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Reactive Pseudosarcomatous Lesions of Soft Tissues: Clinicopathologic Study of 13 Cases

Yumuşak Dokunun Psödosarkomatöz Lezyonları: Klinikopatolojik Çalışma

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ABSTRACT

Reactive pseudosarcomatous lesions of soft tissues are uncommon and challenging entities. They mimic sarcomas because of the clinical history of rapid growth and spindle cell proliferation. Some of these lesions are characterized by new bone or osteoid formation. In this report the clinical, histological, histochemical and immunohistochemical features of 13 cases of these reactive fibroproliferative lesions composed of an ossifying fasciitis, an aneurysmal bone cyst of soft tissue, 1 myositis ossificans, 3 proliferative fasciitis and 7 nodular fasciitis cases with follow ups between 8 months to 14 years, were analyzed. Some of those cases had a history of trauma. These lesions were collagen rich in Masson's trichrome.

Immunohistochemically; smooth muscle actin and vimentin were strongly positive. Our case of ossifying fasciitis is the 13th cases and aneurysmal bone cyst of soft tissue case is the 15th cases of the literature. As a result; clinical and morphological features of those entities were found similar to each other. Finally a unifying concept of fibroblastic and myofibroblastic proliferation in response to trauma, genetic and/or an unknown factor are proposed.

Key Words: *Proliferative fasciitis, Ossifying fasciitis, Aneurysmal bone cyst of soft tissue, Myositis ossificans, and Nodular fasciitis.*

ÖZET

Yumuşak dokunun reaktif psödosarkomatöz lezyonları ender görülen ve ilginç lezyonlardır. Klinikte hızlı büyüme hikayeleri ve histopatolojik olarak iğsi hücre proliferasyonu nedeniyle sarkomları taklit ederler. Bu lezyonların bazıları yeni kemik yapımı veya osteoid oluşumuyla karakterizedir. Bu makalede klinik takipleri 8 ay ile 14 yıl arasında değişen, birer ossifiyan fasiit,

yumuşak dokunun anevrizmal kemik kisti ve miyozitis ossifikans, 3 proliferatif fasiit ve 7 nodüler fasiit olgusundan oluşan yumuşak dokunun reaktif psödosarkomatöz lezyonlarından toplam 13 olgu klinik, histolojik, histokimyasal ve immünhistokimyasal özellikleri araştırılarak incelenmiştir. Bu olguların bazılarında travma öyküsü mevcuttur. Bu lezyonlar Masson trichrome ile kollajenden zengindir. Immunhistokimyasal olarak; düz kas aktini ve vimentin kuvvetli pozitiftir. Ayrıca ossifiyan fasiit vakamız literatürde şimdiye kadar bildirilmiş 13. vaka olurken, yumuşak dokunun anevrizmal kemik kisti vakamız ise literatürde şimdiye kadar bildirilmiş 15. vaka olma özelliğindedir.

Sonuç olarak; tüm bu lezyonların klinik ve morfolojik özellikleri birbirlerine benzer nitelikte bulunmuştur. Oluşum mekanizmaları konusunda travmaya cevaben ortaya çıkan fibroblastik ve miyofibroblastik proliferasyon, genetik ve/veya henüz bilinmeyen başka faktörlerin varlığı düşünülmektedir.

Anahtar kelimeler: *Proliferatf fasiit, Ossifiyan fasiit, Yumuşak dokunun anevrizmal kemik, Miyozitis ossifikans ve Noduler fasiit.*

INTRODUCTION

Nodular fasciitis (NF), proliferative fasciitis (PF), ossifying fasciitis (OF), myositis ossificans (MO) and aneurysmal bone cyst of soft tissues (ABC of ST) are uncommon, reactive, fibroproliferative, pseudosarcomatous, self-limited, non-recurrent lesions of soft tissues. There is a myofibroblastic spindle cell proliferation and a clinical history of rapid growth in all of these lesions; therefore the morphologic and clinical features mimic sarcomas. Some of these lesions are characterized by new bone or osteoid formation. The etiology of these lesions is still not clear. In some previously reported articles trauma was suspected as the trigger in these lesions. We report certain common clinicopathologic and immunohistochemical features of 13 of these reactive pseudosarcomatous soft tissue lesions.

