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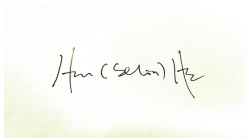

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Primary Nonkeratinizing Squamous Cell Carcinoma of the Scapular Bone: Report of a Rare Case and Literature Review

Abstract

Primary squamous cell carcinoma (SCC) of bone most frequently involves the skull bones, and primary involvement of other sites in the skeletal system is extremely rare. We describe a very rare case of primary SCC of the scapular bone in a 76-year-old Chinese man, which to our knowledge, represents the fourth case of primary SCC of a bone outside the skull and the first case of primary nonkeratinizing SCC of the scapular bone. Wide excision of the right scapular bone was performed, and pathological examination of the surgical specimen confirmed the diagnosis. The patient was doing well at the last follow-up, 22 months after treatment. Our findings suggest that clinicians must exhaust all available means for the diagnosis of primary SCC of bone to facilitate its timely and effective management. Regular and adequate follow-up is essential to help rule out metastasis and judge the prognosis.

Key words: primary squamous cell carcinoma; keratin pearls; scapular bone; diagnosis; immunohistochemistry

Introduction

Squamous cell carcinoma (SCC) is the second most common non-melanoma skin cancer. Although SCC can metastasize to other organs such as bone [1-4], primary SCC of bone is rare due to the absence of native squamous epithelium in osseous tissue [5]. When primary SCC does occur in bone, the most common site of involvement is the skull. Indeed, only three cases of primary SCC at other sites in the skeletal system—namely, the iliac bone, distal tibia, and tarsal bone—have been reported in the English literature [5-7]. The case reported herein is the fourth case of primary SCC of a non-skull bone and also the first case of primary nonkeratinizing SCC of the scapula.

Case presentation

Informed consent was obtained from the patient for the publication of this case, including any necessary photographs.

A 76-year-old Chinese man suffered pain and limited mobility in the right shoulder for 4 months, without an obvious cause. Conservative treatment with oral analgesics and rest was taken by the patient. However, this treatment was ineffective, and the pain in the right shoulder worsened. In October 2018, the patient was referred to our department for therapy. A physical examination revealed significant tenderness in the right scapula. The muscle strength of the right upper limb

was grade II according to the manual muscle test classification. The range of motion of the right shoulder could not be assessed due to severe pain. Three-dimensional computed tomography (CT) reconstruction and magnetic resonance imaging (MRI) revealed an osteolytic destructive lesion in the right scapula with invasion into the surrounding muscles and soft tissues (Fig. 1). After obtaining informed consent from the patient, we performed an ultrasound-guided needle biopsy. Histopathological examination of the biopsy specimen revealed sheets of malignant squamous cells. However, no typical keratin pearls were seen, as the malignant squamous cells were poorly differentiated. Therefore, a diagnosis of nonkeratinizing SCC was made. Immunohistochemical analysis showed that the tumor cells were reactive to cytokeratin 5/6, p63, p40, and vimentin (Fig. 2). Furthermore, CT scans of the lungs, skull, and abdomen as well as single-photon emission CT-CT and positron-emission tomography-CT confirmed that there were no other lesions outside the right scapular bone, which indicated that this was a rare presentation of a primary SCC involving the scapular bone. Therefore, the final diagnosis was primary nonkeratinizing SCC of the right scapular bone.

Surgical protocol

The patient underwent wide excision of the right scapular bone and reconstruction of the resulting defect with the right humeral head, right collarbone, and surrounding muscles. The whole gross specimen measured 7.0×6.5×5 cm. The lesion itself was a dark red ovoid mass that originated

from the right scapular bone and appeared soft and creamy-white on cross section (Fig. 3). No connection to the epidermis was identified.

Rehabilitation

Regular follow-up was continued after surgery. Neither recurrence nor metastasis was found during 22 months of follow-up. Furthermore, the postoperative course was quite good. The patient's severe pain in the right shoulder was significantly relieved, and the mobility and function of the right shoulder were improved.

Discussion

SCC is a tumor of the epithelial tissue that typically originates from the epithelial linings of the skin, respiratory tract, digestive tract, and reproductive tract; thus, SCC can involve the head and neck, esophagus, lungs, cervix, and genital area[8]. Epithelial linings can be divided into layered squamous epithelium and non-squamous epithelium. The squamous differentiation phenotype of SCC depends on the type of oncogenic mutation involved and the cell of tumor origin, and this phenotype determines the degree of differentiation and therefore, the aggressiveness and invasiveness of these tumors[9]. As for most cancers, the initial target cells of the oncogenic mutations as well as the number of cancer stem cells in the tumor are unknown[10]. Therefore, it is difficult to know the source cells for primary SCC in bone. SCC-derived cells share a common

feature in that they originate due to the mutation of proliferative basal cells, which are characterized by their ability to self-renew and produce terminally differentiated cells. Under the influence of oncogenic genes, both stem and progenitor cells can act as the origin cells of cancer[8]. A comparison of different SCCs shows that they are characterized by very similar mutant genes, including *TP53*, *SOX2*, *TP63*, *CDNK2A (P16-INK4A)*, *NOTCH1*, *KMT2D*, *PIK3CA*, and *PTEN*[9].

