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CASE REPORT

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Acromegaly with metastatic renal cell carcinoma: Lung, gluteal and scapular metastasis

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Abstract
The association between acromegaly and increased incidence of malignancy has been reported due to high GH and IGF levels. Although the incidence of all malignancies increases in patients with acromegaly, renal cell carcinoma (RCC) has been rarely reported. Herein, we report an acromegaly case with lung, gluteal and scapular metastatic RCC. The risk of cancer and cancer metastasis is high in uncontrolled acromegaly. At this point, treating acromegaly and controlling the disease progress are both important to enhance the life expectancy of a patient.

Keywords: Acromegaly, renal cell carcinoma, metastasis

Introduction

Acromegaly is an endocrine disorder associated with excess growth hormone (GH) secretion. The secretion of GH is often triggered by pituitary adenomas,which results in an increased secretion of insulin-like growth factor 1 (IGF-1). Increased levels of GH and IGF-1 affect all, but especially cardiovascular, metabolic and gastrointestinal systems. Since these two are known to be involved in regulatory mechanisms of cell proliferation, abnormal growth, apoptosis and angiogenesis, they are likely to take a role in tumorigenesis and cancer progression [1]. IGF-1 is a potent proliferative agent for almost all cell types. One of its predominant but not exclusive effects is mediated via the mitogen-activated protein (MAP) kinase signaling pathway.

Acromegaly has been associated with 1.6- to 3.3-fold increase in mortality related to aging, and 10-year of life expectancy reduction. One of the causes in increasing mortality is the association between acromegaly and cancer. The most common cancers are colorectal cancer, breast, thyroid, prostate cancer in acromegalic patients [2,3]. Renal cell carcinoma (RCC) prevalence is about 2-3% of all adult malignant tumors. The most common histological type of RCC is clear cell renal cell carcinoma (ccRCC) [4]. The cancerogenetic role of IGF-1 and its receptors on RCC have been demonstrated by many studies [5]. One mechanism in multiple cancers including RCC has been reported as the deregulation of IGF-1 receptor (IGF1R) kinase activity, and its overexpression, causing the loss of tumor suppressor genes or increase in oncogenetic actions [6]. A 70 % increased risk of mortality was reported in ccRCC patients with IGF1R overexpression compared to those without IGF1R expression. Resistance against chemotherapeutics is more pronounced in RCC cells with high expression of IGF1R compared to low expression [7]. In the current report, we present an acromegaly case complicated with metastatic ccRCC involving lungs, gluteal and scapular regions.

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Case Report

A 41-year-old male had admitted to our hospital with gluteal and scapular masses. He had been diagnosed with acromegaly two years ago, and treated with transsphenoidal surgery. Remission was not achieved after the surgery, and he did not have any control medical visits afterwards.

On physical examination, he had typical acromegalic features. There were palpable masses on right gluteal and scapular regions, noticed by the patient about two months before admission to our hospital (Figure1). Laboratory examination revealed high levels of GH (10.8 ng/ml) and IGF-1 (1072 ng/ml). Other pituitary, thyroid and parathyroid hormone levels, and biochemical tests were within normal ranges. A thyroid nodule was detected by ultrasonography, biopsy was performed, and histological features were benign. In colonoscopy, multiple hyperplastic polyps were detected.

Abdominopelvic computed tomography (CT) revealed a 93x68

millimeter (mm) mass on the upper-middle pole of the right kidney, and a 100x 65 mm mass on the right gluteal region. Thorax CT revealed metastatic nodular lesions in the right lung, and a mass of 200x80 mm in size on the right scapular region (Figure2). The diagnosis of metastatic ccRCC was verified by gluteal and scapular biopsies. Pituitary magnetic resonance imaging (MRI) revealed residual macroadenoma of 18x16 mm in size. Octreotide LAR treatment for acromegaly with a dose of 30 mg every 28 days was initiated. The patient underwent radiation therapy for the tumors on the right scapular and gluteal regions because of severe pain. At the same time he received interferon-alpha (IFN-alpha) for the treatment of metastatic ccRCC.