MATERIALS AND METHODS

We have studied 13 cases of reactive fibroproliferative lesions clinically, morphologically, histochemically and immunohistochemically; including one MO (Case 1), ABC of ST (Case 2), OF (Case 3), three PF (Cases 4-6) and seven NF (Cases 7-13) cases with follow ups between 8 months to 14 years. The clinical and pathological features of the cases are summarized in Table-1.
Histochemically Masson's Trichrome and immunohistochemically pan-cytokeratin (CK, DAKO, Denmark), CD-34 Class II (CD-34, DAKO, Denmark), desmin (1/25, Zymed Laboratory, San Francisco, CA, USA), smooth muscle actin (SMA; 1/40, Novacastra, Newcastle-upon-Tyne, UK), vimentin (1/40, Novacastra, Newcastle-upon-Tyne, UK), S-100 protein (1/150, DAKO, Denmark) and Myeloid/Histiocyte antigen (Clone Mac-387, 1/10, DAKO, Denmark) were applied to the paraffin sections of these cases. The histochemical and immunohistochemical results were summarized in Table-2.

CLINICAL AND PATHOLOGICAL FINDINGS

Case 1

An 11-months-old male presented with limitation of movement, pain and tenderness in his right knee that has started 20 days before admission. He had a history of falling out of his bed for four times. During physical examination there were limitation of movement, tenderness, pain and an increase in local heat in his right knee region. A deformity in the soft tissue around the right knee region was detected.

On X-ray a fracture at the distal epiphyseal plate and metaphysial destruction in the right femur was found. On the same day, surgical excision was performed. During operation the fracture at the distal epiphysis was detected and irregularly shaped brown colored tissue from the periphery of femur was removed. Histopathologic examination revealed osteomyelitis. Postoperatively during antibiotic treatment a purulent drainage from the operation site was determined and a second surgery was performed. During this operation synovium of the right knee joint was found to be hypertrophic. The surrounding muscle tissue was firm and pale. A firm fibrotic and calcified tissue surrounding the femoral body was removed from the muscle tissue. The material of the second operation was a fragmented tissue composed of irregular; grey to white colored in which the largest fragment measured 6 x 4 x 1.3 cm was extracted from the right distal femoral region.

Table 1: Clinicopathological findings of case materials

Patient No	Age / Sex	Location	Preoperative Diagnosis	Final Pathological Diagnosis	Follow-up*
1	11 months old / Male	Right knee	Osteomyelitis	Myositis Ossificans	9 years
2	23 year old / Female	Left groin	Synovial sarcoma	Aneurysmal Bone Cyst of Soft Tissue	3 years
3	57 year old / Male	Left groin	Lymph adenopathy	Ossifying Fasciitis	5 years
4	27 year old / Female	Left lower abdominal wall	Unknown mass	Proliferative Fasciitis	9 years
5	57 year old / Female	Left arm	Metastatic carcinoma of breast	Proliferative Fasciitis	3 years
6	51 year old / Female	Left arm	Neurofibroma	Proliferative Fasciitis	2 years
7	23 year old / Female	Anterior neck triangle	Lymph node	Nodular Fasciitis	7 years
8	16 year old / Male	Right scapular region	Sarcoma	Nodular Fasciitis	11 years
9	42 year old / Female	Right cheek	Pleomorphic adenoma of parotid gland	Nodular Fasciitis	4 years
10	50 year old / Female	Right hand dorsal area	Fibroma	Nodular Fasciitis	3 years
11	36 year old / Female	Left knee	Unknown mass	Nodular Fasciitis	1 year
12	52 year old / Female	Left arm	Fibroma	Nodular Fasciitis	10 months
13	67 year old / Male	Left brachio-radial region	Neuroma	Nodular Fasciitis	8 months

