Tepecik Eğit. ve Araşt. Hast. Dergisi 2016; 26(1):73-76
doi:10.5222/terh.2016.073

Olgu Sunumu

Widespread osseous metaplasia in malign tumors: High grade papillary urothelial carcinoma of the bladder and metastatic colonic adenocarcinoma

Malign tümörlerde yaygın osseöz metaplazi: Mesanenin yüksek dereceli ürotelyal karsinomu ve metastatik kolon adenokarsinomu

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ABSTRACT

Osteoid metaplasia is a rarely seen characteristic feature among all tumor types. Dystrophic calcifications can be occasionally seen in necrotic areas of tumors. However actual bone formation also termed as osteoid metaplasia or heterotopic bone formation is a rarely developed incidental microscopic finding.
In this case report we presented a case diagnosed as a high grade papillary urothelial carcinoma of the bladder associated with osteoid metaplasia, and another one with diagnosis of metastatic adenocarcinoma of colon.
In both cases, presence of diffuse osteoid metaplasia accompanying malignant tumors is a remarkable finding. Two cases with incidentally detected osteoid metaplasia associated with different histopathological diagnosis were presented. Osteoid metaplasia is a rare entity which accompanies both benign and malignant tumors and its etiopathogenesis is still unknown. However osteoid metaplasia is an important incidental finding in that it can lead to misinterpretations as bone invasion when it accompanies malignant tumors.

Key words: Osseous metaplasia, malign tumour

ÖZ

Osteoid metaplazi tüm tümör tiplerinde görülebilen ender bir özelliktir. Tümörlerin nekrotik alanlarında zaman zaman distrofik kalsifikasyon görülebilir. Ancak osteoid metaplazi ya da heterotopik kemik formasyonu olarak adlandırılan gerçek kemik oluşumu ender olarak gelişir ve insididental olarak saptanan mikroskopik bir bulgudur.
Bu sunumda osteoid metaplazinin eşlik ettiği "mesanenin yüksek dereceli papiller ürotelyal karsinomu" ve "metastatik kolon adenokarsinomu" olarak tanı alan iki olgu sunulmuştur.
Her iki olguda da malign tümörlere eşlik eden yaygın osteoid metaplazi varlığı dikkat çekmektedir. Farklı patolojik tanılara eşlik eden ve insidental olarak saptanan osteoid metaplazi görülen iki olgu sunuldu. Osteoid metaplazi hem benign hem de malign tümörlere eşlik eden ender bir antitedir ve etiopatogenezi halen bilinmemektedir. Ancak osteoid metaplazi, malign tümörlere eşlik etmesi durumunda kemik invazyonu açısından yanlış yorumlara neden olabileceği için önemli bir bulgudur.

Anahtar kelimeler: Osseöz metaplazi, malign tümör

Alındığı tarih: 31.08.2015
Kabul tarihi: 16.12.2015

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INTRODUCTION

Osseous metaplasia is a rarely seen feature for any type of tumor. Necrotic areas of tumors occasionally represent dystrophic calcifications, but mature bone formation also known as osseous metaplasia or hete-

rotopic bone formation is a rare feature. In all these cases osseous metaplasia is an incidental finding detected during microscopic examination which can not be identified by any specific clinical features or tests. Etiopathogenesis of osseous metaplasia is still a mystery. However many factors have been speculated to be effective in the pathogenesis of osseous metaplasia as chronic ischaemia, trauma, chronic inflammation, non-resorbed haematoma, cancer, hypercalcaemia and hypervitaminosis D [1].

It is necessary to be aware of osseous metaplasia to avoid overdiagnosis of bone invasion in malignant tumors or misdiagnosis as heterologous differentiation in a carcinosarcoma like our cases of bladder carcinoma and metastatic colon adenocarcinoma. Osseous metaplasia is defined as the formation of stromal mature bone in the neoplasm. This rare finding has been reported in benign and malignant tumors of various organs. Osseous metaplasia has been detected in gastric hyperplastic polyps, colon adenoma and polyps, endometrium and vagina, choroid plexus, nasal polyp, tympanium, labyrinth, parotid gland, kidney, aorta, abdominal wall, lung, lipoma, ischaemic myocardium, pituitary adenoma, melanoma and basal cell carcinoma [1]. Osseous metaplasia has been seen mostly in adenocarcinomas occurring in the gastrointestinal tract, lung, breast, thyroid, parotid and pancreas [2]. The overall incidence of osseous metaplasia in malignant tumors is approximately 0.4% as suggested by Dukes [3].

We report two cases of osseous metaplasia which were seen with high grade papillary urothelial carcinoma in the first,and with metastatic adenocarcinoma of colon in the second case.

CASE PRESENTATION

CASE 1: A 75-year-old male patient was admitted to urology clinic with complaints of haematuria and dysuria. Cystoscopy was performed which revealed a large polypoid tumor at the bladder base. Transurethral bladder tumorectomy (TUR-BT) was performed. Cytoscopic resection specimen was irregularly shaped, pale pink sample with a volume of 4cc. Histopathological diagnosis was reported as high grade papillary urothelial carcinoma of urinary bladder with diffuse invasion of lamina propria and muscle tissue. In addition to these findings, areas of osseous metaplasia were detected in the stroma of some tumor fragments (Figure 1).

