

Computed Tomography Findings of a Tuberos Sclerosis Complex with Coexistent Multiple Myeloma: Case Report

Tuberöz Sklerozis Kompleks ve Eşlik Eden Multipl Miyeloma Olgusunda Bilgisayarlı Tomografi Bulguları

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ABSTRACT Tuberos sclerosis complex (TSC) is an autosomal dominant neurocutaneous disorder presenting with diverse clinical symptoms and multiple hamartomatous lesions in several organs. Imaging modalities play an important role in the assessment of TSC patients and reveal characteristic lesions in various organs. In our case report, we presented a 38 year-old female patient who exhibited clinical and computed tomography (CT) findings that were suggestive of TSC and also manifested with Multiple myeloma (MM) disease. We have described brain and thoraco-abdominal imaging findings of both diseases and briefly discussed TSC. In the literature, although various other tumors occurring with TSC have previously been reported, coexistence of TSC and MM disease seems to be a rare association.

Keywords: Angiomyolipoma; lymphangiomyomatosis; plasmacytoma; tuberous sclerosis

ÖZET Tuberöz sklerozis kompleks (TSC) çeşitli klinik semptomlar ve bazı organlarda multipl sayıda hamartomatöz lezyonlar ile ortaya çıkan otozomal dominant karakterde nörokütanöz bir hastalıktır. Görüntüleme modaliteleri TSC hastalarının değerlendirilmesinde ve çeşitli organlardaki karakteristik lezyonların ortaya konmasında önemli rol oynayabilir. Olgu bildirimizde, klinik ve bilgisayarlı tomografi bulguları TSC açısından anlamlı olan ve ayrıca multipl miyeloma (MM) hastalığı da bulunan 38 yaşında bir kadın hastayı tanımladık. Burada her iki hastalığın beyin ve torako-abdominal görüntüleme bulguları eşliğinde kısaca TSC hastalığını tartıştık. Literatürde TSC hastalığına eşlik eden çeşitli diğer tümöral lezyonların daha önce bildirilmiş olmasına karşın, TSC ve MM birlikteliğinin nadir olduğu düşünülmektedir.

Anahtar Kelimeler: Anjiyomyolipom; lenfanjiyoleiomyomatözis; plasmositom; tüberosklerozis

Tuberous sclerosis complex (TSC) is an autosomal dominant disorder characterized by mental retardation, seizures, skin lesions and formation of hamartomatous lesions in multiple organs such as the skin, liver, kidney, heart, lung and brain. It is regarded as the second most common neurocutaneous disorder after neurofibromatosis type 1 (NF 1). It has an incidence of 1/6.000-1/10.000 live births.¹ Approximately 2/3 of the cases occur due to spontaneous mutation of either the TSC1 (located on 9q34) or TSC2 (located on 16p13.3) genes. The diagnostic criteria of the disease was redefined in 2012 by the International Tuberos Sclerosis Complex Consensus Group.² In our case report, we presented a 38 year-old female patient who had TSC with coexisting multiple myeloma (MM) disease and discussed her computed tomography (CT) findings.

CASE REPORT

A 38 year-old female was admitted to our hospital due to bilateral flank pain, headache, cough and chest pain persisting for several weeks. Her intelligence was under normal level and she had a history of seizures for a long time. On physical examination, multiple adenoma sebaceum on the face and periungual fibromas on the feet were detected. Laboratory examination and chest x-ray evaluation were found within normal limits. Eventually, for further investigation the patient was referred to the CT department for brain and thoraco-abdominal imaging using a multi-detector row helical CT scanner (Somatom Sensation 16, Siemens Medical Systems, Erlangen, Germany). Informed consent was obtained from the patient prior to examination. Both un-enhanced and contrast-enhanced CT studies were performed. Contrast-enhanced CT images were obtained following 150 mL of nonionic contrast material administration (Ultravist 300, Iopromide injection 300 mg I/mL) by using a power injector at a rate of 2-4 mL / sec. Brain CT disclosed multiple subcentimeter calcified nodules along the subependymal surface of both lateral ventricles and calcified cortical tubers in the frontal and occipital lobes (Figure 1). A huge mass lesion measuring 80 x 60 x 50 mm in diameter originating from the right maxillary and sphenoid bones was detected. It was thought an extra-cranial and extra-axial lesion, but also involved the right fronto-temporal lobes and extended into the suprasellar and right orbital region. It showed heterogenous contrast enhancement and led to massive bone destruction (Figure 2). There was no any other contrast - enhanced lesion in the brain. On thorax CT examination, bilateral multiple thin-walled cystic lesions scattered throughout the lung parenchyma were found compatible with lymphangiomyomatosis (LAM) (Figure 3). Abdomen CT revealed bilateral enlarged kidneys with lobulated contours. A few simple cysts in both kidneys and a right adrenal fat density mass lesion suggestive of adenoma were detected. Besides, multiple fat-containing mass lesions indicating angiomyolipomas (AML) were present in