*Without evidence of the disease

Table 2: Histochemical and immunohistochemical findings

Case No	Pathological Final Diagnosis	Masson's Trichrom	Vimentin	S-100	Mac-387	SMA	Desmin, CD-34 and CK
1	Myositis Ossificans	Collagen Rich	(+) in chondroida and osteoid areas	Focal (+) in chondroid areas	(-)	(-)	(-)
2	Aneurysmal Bone Cyst of Soft Tissues	Collagen Rich	(+)	(-)	Focal (+) in histiocytes	(+)	(-)
3	Ossifying Fasciitis	Collagen Rich	(+)	(-)	Focal (+) in histiocytes	(+)	(-)
4-6	Proliferative Fasciitis	Collagen Rich	(+)	(-)	Focal (+) in histiocytes	(+)	(-)
7-13	Nodular Fasciitis	Collagen Rich	(+)	(-)	Focal (+) in histiocytes	(+)	(-)

Histologically, mature chondroid tissue and osteoid formation within the focal hemorrhagic areas were seen. In the periphery of the lesion a well formed lamellar bone gradually maturing from poorly formed trabeculae of osteoid in the middle zone and in the centre a fibroblastic proliferation composed of plump to spindle shaped fibroblasts within a myxoid matrix could be seen (Figure-1). An inflammatory reaction composed mostly of mononuclear cells in the periphery of the lesion was also detected.

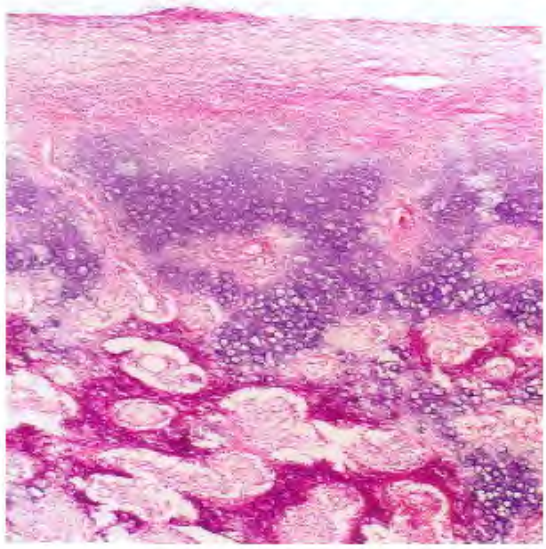

Figure 1: *The typical zonal pattern of myositis ossificans, H&E (x40)*

Case 2

A 23-year-old female complained of 3-months' history of pain and swelling in her left groin. There is no history of trauma. On physical examination a painful, firm, poorly demarcated mass measuring approximately 6 cm in diameter was palpated in the left inguinal area. On ultrasound; a calcified cystic mass measuring 5 cm in diameter located in the left pectineus muscle was demonstrated. On magnetic resonance imaging a mass measuring 8x7x6 cm, that pushed left femoral vessels medially, was located at the anterior side of the hip joint, between the iliacus and rectus femoris muscles was found. Biopsy was performed with a preliminary clinical diagnosis of sarcoma. After the pathological diagnosis revealing "aneurysmal bone cyst" total excision was performed. During operation a mass measuring 10 cm in diameter with a calcified outer surface that was located in soft tissue between muscles was removed.

On gross examination; it was a fragment of grey to brown-colored, solitary well-circumscribed mass separated from the surrounding soft tissues by an egg shell-thin layer of bone, which measured 9x6.5x6 cm. When sectioned, the lesion showed multiple anastomosing cavernous spaces separated by fibrous septa and filled with bloody viscous material (Figure-2).