Primary SCC of the bone is commonly seen in the head and neck region[11], and it is rarely found elsewhere in the skeletal system. According to the literature, the present case is only the fourth case ever reported of primary SCC of a bone outside the skull and the first case of a primary nonkeratinizing SCC of the scapula (Table 1). It is not easy to make a diagnosis of primary SCC of a non-skull bone, as this depends on not only pathological and immunohistochemical examinations but also extensive workup to rule out metastasis. In addition to metastasis, the differential diagnosis of primary SCC should also include SCC caused by chronic osteomyelitis[12]. Keratin pearls are the pathological features of highly differentiated SCCs, and their presence in histopathological sections of well-differentiated SCCs is a common phenomenon[13]. Unlike the three cases of primary SCC of a non-skull bone reported previously, our case was unique in that no keratin pearls were found. This is because our patient had a poorly differentiated SCC, while the previous three patients had well-differentiated SCCs with keratin pearl formation. The immunohistochemical features of the previous three cases were also similar

to those of our case[5-7], in that the tumor cells were reactive to cytokeratin 5/6, p63, and p40[14]. However, in our case, the tumor cells were also reactive to vimentin, which may be related to the metastatic capability and invasiveness of the primary SCC[15]. In our patient, the final diagnosis of a primary SCC of the bone was supported by the immunohistochemical findings, the extensive workup for the identification of a primary source, and the fact that the patient remained disease-free during a 22-month follow-up period.

For patients with primary SCC, the choice of treatment depends on the specific tumor characteristics, and an effective personalized treatment strategy must be devised. For most patients with primary SCC of the bone without metastasis, a negative tumor margin of at least 2 cm must be achieved during surgery[16]. For patients with SCC of the temporal bone, this margin may be difficult to achieve, as many important structures are located nearby, and the anatomical structure of the temporal bone is complex. In such patients, adjuvant radiotherapy may help control minimal residual disease[17]. In our patient, as the SCC originated from the relatively independent anatomical structure of the scapula[18], it was easier to achieve complete resection of the tumor. Surgical resection is the most important treatment method for this type of tumor, and postoperative adjuvant treatment can be individualized according to the immunohistochemical characteristics of the tumor. For example, cetuximab is a monoclonal antibody that targets the epidermal growth factor receptor, and compared with conventional radiotherapy, cetuximab combined with radiotherapy may help achieve good outcomes in some patients with SCC[19]. In

addition, cisplatin, 5-fluorouracil, and docetaxel constitute an effective combination chemotherapy regimen[20]. These adjuvant treatments can improve local control and reduce the mortality of advanced head and neck cancers, but due to the paucity of reports of primary SCCs outside the head and neck, there is still a lack of definitive clinical research evidence.

There is still no consensus on the standard treatment method or prognosis of primary SCC of non-skull bones because of the rarity of such cancers, with only a few cases having been reported and followed up. Our findings demonstrate that clinicians must exhaust all available means for the diagnosis of primary SCC of bones, to facilitate timely treatment and effective management. Regular and adequate follow-up is essential to help rule out metastasis and judge the prognosis.

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TABLE

Table 1. Published cases of primary squamous cell carcinoma of bones outside the skull

FIGURE LEGENDS

Fig. 1. Three-dimensional computed tomography reconstruction (a–c) and magnetic resonance imaging (d) showing an osteolytic destructive lesion in the right scapular bone, invading into the surrounding muscles and soft tissues.

Fig. 2. Histopathological staining of the biopsy specimen showing malignant tumor cells in the trabecular bone space but no typical keratin pearls (stain, hematoxylin and eosin; original magnification, ×100) (a). Immunohistochemical staining images showing that the tumor cells were reactive to cytokeratin 5/6, p63, and p40 (stain, hematoxylin and eosin; original magnification, ×40) (b–d).

Fig. 3. Photograph of the surgically resected specimen showing that the lesion was a dark red ovoid mass that originated from the right scapular bone and appeared creamy-white and soft on cross section (a). The right humeral head, right collarbone, and surrounding muscle were put together and used to reconstruct the resulting defect (b).