FIGURE 1: Brain CT image reveals subependymal calcified nodules and a calcified subcortical tuber in the occipital region.



FIGURE 2: Brain CT image, a slightly hyperdense huge extra-axial solid mass in the right temporal region extending to inferior frontal lobes, right orbita and sphenoid sinus causing destruction of bony structures as consistent with plasmocytoma.

the right kidney, whereas the left kidney showed a grade 4 hydronephrosis with massive parenchymal atrophy (Figure 4 a, b). On bone window targeted images, numerous sclerotic and lytic lesions were detected in multiple vertebral bodies and also a lytic expansile mass lesion in the xyphoid bone was found (Figure 5). These lesions were thought to be multiple bone metastases. The patient underwent a biopsy procedure for the right fronto-temporal mass lesion which revealed extramedullary plas-



FIGURE 3: Thorax CT image shows multiple, thin-walled cystic lesions throughout the bilateral lung parenchyma indicative of pulmonary LAM. There are also bilateral ground-glass opacities and septal thickening.

mocytoma. Consequently, the patient was diagnosed as having MM. On the other hand, based on the clinical and CT imaging findings consisting of subependymal calcified nodules, calcified cortical tubers, LAM and renal AML and cysts, the patient was also regarded as having TSC.

DISCUSSION

TSC is the second most common neurocutaneous syndrome after NF type 1. It is characterized by histologically benign hamartomas and low grade neoplasms occurring in multiple organs such as skin, brain, lung, liver and kidney. Cutaneous stigmata of the TSC including hypomelanotic macules, fibrous plaques, adenoma sebaceum and periungual fibromas are frequently found in patients and have no risk of any malignant transformation.³ In the central nervous system; cortical tubers, white matter heterotypes (dysplastic or demyelinating white matter lesions), subependymal nodules and subependymal giant cell astrocytoma (SEGA) are regarded as characteristic lesions.^{4,5} Cortical tubers are usually located in the frontal and temporal lobes and thought to be related to the seizures and behavioral problems seen in these patients. They do not show malignant transformation, but may calcify in time.^{4,6} Subependymal nodules are found in 80%-90% of patients with TSC.^{4,6} They are usually smaller than 1 cm in diameter and located along the surface of the third ventricle and lateral ventricles.