Figure 2: *The multiple cavernous spaces that could be seen on cut surface of the aneurysmal bone cyst of soft tissue*

Histologically, the lesion consisted of anastomosing cavernous blood channels surrounded by muscle and connective tissue and mature lamellar bone trabeculae with prominent osteoblastic rimming in the periphery. These cavernous blood channels were not covered with endothelial lining and were separated by fibrous septa composed of fibroblasts, multinucleated giant cells and a lacework of osteoid trabeculae (Figure-3). In the lumen of these cavernous spaces erythrocytes and fibrin could be identified. Some of these septa contained mature lamellar bone trabeculae and bone marrow proliferation within these bone trabeculae were identified. Osteoclastic giant cells were included in the cystic spaces and they sometimes lined the septa.

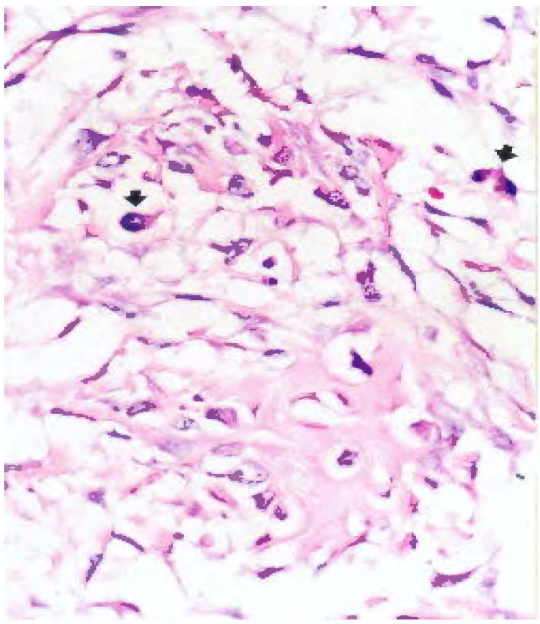

Figure 3: *Cavernous spaces, osteoid trabeculae and fibrous septa, H&E (x40)*

Case 3

A 57-year-old male complained of pain in the left lower extremity that had become more prominent during the last 3 months. The pain was alleviated with rest. He had a history of bilateral inguinal hernia operation 13 years before and a history of previous angiography through the left femoral region in the same year. During physical examination pulses could not be felt in the popliteal, posterior tibial and dorsalis pedis arteries of his left lower extremity. Pulses were present in both of the femoral arteries. Angiography was performed using left groin approach and bilateral occlusive disease of femoral arteries was found. One month later, a left femoropopliteal by-pass and right femoral embolectomy was performed. During the operation surgeon encountered a firm cylindrical mass in the left groin and removed this mass with a preliminary diagnosis of lymphadenopathy.
It was a fragment of grey-yellow irregular, solitary soft tissue fragment, which measured 5x3x2.5 cm.

Histologically, a hyperplastic lymph node and an irregular lesion beneath perinodal fat tissue could be seen. Plump fibroblastic cells were arranged in short interlacing fascicles. The fibroblasts were spindle shaped and pleomorphic. They frequently had nucleoli. Occasional mitotic figures were seen within fibroblasts but no abnormal mitotic figures were identified. In some areas, the proliferating fibroblasts were separated by clear, granular or basophilic myxoid matrix. In other areas the lesion extended into adjacent adipose tissue. Skeletal muscle was not identified in the lesion. Within this fibroblastic proliferation foci of immature woven bone composed of irregular osteoid showing chondroid differentiation and calcification were seen (Figure-4). The osteoid trabeculae were rimed by plump osteoblasts. There were extravasated erythrocytes and macrophages within the lesion.