Figure 1. (A) Physical examination of the patient had typicial acromegalic features (B) Metastatic mass on the right scapular region

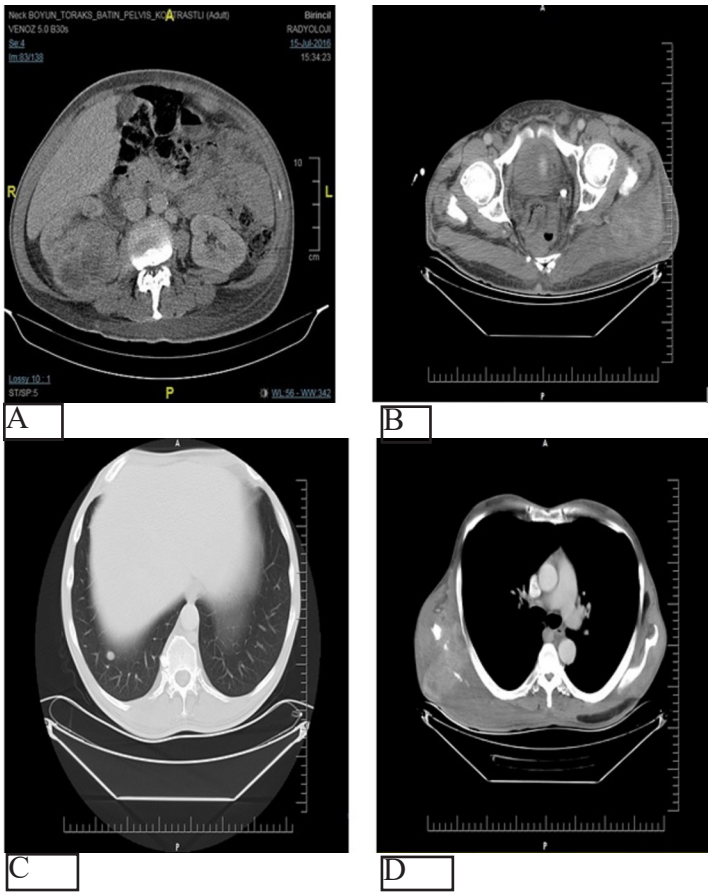

Figure 2. Abdominopelvic CT: (A) image showing 93X68 mm large mass on the right kidney (B) 100x 65 mm mass on the right gluteal region.
Thorax CT: (C) metastatic nodüler lesions on the right lung. (D) 200x80 mm mass on the right scapular region.

Evaluation of the patient after three months of IFN-alpha treatment, it was detected that the masses on scapular and gluteal regions regressed, while the renal mass and pulmonary metastasis progressed. Therefore, sunitinib treatment was immediately added. The patient died due to severe pleural effusion and respiratory failure in the first month of the treatment.

Discussion

Increased malignancy risk in acromegaly patients has been reported in previous epidemiological studies. The two marked studies are by Nabarro and by Orme et al. [8,2]. Nabarro reported that breast cancer incidence markedly increased among acromegaly patients [8]. Orme et al. in their large-scaled retrospective cohort study of 1362 patients with acromegaly have demonstrated an increased mortality of colon and breast cancers. One conclusion by the authors was the association between higher post-treatment GH levels and the increased risk of mortality of all malignancies, particularly colon cancer, for which they assumed modification of the progression of existing cancer by GH hypersecretion [2]. Also, increased expression of IGF-1 receptors and the increased secretion of GH have been associated with poorer radio-and chemotherapy responses [9]. A recent survey study from Italy demonstrated an increased incidence of all malignancies in acromegalic patients, as well as differences in the incidence of malignancy types according to gender, with increased incidences of thyroid, colorectal and breast cancerin females, while thyroid, kidney and colorectal cancer in males [10].

The stimulating effects of GH and IGFs on tumor growth is either by directly affecting cell proliferation, differentiation, and survival or by indirectly by interacting with some other growth factors. IGFs also have angiogenic actions promoting metastases development. Further confirmation was reported of the role of IGF-1 and its receptors on RCC cancerogenesis [5,7]. It has been recently shown that in human RCC cell lines, the growth-promoting effects of IGF-I are regulated by IGF-binding protein 3 (IGFBP-3), where IGF-I enhances the transforming growth factor-β (TGF-β) signaling and TGF-β promotes IGFBP-3 production [11]. The pathological regulation of the IGF1R activity results in loss of tumor suppressor gene or the oncogenetic activity [6].

IGF-1 locally synthesized in connective tissue adjacent to renal epithelial cells acts as a paracrine or autocrine factor in kidney. The degree of the IGF1R gene expression is different in the whole nephrogenic zone, with a stronger expression in the glomeruli and the tubular epithelium of medulla, and weakest expression in the proximal tubules [12]. The IGF1R has an effect on transformation of renal cells to malignancy by inducing cell proliferation, dedifferentiation and inhibiting apoptosis. RCC cells are responsive to exogenous IGF-1 stimulation. IGF1R expression and ccRCC development was shown to be associated, indicating that it may be possible molecular prognostic marker as well as potential target for new therapeutic interventions [13].

