Malignant Mixed Tumor of the Soft Tissue Occurring After Total Knee Arthroplasty

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Abstract

A 70-year-old woman developed a malignant mixed tumor of the soft tissue 2 years after total knee arthroplasty. A 5×3×3-cm elastic hard tumor at the lateral side of the surgical scar was resected. The tumor showed focal infiltration into surrounding adipose and fibrous tissues, focal necrosis, and vascular infiltration. It was diagnosed as malignant. Mixed tumor, or myoepithelioma, of the soft tissue is a relatively rare tumor that was recently recognized as a disease entity; the vast spectrum of myoepithelial cell differentiation and the resultant morphologic diversity might increase the difficulty of the histological diagnosis. Postoperatively, the patient did not receive adjuvant therapy and no recurrence of the tumor was observed for 6 years. Range of motion of her left knee is –5° extension and 90° flexion; however, her activities of daily living are restricted because of general fatigue, partly due to hepatoma and chemotherapy.

Despite the increase of artificial implant use worldwide, reports of peri-implant tumor formation are rare. Although we do not know the exact mechanism of tumor genesis, we consider the fibroblast formation in the routine healing process to be a possible mechanism. Further investigation is necessary to identify coexisting factors that increase the risk of tumor formation after implantation.

Figure: AP radiograph did not show the tumor at the lateral side of the implant of the left knee.

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The oncogenic potential of artificial implants has long been a concern, but the precise risk of tumor formation after implantation is unclear. However, several case reports and animal model studies may provide information about the tumorigenic risk after implantation. Formation and dissemination of metal particles originating from the implant and chronic inflammation have been discussed as causes of implant-inducing tumorigenesis.

Myoepithelioma is a neoplastic proliferation of myoepithelial cells commonly observed in the salivary glands, also known as pleomorphic adenoma. Myoepithelioma is also reported in soft tissue, skin, lungs, and breasts. In soft tissue, myoepithelioma shows reticular growth of epithelioid, ovoid, and spindle cells in collagenous or chondromyxoid stroma. Tumors with ductal differentiation are known as mixed tumor, and those without ductal differentiation are known as myoepitheliomas; these 2 tumors are considered to lie on a morphologic continuum.

The criteria of malignancy in myoepithelioma and mixed tumors of the soft tissue are slightly different from that in myoepithelioma and mixed tumors of the salivary glands. In the salivary glands, tumors showing cytologic atypia, increased mitotic activity, or infiltration into surrounding tissue are regarded as malignant. Infiltration is not a criterion for malignant myoepithelioma or mixed tumors of the soft tissue.

**CASE REPORT**

A woman underwent bilateral total knee arthroplasty (TKA) because of osteoarthritis. Two years after the TKA, at age 70, she noticed a lump in her left knee with associated pain and numbness. Tinel’s sign was observed. A 3.5-cm mass that was elastic hard on palpation was found on the lateral side of the surgical scar (Figure 1). Magnetic resonance imaging and computed tomography scanning were not performed because TKA had been performed. 201Tl Scintigraphy (GE Healthcare, Chalfont St Giles, Buckinghamshire, United Kingdom) showed high radioactivity, suggesting the possibility of malignancy. Cytologic examination and biopsy were performed.

Histological examination suggested a mesenchymal tumor because there was proliferation of stromal cells in the prominent fibrous tissue. Examination also did not suggest a diagnosis of malignancy. With these findings, surgical resection of the tumor with wide local margin was performed, including the fascia on the medial margin and a part of capsule on the distal margin. The tumor was located close to the implant; however, no direct contact of the tumor with the implant was observed. The implant was exposed during the operation, and irrigation was performed to avoid infection.

Postoperatively, the wound healed well with no infection, and pain was controlled. Three months postoperatively, range of motion (ROM) of the knee joint was –5° extension and 90° flexion, and slight weakness of quadriceps was observed. Because of the resection of the lateral collateral ligament, lateral instability of the knee joint was observed. With the use of knee brace and a cane, the patient’s gait became stable.