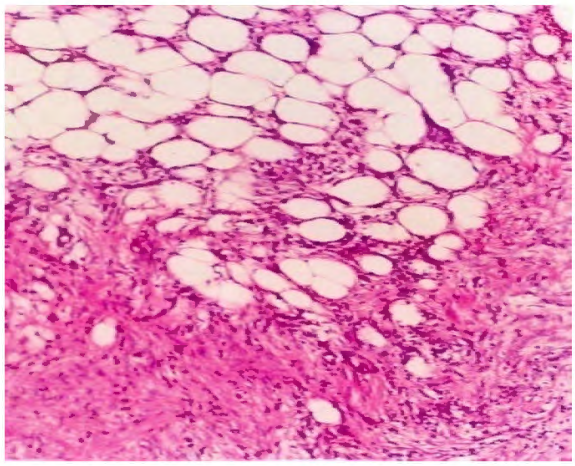

Figure 4: *Irregular osteoid formation within fibroblastic stroma, H&E (x460).*

Case 4

A 27-year-old female complained of feeling a palpable mass without pain in the left lower quadrant of abdominal wall. She had no history of trauma. During the physical examination a firm mass measuring 2x1x1 cm adjacent to the overlying skin was found in the left lower abdominal wall. Complete excision of this poorly demarcated mass was performed.

Case 5

A 57-year-old female, with a history of infiltrative ductal carcinoma, complained of a painless palpable mass in the left arm. Left mastectomy and axillary lymph node excision was performed five years ago. On physical examination a firm mass measuring 1.5x1x1 cm adjacent to the overlying skin was detected. Complete removal was performed with a preliminary diagnosis of metastatic carcinoma of breast.

Case 6
A 51-year-old female, complained of a painless palpable mass in the left arm. She considered that she hit her arm to the door 3 months before. During the physical examination a firm mass measuring 2x1x1 cm adjacent to the overlying skin was found in the left arm. Biopsy was performed with a preliminary diagnosis of neurofibroma.

Pathological findings of cases 4-6:
The surgical specimens of the Cases 4-6 were similar each other. Each was fragment of grey to brown-colored, irregularly shaped fibro-adipose tissues. Grey colored, irregular, poorly demarcated firm mass were identified in the central part of these tissues.

Histologically, Cases 4-6 were sharing the same features. Irregular lesion beneath the adipose tissues could be seen. Plump fibroblasts were arranged in interlacing fascicles. The fibroblasts were satellite or polygonal in shape. They had abundant eosinophylic cytoplasm surrounding large but oval to round vesicular nuclei with prominent nucleoli. Some of them were resembled ganglion cells. There were occasional mitotic activity but there is no atypia. These fibroblasts were dispersed singly within a slightly myxoid stroma. A central fibrinous area could be seen. There was an inflammatory reaction around this lesion especially prominent in the areas of infiltration into the subcutaneous adipose tissue (Figure-5). No metastatic carcinoma was found in case 5.

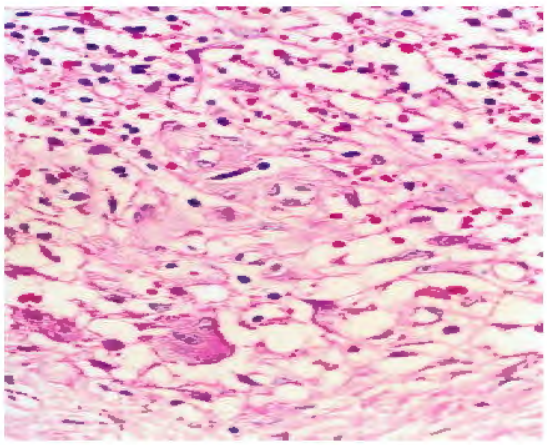

Figure 5: *The extension of the fibroblastic proliferation into the adipose tissue, H&E (x40).*

Case 7
A 23-year-old female complained of feeling mass without pain in her neck. She had a history of sensory neural deafness and no other illnesses. During physical examination a firm mass measuring 1.5 cm in diameter was found in the anterior triangle of neck. This subcutaneous lesion was removed with the overlying skin.

