]. These growth factors and signaling pathways are closely correlated with the development of neoplasms. Additionally, hypoxia frequently occurs in mechanically challenged tissue; this induces the expression of hypoxia inducible factor-1 α , upregulating several genes involved in promoting epithelial-mesenchymal transition and stem-like characteristics in tumor cells[21]. The compression force can lead to extracellular matrix stiffness, activating TGF- β [22], WNT[23], and Hippo signaling[24]. These biological processes can promote the proliferation of tumor cells.

In contrast to a number of studies on these types of carcinogenic mechanisms, only a few studies are available on molecular mechanisms involved in the tumorigenesis of MFH[25]. Idbaih *et al*[26] identified a high level of genomic complexity with the recurrent amplification of the 5p chromosome region, the biological significance of which is unknown. Perot *et al*[27] found that MFH was associated with the inactivation

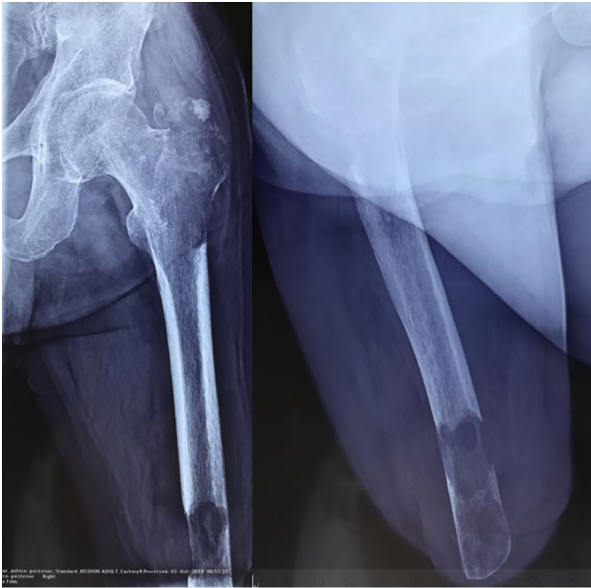


Figure 1 X-ray radiograph revealing a soft tissue mass and bone lesions.

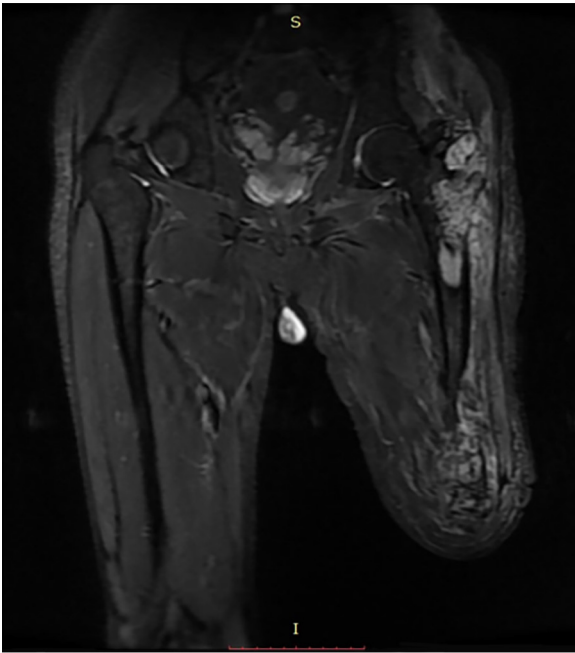


Figure 2 Magnetic resonance imaging of the residual limb showed abnormal signals.

of the *RB1* gene or frequent loss of p53 function. Matsuo *et al*[28] detected telomerase activity and the expression of human telomerase reverse transcriptase in tumor samples. Current studies have shown no association with signaling pathways related to wound healing and mechanical force.

The amputated femur of the patient showed two separate lesions in the greater trochanter and the residual limb. The two lesions were not connected by any intramedullary or extraosseous tissue. This is common in musculoskeletal tumors[29]. In the literature, multiple lesions in one bone are usually described as skip metastasis or synchronous multifocal tumors[29,30].

Skip metastasis can occur in osteosarcoma, Ewing sarcoma, and rarely in chondrosarcoma[29]. It presents as intramedullary lesions separated by normal marrow without any distant metastasis, such as lung metastasis. Skip metastasis usually emerges in the same bone, while those occurring in different bones are named transarticular skip metastasis. Synchronous multifocal lesions refer to more than one lesion at presentation without visceral metastasis[31,32]. Synchronous multifocal

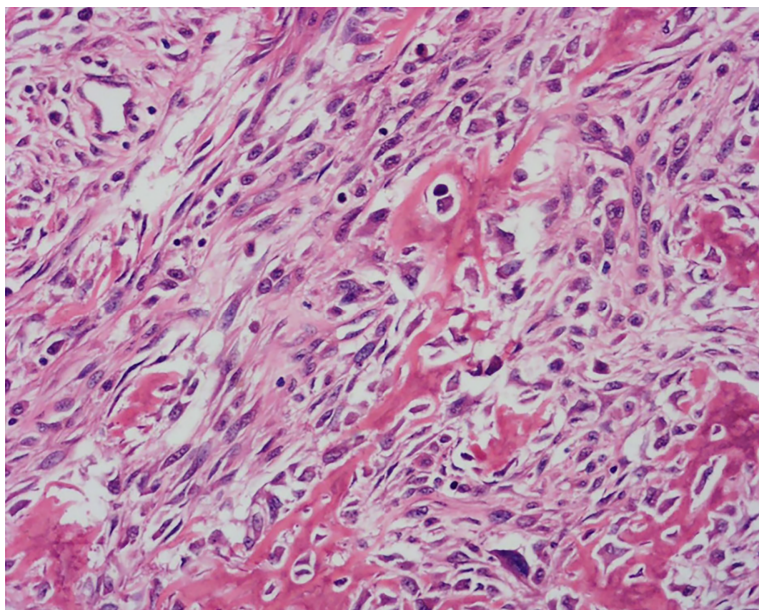


Figure 3 Biopsy results confirmed a diagnosis of malignant fibrous histiocytoma.

lesions have been reported in osteosarcoma, MFH, and chondrosarcoma[30]. Whether skip metastasis (or synchronous multifocal lesions) is metastasis in the traditional sense or multicentric tumorigenesis lacks strong evidence for differential diagnosis. The patient described in this paper exhibited two lesions in his greater trochanter and residual limb. The two lesions presented similar radiographic characteristics on MRI and looked similar pathologically. Therefore, we think that the lesions were more likely to be synchronous.

CONCLUSION

In this case, a 66-year-old man developed MFH 6 years after amputation. The disease course may suggest that the mechanical force from the prosthesis can promote MFH. However, based on the patient's demographic characteristics, the tumor could also have occurred spontaneously without any correlation to the previous amputation surgery. More investigation is needed to determine whether the prosthesis or other types of local stimulation affect MFH after surgery.

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