During the 6-year follow-up period, no local recurrences or distant metastases were observed. However, hepatocellular carcinoma was diagnosed 5 years postoperatively and the patient was receiving chemoradiotherapy for it. At 6 years postoperatively, ROM of the left knee was –5° extension to 90° flexion; however, the patient’s activities of daily living were restricted because of general fatigue, partly due to the hepatoma and chemotherapy.

Biopsy specimen showed mesenchmal cell proliferation surrounded by fibrous tissue (Figures 2A, B). The cells were immunohistochemically negative for cytokeratin AE1/3, CD31, CD34, desmin, S100 protein, and CD68. Although a mesenchymal tumor was surmised, histological subtype and malignant potential of the tumor could not be decided.

After the resection, the tumor was macroscopically and microscopically examined. The 5×3×3-cm tumor, which was located in the articular capsule, contained the myxomatous area and was circumscribed by a 4- to 5-mm thick white and amorphous layer (Figure 3). Microscopically, tumor cells grew in lobules, showing a predominantly reticular growth pattern with intersecting cords of epithelioid, ovoid, or spindle cells with partial...
hyalinization, collagenous stroma, and ductal differentiation (Figures 2C, D). The tumor showed focal infiltration into the surrounding adipose and fibrous tissues, focal necrosis, and vascular infiltration (Figures 2E, F).

Tumor cells were immunohistochemically positive for cytokeratin AE1/3, S100 protein, vimentin, epithelial membrane antigen, and muscle actin (HHF35) (Figures 2G-J). Mixed tumor of the soft tissue with malignant potential was diagnosed. Tumor cells were not observed in the resected margin. No metal particles or inflammatory features were observed in the tumor or surrounding tissue.

**DISCUSSION**

Malignant tumor formation around artificial implants was first described in 1956 by McDougall, who reported a malignant bone neoplasm resembling an Ewing sarcoma occurring at the site of bone plating. Since then, the incidence of surgical use of artificial implants has dramatically increased worldwide; however, reports of tumor formation concerning implants are rare. In this respect, risk of tumor formation after implantation seems to be negligible. In fact, several cohort studies on patients receiving hip or knee arthroplasty indicate no increases of cancer risk by implantation.

However, several case reports, including the current report, clearly demonstrate the correlation between implants and tumor formation. Furthermore, experimental studies in rats have shown that implantation of cobalt, chromium, nickel, polyethylene, and methylmethacrylate can induce the development of sarcomas.

In the current study, the tumor was located close to the implant; however, no direct contact of the tumor with the implant was observed. This is distinct from the previous reports of implant-induced tumors arising close to the implants. However, the close location of the tumor to the implant indicates the fibroblast formation in the routine healing process in the surgery area might have triggered tumorigenesis. Nevertheless, it should be recognized that this finding was entirely coincidental; thus, further studies are necessary.

Mixed tumor, or myoepithelioma of the soft tissue, is a relatively rare tumor that was recently recognized as a disease entity. Before the report by Hornick and Fletcher, myoepithelioma of the soft tissue was a difficult tumor to diagnose, mainly due to the vast spectrum of myoepithelial cell differentiation and the resultant morphologic diversity in myo-
epithelial tumors. Despite the broad morphologic spectrum, most cases of myoepithelioma of the soft tissue show a positive reactivity for cytokeratin, vimentin, and S100 protein, which is diagnostically useful. The current case showed positivity in these immunohistochemistry.

Because of the rarity of the tumor, establishment of criteria for malignancy in myoepithelioma of the soft tissue is difficult. In the salivary gland, tumor infiltration into adjacent normal tissue is the most important criterion for malignancy, with or without the cytologic atypia. However, this criterion was challenged in myoepithelial lesions of the soft tissue by Hornick and Fletcher, who argued that infiltrative growth is insufficient for the diagnosis of malignancy but that cytologic atypia is essential in the diagnosis of malignancy. The current case did not show apparent cytologic atypia; however, the tumor was diagnosed as malignant because necrosis and vascular invasion were observed.

Further case collection and prospective studies are needed to determine whether this tumor was simply coincidental or whether a true association exists between myoepithelioma and TKA.

REFERENCES