Case 8
A 16-year-old male complained of painless swelling on his right scapular area. He had given a history of playing basketball and many traumas during competitions. During physical examination a solitary, firm mass measuring approximately 4 cm in diameter was found above his right scapula. This subcutaneous mass was removed with the overlying skin with a preliminary diagnosis of sarcoma.

Case 9
A 42-year-old female complained of a painless swelling in her right cheek. She did not remember a trauma history clearly. Physical examination revealed a painless, firm, nodular, solitary mass in the right parotid region. All other physical findings were normal. Surgical excision with a preliminary clinical diagnosis of pleomorphic adenoma of parotid gland was performed. During operation no gross pathological abnormality was detected in parotid gland but a well-circumscribed, solitary mass measuring 1 cm in diameter was found within the right masseter muscle.

Case 10
A 50-year-old female complained of a painless swelling in the right hand with a history of many minor traumas to the right hand. During physical examination a painless, firm, nodular, solitary mass measuring 1.5 cm in diameter was found in the right hand dorsal area. All other physical findings were normal. Complete excision of the lesion was performed with a preliminary diagnosis of fibroma.

Case 11
A 36-year-old female complained of a painless mass in the left knee. She did not remember any recent trauma to the related site. During physical examination a painless, firm, nodular, solitary mass was found in the medial site of the patella in the left knee. All other physical findings were normal. Total excision of the lesion was performed.

Case 12
A 52-year-old female complained of a painless swelling in the left forearm. During physical examination a painless, firm, nodular, solitary mass measuring 1.2 cm in diameter was found in the left forearm. All other physical and laboratory findings were normal. Total removal of the lesion was performed with a preliminary diagnosis of fibroma.

Case13
A 67-year-old male complained of a painless swelling in the left arm. During physical examination a painless, firm, nodular, solitary mass measuring 1.7 cm in diameter was found in the brachioradial area of the left arm. All other physical findings were normal. Complete excision of the lesion was performed with a preliminary diagnosis of neuroma.

Pathological findings of cases 7-13:
On the gross examination, cases 7-13 were nodular, solitary and firm. The cut surfaces of the tissues were grayish white, hard, nodular and well-demarcated.

Histologically, they were composed of spindle shaped or plump fibroblasts arranged in randomly interlacing fascicles within a myxoid matrix. Long cytoplasmic processes were detected in most of those fibroblasts. Numerous plump fibroblasts have abundant cytoplasm, large nuclei, and small nucleoli and diffuse light chromatin pattern. A zonation effect with a hypo-cellular hyalinization center and more hyper-cellular periphery could be identified in all of these lesions (Figure-6). At the periphery of the lesions inflammatory cells composed of small collections of mononuclear cells were also seen. Occasional mitotic activity was determined but there was no atypia. Infrequent multinuclear giant cells were also revealed within these lesions.

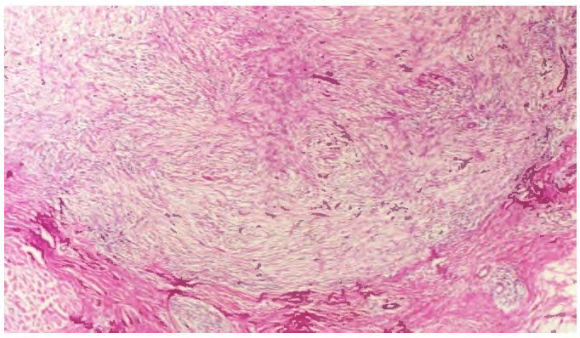

Figure 6: *Well-circumscribed nodular lesion, Masson's Trichrome (x40).*

DISCUSSION

NF is a reactive, fibroproliferative lesion, which is a self-limited pseudosarcomatous proliferation of fibroblasts occurring in subcutaneous or deep fibro-connective tissue (1-6). Most of the NF cases occur between the ages of 20 and 30 years and affect males and females equally. NF is commonly located on the forearm, arm, face and shoulder and is characterized by its rapid growth in a very short period of time, as a matter of weeks. Few of the patients complain of pain and a history of trauma to the related area (2,4,5). The largest NF series were reported by Bernstein and Lattes (2) and composed of 134 NF cases including 7 OF cases. Another NF series composed of 42 cases including 3 OF and 3 PF cases were reported by Samaratunga et al.(5). In previous reports of NF; OF and PF were reported as variants of NF (2,4,5,7).

