Olgu / Case

Primitive Neuroectodermal Tumor of Kidney: success of neoadjuvant chemotherapy in an unresectable tumor?

Böbreğin Primitif Nöroektodermal Tümörü: Rezektabl Olmayan Bir Tümörde Neoadjuvan Kemoterapinin Başarısı

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Geliş tarihi (Submitted): 15.05.2015
Kabul tarihi (Accepted): 08.10.2015

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Abstract

Objective: Primitive neuroectodermal tumors (PNET) of the kidney are very rare tumors with aggressive behavior. They usually are associated with poor prognosis.

Case: A 26-year old male patient presented to our clinic with right flank pain, microscopic hematuria and moderate-heavy nausea complaints. CT imaging studies showed a tumor with 17x13x18 cm dimensions. A mass excision was not possible caused by tumor spread to liver surface and duodenum and the tumor could not be separated from these surfaces. The operation was finished with an excisional biopsy.

The patient received 7 cycles of alternating IE/VAC chemotherapy sessions. At 5th month of follow-up, PET-CT scans showed that the tumor was regressed to 8x6x7 cm dimensions. Following this outcome, radical nephrectomy was performed without risking any other organs.

Conclusion: Neoadjuvant chemotherapy can be employed prior to radical nephrectomy in such cases in order to radically/efficiently/drastically reduce the tumor mass

Key Words: neuroectodermal tumor, kidney, neoadjuvant chemotherapy

Özet

Amaç: Böbreğin primitif nöroektodermal tümörü oldukça seyrek ve agressif davranışlı ve kötü prognozludur.

Olgu: 26 yaşında erkek hasta, hafif sağ yan ağrısı, mikroskopik hematüri ve hafif kusma yakınmaları ile kliniğimize refere edildi. BT de; 17X13X18 cm boyutlarında, sağ böbreği tümüyle saran ve sağ hipokondriumu dolduran bir tümör saptandı. Tümör, karaciğer yüzeyinden ve duodenumdan disseke edilemediği için eksize edilemedi, eksizyonel biyopsi yapılarak operasyon sonlandırıldı.

IE/VAC alterne kemoterapi 7 siklus boyunca uygulandı. Tedavinin 5. ayında çekilen PET-CT de tümörün 8X6X7 cm boyutlarına küçüldüğü gözlendi. Herhangi bir komşu organa zarar verilmeden radikal nefrektomi yapıldı.

Sonuç: Bu tip tümörlerde neoadjuvan kemoterapi, radikal nefrektomi öncesinde kitle küçültmek amaçlı olarak kullanılabilir.

Anahtar Kelimeler: nöroektodermal tümör, böbrek, neoadjuvan kemoterapi

Introduction

Primitive neuroectodermal tumors (PNET) of the kidney are very rare and they are associated with poor prognosis by aggressive behavior (1). They are very prone to metastasize, despite medical (chemotherapy), surgical (radical nephrectomy) or, in some cases, with radiotherapy treatments. In this case report, we present a giant kidney tumor in a 26-year old male patient. The complaints of the patient were relatively new, ongoing for just one month.

Case

A 26-year old male was referred to our clinic from another hospital. Patient's complaints included mild right flank pain, microscopic hematuria and a moderate-to-heavy nausea. A huge/large mass with a very wide circumference that filled up the right hypochondrium was palpated during physical exam.

CT scan showed a tumor with 17X13X18 cm dimensions, replacing the right hypochondrium and completely surrounding the right kidney; with extension and metastasis to several lymph nodes with a 4 cm diameter. The mass was compressing liver, pancreas and duodenum and was also pushing the medial line towards vena cava (Fig.-1). Following an transperitonal anterior subcostal incision, right hemicolon and colon flexura were medially dissected. However, a mass excision was not possible since the tumor could not be separated from liver surface and duodenum. Operation was ended with an excisional biopsy.

Our plan after that was to employ neoadjuvant chemotherapy or radiotherapy depending on histopathological diagnosis in order to reduce the tumor size and reattempt another surgical intervention.

The immunohistochemical evaluation revealed a diffuse membranous CD99 positivity-primitive neuroectodermal tumor of the kidney (Fig. – 2). Synaptophysin, vimentin focal (+), CD56, TTF-1 and chromogranin markers were all negative.

