

Osteosarcoma In A Patient With Tuberous Sclerosis

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Citation

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Abstract

The tuberous sclerosis complex (TSC) is an autosomal dominant disorder characterized by benign para nasal angiofibroma and benign tumors of the periungual area ,brain, heart, that can be associated with seizures, mental retardation, and many benign tumors of kidney. Malignant tumors also can occur in patients with tuberous sclerosis .TSC is now known to be associated with benign tumor, but rarely malignant tumor. We report a case of TSC with osteosarcoma and death due to pulmonary metastases, and a short review of recent literatures regarding the conditions.

INTRODUCTION

Tuberous sclerosis complex is a hamartomatous disease that affects the skin and internal organs. Cutaneous manifestations include angiofibromas, fibrous plaques, collagenomas (shagreen patches), periungual fibromas (Koenen tumors), gingival fibromas, dental enamel pits, hypopigmented macules (ash-leaf and confetti), and café-au-lait macules(.).Tuberous sclerosis is not a rare disease, but It's association with osteosarcoma has not been reported in medical literature . This complex is thought to have inhibitory effects on cell growth, cell proliferation, intracellular trafficking, cell adhesion, and cell migration.)_{1,2,3}). The TSC is an autosomal dominant disorder characterized by benign facial angiofibroma and benign tumors of the periungual area, brain, heart, that are associated with seizures, mental retardation, and many benign tumors of kidney. The disease is now accepted as a complex syndrome with multiple organ involvement and the patient's clinical symptoms/signs may lead us to investigate a certain system (4). Malignant tumors also can occur in patients with tuberous sclerosis, particularly in the kidney, although they occur less frequently (0.5% of all TSC cases) in compare with benign tumors. 10 malignant tumors from 8 TSC patients are reviewed (everyone of two cases had two malignancies). Seven tumors were renal, carcinoma, one case was association of TSC with unknown malignancies located in inguinal region, and one was from the brain (4,5,6). We report a case of TSC in association with tibial osteosarcoma. Amputation has done but metastases to the lung caused death to him Our case is a 15 year old girl with TSC girl associated with osteosarcoma of tibia so (leg)

which has been expired due to pulmonary metastases .

Thinking about premature osteosarcoma in a patients with TSC can guide that this complex may be a risk for developing malignant transformations by oncogenic predomination in them (6,7).

CASE REPORT

A 15 year old girl, has been admitted first in the surgery ward of Kerman Darman hospital in Iran with chief complain of a mass on her left shin at 8 months ago. Radiologic & pathologic investigation has been done on this mass confirmed impression of tibial osteogenic sarcoma. Amputation of left thigh has been done and following up of him after 8 sessions of chemotherapy showed that her chief complain changed to left shoulder pain with mild dyspnea and second hospital admission was done. Chest x-ray showed a dense radiological pulmonary mass, most probably metastasis to the lung. In bronoscopic examination and taking a biopsy metastatic osteosarcoma approved and totally excision of pulmonary mass was done and in pathological report of cut section pulmonary metastasis of osteosarcoma has been approved (Fig. 1-2-3). Before she has been discharged of hospital a dermatological consultation for therapy of acne like lesion has been done, and in examination centro-facial due mono morph verrucos lesions specially on para nasal area that has been observed that they has been appeared when she was 7 years old. In general examination, low intelligence in association history of epilepsy, with multiple dark red papules has been observed in her centro facial area, a few ash leaf hypo pigmented patches are seen over the remain leg and on her back. One of nasolabial papule has been excised and pathological report

of these lesion was compatible with an angiofibroma (association of osteogenic carcinoma and tuberous sclerosis complex in a case). She has being followed till on the 5th post-operative day, she has been expired 3 months later after discharging of hospital.