RCC has been reported rarely in several large-scale epidemiological studies of incidence and prevalence of neoplastic diseases in acromegalic patients [2]. On the other hand, RCC has a widespread and unpredictable metastatic potential. It is mostly metastasized in the lungs, lymph nodes, bones, liver, and brain. The rarest metastatic sites of RCC are gluteal striated muscle and scapula.

In only few reports, gluteal RCC metastases have been seen [14]. Here, we report a very rare case of acromegaly complicated with metastases of RCC to lung, gluteal and scapular sites. Our case, unlike the others, had metastases in unexpected regions. It may be meaningful in our case that acromegaly is accompanied by RCC.

Conclusion

We would like to draw particular attention to the finding that in acromegalic patients, malignant neoplasms may diagnosed at any time in their life during follow-up. The normal cell and tissue growth mediating role of GH-IGF-1 axis has been clearly documented; yet, it remains still unclarified increased cancer risk in acromegalic patients. We have reported an acromegaly case complicated with lung, gluteal and scapular metastatic RCC. Therefore, treatment of acromegaly and control of disease progression in acromegalic patients with any type of cancer is mandatory.

Competing interests
The authors declare that they have no competing interest

Financial Disclosure
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References

1. Cohen P, Clemmons DR, Rosenfeld RG. Does the GH–IGF axis play a role in cancer pathogenesis? Growth Horm IGF Res. 2000;10:297–305.
2. Orme SM, McNally RJ, Cartwright RA, et al. Mortality and cancer incidence in acromegaly: a retrospective cohort study. United Kingdom Acromegaly Study Group. J Clin Endocrinol Metab. 1998;83:2730-4.
3. Colao A, Ferone D, Marzullo P, et al. Systemic complications of acromegaly: epidemiology, pathogenesis, and management. Endocrine Reviews. 2004;25:102–52.
4. Escudier B, Szczylik C, Porta C, et al. Treatment selection in metastatic renal cell carcinoma: expert consensus. Nat Rev Clin Oncol. 2012;9:327–37.
5. Tao Y, Pinzi V, Bourhis J, et al. Mechanisms of disease: signaling of the insulin-like growth factor 1 receptor pathway–therapeutic perspectives in cancer. Nat Clin Pract Oncol. 2007;4:591–602.
6. Werner H, Shalita-Chesner M, Abramovitch S, Idelman G, Shaharabani-Gargir L, Glaser T. Regulation of the insulin-like growth factor-I receptor gene by oncogenes and antioncogenes: implications in human cancer Mol Genet Metab. 2000;71:315–20.
7. Adam F.Tracz, Szczylik C, Porta C, et al. Czarnecka. Insulin-like growth factor-1 signaling in renal cell carcinoma. BMC Cancer. 2016;16:453.
8. Nabarro JD. Acromegaly. Clin Endocrinol (Oxf). 1987;26:481-512.
9. Clayton PE, Banerjee I, Murray PG, et al. Growth hormone, the insulin-like growth factor axis, insulin and cancer risk. Nat Rev Endocrinol. 2011;7:11–24.
10. Terzolo M, Reimondo G, Berchialla P, et al. Italian Study Group. of Acromegaly. Acromegaly is associated with increased cancer risk: a survey in Italy. EndocrRelat Cancer. 2017;24:495-504.
11. Rosendahl AH, Forsberg G. IGF-I and IGFBP-3 augment transforming growth factor-beta actions in human renal carcinoma cells. Kidney Int. 2006;70:1584–90.
12. Kamenicky P, Mazziotti G, Lombes M, et al. Growth hormone, insulin-like growth factor-1, and the kidney: pathophysiological and clinical implications. Endocr Rev. 2014;35:234–81.
13. Parker AS, Cheville JC, Blute ML, et al. Pathologic T1 clear cell renal cell carcinoma: insulin-like growth factor-I receptor expression and disease-specific survival. Cancer. 2004;100:2577–82.
14. Sakamoto A, Yoshida T, Matsuura S, et al. Metastasis to the gluteus maximus muscle from renal cell carcinoma with special emphasis on MRI features. World J Surg Oncol. 2007;5:88.