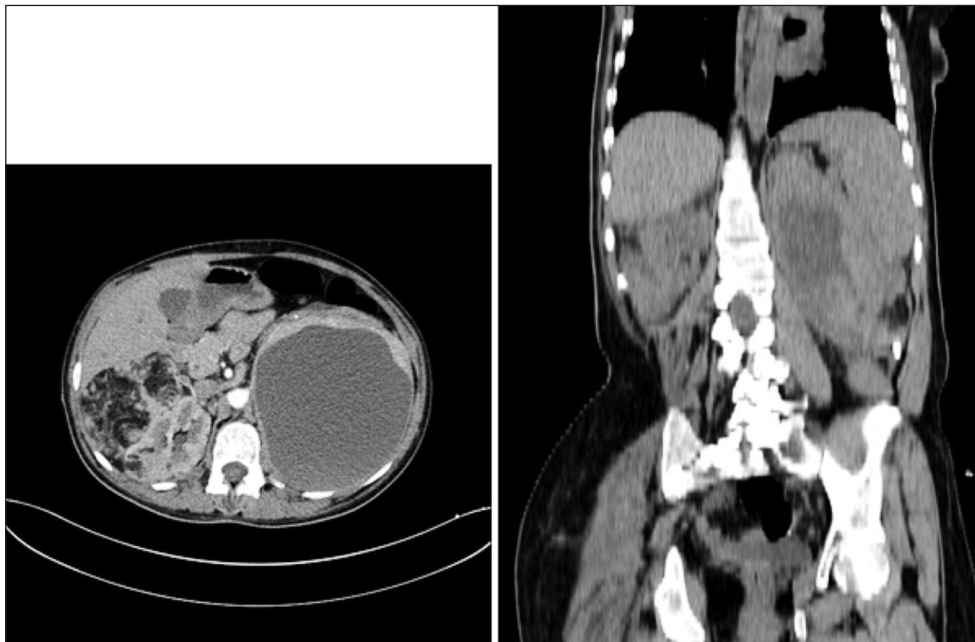


FIGURE 4: a, b) Abdomen CT images, multiple fat-containing hypodense mass lesions in the enlarged right kidney suggestive of AMLs is seen. Also a grade-4 hydronephrosis is present in the left kidney.



FIGURE 5: Sclerotic and lytic lesions were detected in multiple vertebral bodies and a lytic expansile mass lesion in the xyphoid bone was also found.

Although subependymal nodules are almost asymptomatic, they can transform into SEGA in a gradual fashion.⁷ SEGA has been reported to occur in 5% to 14% of TSC patients and also account for 90% of all intracranial tumors associated with TSC.⁵ These tumors usually develop around the foramen of Monro, appear hypointense on T1 and T2 weighted images and show intense contrast enhancement on brain magnetic resonance imaging (MRI).⁷ SEGAs should be removed by surgical intervention, otherwise they can lead to neurological deficits and development of hydrocephalus.⁸ Despite the fact that SEGA is the most common tumor seen in TSC patients, other tumors may also accompany this patient population. For instance, choroid meningioma and malignant melanoma cases have been reported in TSC.^{9,10} Although rare, other tumors such as glioblastoma multiforme, astroblastoma and hemangioma have also been reported in these patients.¹¹ TSC has also been associated with gastric, testicular, breast, hepatocellular, somatostatinoma and sarcoma types of cancer. But TSC with accompanying MM disease, we think would be a rare association in the literature. Because only one case has been reported by Soryal et al. in a 66 year old male patient who had a history of TSC presented with acute kidney injury and renal impairment due to MM disease.¹² In TSC patients, renal lesions are frequently encountered including AML, cysts and renal cell carcinoma (RCC). AMLs are the

most common renal lesions in TSC (55%-75%) and may lead to death.¹³ Patients have a high risk of serious complications such as life-threatening hemorrhages which occur in 25% to 50% of patients. As the disease progresses, chronic renal failure that requires hemodialysis may develop. RCCs may develop within dysplastic epithelial cysts in 2%-3% of these patients.¹⁴ TSC related RCC is usually bilateral and more often seen in women. However, in this patient population, it is usually hard to differentiate RCC from poor-fat containing AML on the basis of imaging studies alone and this sometimes may lead to an over-called diagnosis. The characteristic cardiac finding seen in TSC patients is rhabdomyomas. These tumors are benign and usually multiple.¹⁵ They typically develop in the in-utero period and are generally diagnosed by means of prenatal ultrasound.² All of these lesions regress spontaneously even the ones who have presented with symptoms before.¹⁶ LAM is the major lung disease seen in TSC patients. It is characterized by cystic destruction of the lung parenchyma due to infiltration by smooth muscle cells. Sporadic LAM is rarely seen in patients without having TSC. In a study performed by Moss et al. a high prevalence of 34% LAM was reported in TSC patients. Costello et al. found that 20% of the TSC patients in their series had developed LAM.^{17,18} Pulmonary LAM mainly affects females of reproductive age with dyspnea and pneumothorax as the most common clinical manifestation. Herein, we have reported a female patient diagnosed with an unfamiliar association of TSC and MM disease. We have also described the clinical and CT features of TSC with a review of the related literature.

Conflict of Interest

Authors declared no conflict of interest or financial support.

Authorship Contributions

All authors have contributed in the preparation and writing of the article.

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