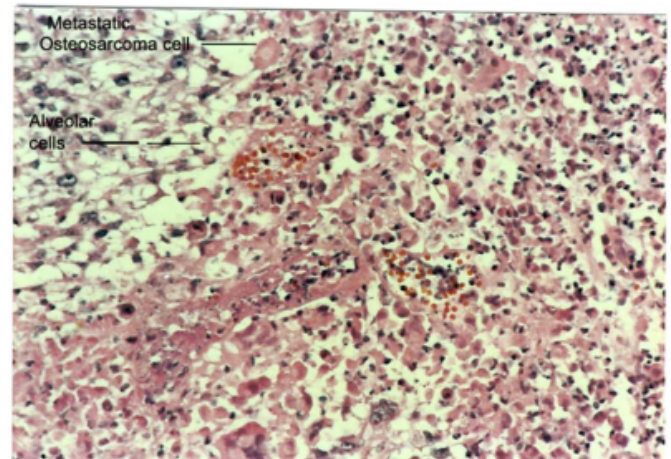
Figure 1



Figure 2



Figure 3



DISCUSSION

Overlap of osteosarcoma in a case with tuberous sclerosis may be usually a consensus association of these disorders, but we can think about their correlation of them, because of increasing prevalence of malignancies such as astrocytoma in patients with tuberous sclerosis has been reported. Our case is a missed one of tuberous sclerosis that has been admitted in hospital due to her major progressive problem with metastases to the lung. TSC is a genetic disorder with hamartomatous in many organs, in particular the skin, brain, eye, kidney and heart^(1,2). Classically skin lesions are not invariably seen in association with epilepsy and mental retardation^(7,8,9). Cystic lesions of phalanges and long bones are not uncommon in TSC. Our patient is the first documented case that being report as a transformation of tibial osteosarcoma in a case with tuberous sclerosis complex. She has been expired due to pulmonary metastasis of osteosarcoma. An extensive review of medical literature by Berger M.S. in Netherlands, Gutmann-DH in Spain and Xiao-GH et al in 1997 has shown that pediatric brain tumors occur with a frequency of 24 to 27 cases/year in a cohort study of 1 million children and the lesion can be present in the cases of tuberous sclerosis^(7,9,10,11). More literature review showed that malignant transformation is seen in 0.5% of all cases with TSC, but association of osteosarcoma with tuberous sclerosis has not been reported until now. In our case, chest radiography shows cardiomegaly and a metastatic nodule that were seen in lower left lobe of her lung. Although association of TSC with cystic mass in lung was first seen in 1918 by Lutembacher, but he interpreted the bilateral pneumothorax to be the result of metastases from fibrosarcoma of the kidneys^(1,3,4,5). Malignancies are rare in TSC and in literature review as we know this is the first case of osteosarcoma in association with this complex. We think

more about it's correlation of these two disorders against an association event of them.

References

1. Christopher T Cassetty MD Tuberous sclerosis complex (Bourneville disease) *Dermatology Online Journal* 10 (3): 17
2. Narayanan V. Tuberous sclerosis complex: genetics to pathogenesis. *Pediatr Neurol* 2003; 29: 404.
3. Birchenall-Roberts MC, et al. Tuberous sclerosis complex 2 gene product interacts with human SMAD proteins: a molecular link of two tumor suppressor pathways. *J Biol Chem* 2004 Apr 2 [Epub ahead of print].
4. Al Saleem T, Wessner LL, Scheithauer BW, Patterson K, Roach ES, Dreyer SJ, Fujikawa K, Bjornsson J, Bernstein J, Henske EP: Malignant tumors of the kidney, brain, and soft tissues in children and young adults with the tuberous sclerosis complex. *Cancer* 1998, Nov 15 ;83(10); 2208-2216.
5. Narayanan V. Tuberous sclerosis complex: genetics to pathogenesis. *Pediatr Neurol* 2003; 29: 404.
6. Peh, W.C.G., Shek, T.W.H., Wang, S.C., Wong, J.W.K. and Chien, E.P. Osteogenic sarcoma with skeletal muscle metastases. *Skeletal Radiology*, 1999, 28: 298-304.
7. Birchenall-Roberts MC, et al. Tuberous sclerosis complex 2 gene product interacts with human SMAD proteins: a molecular link of two tumor suppressor pathways. *J Biol Chem* 2004 Apr 2 [Epub ahead of print].
8. Xiao-GH ; Shoarinejad - F ; J in- F ; Golemis - EA ; Yeung - RS : the tuberous sclerosis 2 gene product , tuberin , functions as a Rab5 Gtpase activating protein (GAP) in modulating endocytosis. *J- Biol - Chem.* 1997 Mar 7: 272(10):6097.
9. Wienecke R, Maize JC, Jr, Shoarinejad F, Vass WC, Reed J, Bonifacio JS, Resau JH, de Gunzburg J, Yeung RS, DeClue JE: Co-localization of the TSC2 product tuberin with its target Rap1 in the Golgi apparatus. *Oncogene* 1996, 13:913-923
10. Laass MW, et al. Tuberous sclerosis and polycystic kidney disease in a 3-month-old infant. *Pediatr Nephrol* 2004 Mar 9 [Epub ahead of print].
11. Shepherd CW, Gomez MR, Lie JT, Crowson CS: Causes of death in patients with tuberous sclerosis. *Mayo Clin Proc* 1991, 66:792- 796.

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