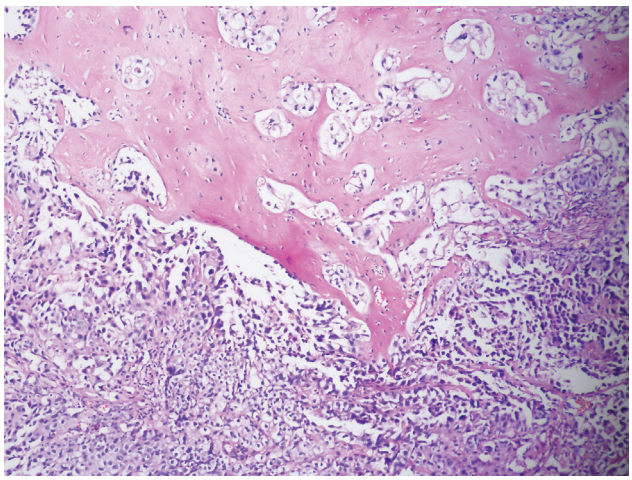

Figure 1. Areas of osseous metaplasia in the stroma of tumor fragments, H&Ex400.

CASE 2: A 51-year-old male patient with a medical history of colonic adenocarcinoma metastasized to the subcutaneous layer of the abdominal wall in the year 2001 which progressed, and invaded into the subcutaneous tissue of the right inguinal region in the year 2002.

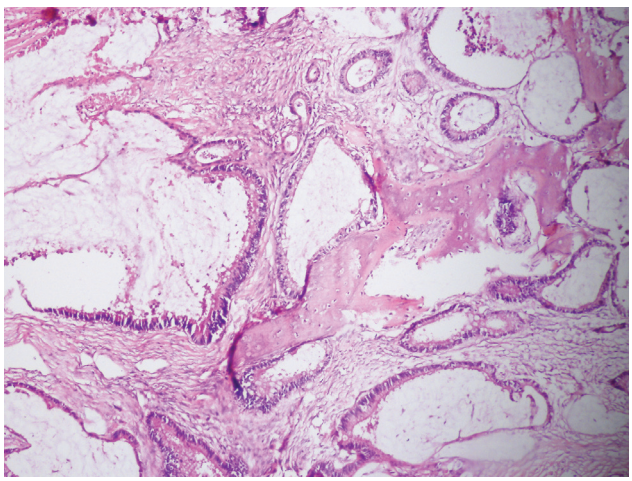

Figure 2. Adenocarcinoma including mucinous component with osseous metaplasia, H&Ex100.

Macroscopically excision material measuring 13x9x9 cm consisted of layers of skin and subcutenous tissue. Skin lesion was 1 cm in length and 0.5 cm in depth. Serial sections of the specimen disclosed a mucoid, fibrotic and partially calcific tumor in the subcutenous fat tissue with dimensions of 7x4.5x3 cm. Microscopic evaluation revealed a metastatic lesion stemmed from colonic adenocarcinoma including a mucinous component in the subcutaneous tissue that spred to the skin with osseous metaplasia (Figure 2).

Both of the cases were diagnosed as malignant tumors with osseous metaplasia which were high grade papillary urothelial carcinoma in the first case and metastatic adenocarcinoma of colon in the second case.

DISCUSSION

Osseous metaplasia is a living tissue which contains cells, unlike ectopic calcifications with apathetic calcium pyrophosphate deposits. Extraskeletal bone formation is a process of multiple steps. A mesenchymatous pluripotent cell differentiates into an osteoblast under the influence of paracrine osteogenic signal in the first step. The nature of this primary signal is not known. After this step, an osteogenic signal stimulates osteoblasts to induce secretion of bone matrix. As the last step, local environment must sustain sustained production of the heterotopic bone [1,4].

The stroma or metastases of urothelial carcinomas may rarely represent osseous or cartilaginous metaplasia [5]. These metaplasias should not be misdiagnosed as heterologous differentiation in a sarcomatoid carcinoma (carcinosarcoma). In these cases bone or cartilage appears as mature structures, and lacks cytologic atypia [6,7].

Ossification can be seen in both neoplastic and non-neoplastic lesions of the gastrointestinal system as is the case with colonic polyps, mucocele of the appendix, gastric carcinoids and adenocarcinomas [8-10]. Osseous metaplasia is a more common feature of lower gastrointestinal tract lesions and rectum is the most common site [11]. However some cases of osseous metaplasia have been reportedly detected in sigmoid, transverse colon and caecum [12]. Heterotopic bone formation is usually seen in tumors that produces excessive amounts of mucin [9]. It is thought that the extravasation of mucin may stimulate ossification [13,14]. Rhone and Horowitz reported that ossification may be caused by metaplasic transformation of pluripotent mesenchymal cells into osteoblasts [15]. Imai et al studied the immunohistochemical expression of bone morphogenetic protein (BMP) 2 in colon carcinomas and reported that BMP-5 and BMP-6 were barely expressed in the tumor cell cytoplasm, but weakly expressed in the adjacent osteoblast- like cells of the nearby bone [16]. This pattern suggests that the tumor cells mostly produce BMP-5 and BMP-6 that may stimulate proliferation and transformation of mesenchymal cells into BMP-2 and BMP-4 expressing preosteoblastic and osteoblastic cells [14]. BMP-2 and BMP-4 mainly stimulate osteoblastic differentiation when compared with other BMPs [17].

Although dystrophic calcification is seen in many malignant tumors, metaplastic bone formation is a rare feature. Etiopathogenesis of these osseous metaplasia is still a mystery. Thus, metaplastic bone formation in malignant tumors and the prognostic value of metaplastic bone formation should be investigated in larger case series.

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