The patient received 7 cycles of alternating IE/VAC chemotherapy regimens. The regimen consisted of Ifosfamide 1800 mg/m² /day, Mesna 1800mg/m², Etoposide 100mg/ m² for first 5 days, then alternating to 1.5 mg/m² Vincristine, Doxorubicin 75 mg/m², cyclophosphamide 1200 mg/m²/day, Mesna 1200 mg/m² for the rest of the cycle.

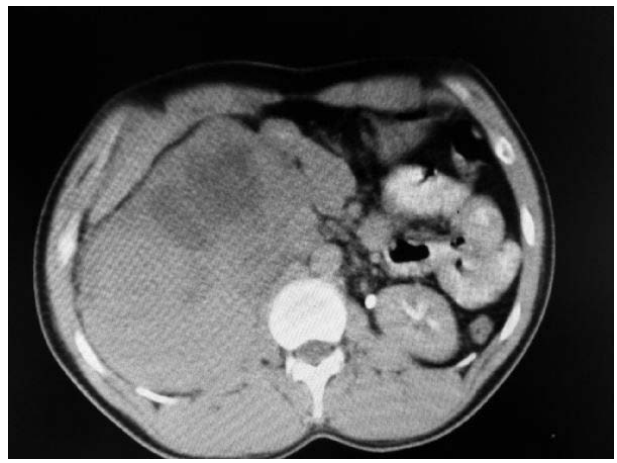

Figure.1: Preoperative appearance of the huge mass on CT
Notice the relationship of the mass between liver, duodenum and vena cava

Following 5 months of treatment, PET-CT scan showed that the tumor regressed to 8x6x7 cm dimensions. In addition, the lymph nodes with 4-cm diameter also regressed to their normal size(Fig.4). Following these outcomes, a radical nephrectomy could be performed without risk of injuring other organs.

Macroscopic examination of the tumor showed a greyish-brown surfaced mass with multiple hemorrhagic, cystic and necrotic areas. The tumor had an overall heterogeneous appearance and was 7x5x4 cm in size.

Microscopic examination showed a proliferation of small round cells in "nests" and "rosettes" which diffusely infiltrated into the renal capsule and perinephric fat tissues.

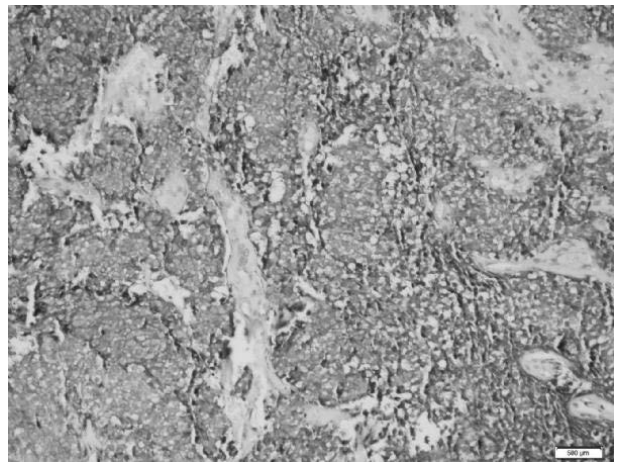

Figure.2: Histopathological appearance of the biopsy material
Immunoperoxidase for CD99 shows the tumor composed of small round cells

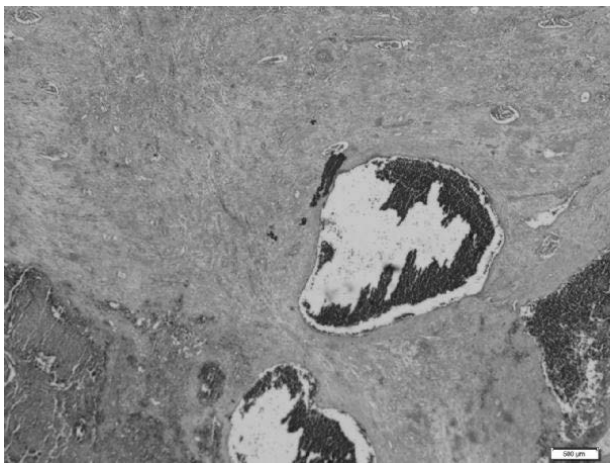

Figure.3: Tumor area in the bottom left of the specimen (HEX20)
The tumor tissue surrounded by congested renal parenchyma

The immunohistochemical evaluation revealed that CD99, CD56,Synaptophysin, TTF1, WT1 and CK 7 were all negative. However, CD99 was diffuse membranous positive on the specimen of the renal pedicle (surgical margin+). The macrophage cells, which comprised of hemosiderin and fibrosis caused by chemotherapy, in addition to about 40% live tumor cells were also found in the specimen.

Following these outcomes, radiotherapy to right renal bed was planned for 30 days. The patient is still alive and no metastatic foci could be detected so far in radiological follow-up.

Discussion

Primitive neuroectodermal tumors (PNET) are usually seen in bones and they share the same microscopic and immunohistochemical properties with Ewing's Sarcoma. Young adults are under the risk of developing these tumors. Another typical finding for such tumors is that they can reach to a very big volume relatively in a short time period. For this reason, they are frequently diagnosed in late-term. Differential diagnosis should include neuroblastoma, rhabdomyosarcoma, Wilms' tumor, small-cell carcinoma, carcinoid tumors, clear cell-carcinoma of the kidney and lymphomas (2). The diagnosis of renal PNET must be considered in young patients with kidney malignancy, especially those with advanced disease at the time of presentation (3). This can be justified by saying that; despite the fact that peripheral location of those tumors are very rare, they are associated with a very aggressive course and high mortality rates.

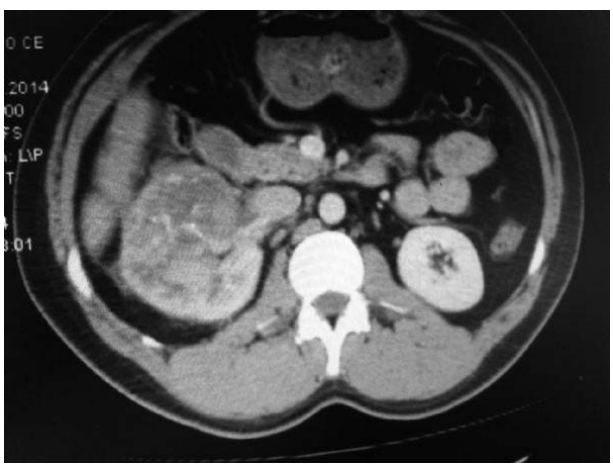

Figure.4: appearance of the mass after chemotherapy
**Distance between the liver and the mass, duodenum and the mass, vena cava and the mass can be seen clearly*

Histological features were generally similar to those of primitive neural tumors with varying amounts of rosettes and neutrophils; however, a large proportion of cases displayed unusual features such as spindle cells, ganglion cells, clear cell sarcoma-like foci, rhabdoid cells, epithelioid cells, and organoid foci (4).

Homer-Wright type rosettes are a typical histological feature for PNET and can address the diagnosis, although they can be found in neuroblastomas as well (5). In order to prove the correct diagnosis, an immunohistochemical evaluation on the specimen is indicated. PNETs show immune reactivity to CD99, meaning that CD99 positivity is enough evidence for the diagnosis, although it can be additionally determined (6).

The therapeutic alternatives for the PNET are radical nephrectomy + adjuvant chemotherapy + radiotherapy for surgical margin positivity or incomplete tumor resection with local tumor recurrences.

In our case, since radical nephrectomy was not possible in our initial attempt, we employed neoadjuvant chemotherapy to shrink the tumor to an operable size. Following the regression of tumor size to 7x5x4 cm, it was deemed as "operable". In addition, the tumor size regression also provided ease in surgery and also made it easier for us to avoid any laceration or rupture of surrounding organs in tissues. Moreover, we had a chance to observe the effectiveness of chemotherapeutic agents on the tumor and tumor-cell infiltrated lymph nodes.

A 40% live tumor cell rate following 7 cycles of chemotherapy was not a desirable result. The chemotherapy could be deemed as satisfactory or acceptable if the live-cell count in the tumor would be below 10%. Therefore, and in addition to positive surgical margins, we added radiotherapy for complete remission or even cure of the disease.

Conclusion

Neoadjuvant chemotherapy can be employed prior to radical nephrectomy in such cases in order to radically/efficiently/dramatically reduce the tumor mass.

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