The largest PF series composed of 53 cases were reported by Chung and Enzinger (7). They described the morphological features of PF, and reported that some clinical and morphological features of PF have resembled NF but unlike NF; an older age group was affected in PF (7). In PF reactive fibroblasts are more eosinophylic and polygonal in shape and resemble ganglion cells. PF is poorly circumscribed, and giant cells, which are common findings in NF are extremely rare in PF (7).

Metaplastic bone is recognized as an uncommon finding in cases of reactive fibroproliferative lesions (2-5), (8-11). MO, OF and ABC of ST are reactive pseudosarcomatous lesions that are characterized by extra-osseous new bone formation (2), (4-9), (11-22). MO is characterized by a typical new bone forming so called "zonal phenomenon" which is the organization of the lesion into three zones; well formed lamellar bone in the periphery, gradually maturing from poorly formed trabeculae of osteoid in the middle and a fibroblastic proliferation similar to NF in the central portion (11,14,22).In previous reports of MO; trauma was suspected as the cause that triggers the reactive process. Michelsson et al. (14). reported that they had observed heterotopic bone formation as a consequence of repeated forcible distention of previously immobilized soft tissues. MO occurs in patients aged between 20 to 80 years and males are commonly affected. The sporadic form of posttraumatic MO should be distinguished from

the disorder known as "fibrodysplasia ossificans progressive" which is similar to MO microscopically. This disorder begins in childhood and occurs spontaneously (11, 22). MO is an uncommon entity in infants and can be confused with osteomyelitis (16). Our case of MO is an infant with a history of multiple traumas and without a family history of "fibrodysplasia ossificans progressiva"

ABC of ST is an extremely rare entity. Only 12 previously reported cases (Table-3) were found from the literature (12,13,15, 17-21, 23). The largest series of ABC of ST composed of five cases and was published in year 2002 by Nielsen et al. (15). To our knowledge presented ABC of ST case is the 15th case of ABC of ST which has been described in the localization of left groin similar to the case of Amir et al. (12). Like our case all of the reported cases were complained of feeling pain and a palpable mass in the related area and neither of them had a history of trauma (12,13,15,17-21,23). Shannon et al. (20) reported that new bone formation at various stages of maturation within the lesion had raised the possibility that the ABC of ST may arise within a MO. But this new bone formation in ABC of ST did not show the characteristic "zonal phenomenon" of MO. However Lopez-Barea et al. (13) had reported that this lesion could be considered secondary to a trauma that had provoked a hemorrhagic soft tissue's vascular abnormality, which followed by a reactive fibroproliferative process. They have also stated that MO and ABC of ST might be two different morphological responses to the same injury and this difference depended on the type and amount of tissue damage (17). However in previously reported ABC of ST cases there was no history of trauma (12,13,15,17-21,23). Some of the intraosseous ABC cases shows 46, XY, t (17;17) (p13;q12). One of the ABC of ST case had showed this cytogenetic abnormality in the literature but no specific abnormality having been identified in MO (15).

Heterotopic bone formation had also been reported in rare cases of NF series. This uncommon entity is known as OF. The first reported case of OF was a case of NF in which giant cells and ossification were prominent and Kwittken (3) had named this case as "Fasciitis Ossificans". To our knowledge there are 13 reported cases of OF including our case in the literature (2-5, 8,9,11). It has been reported that OF was occurred most commonly in young adults, the upper extremities being mostly involved and in 10-15% of patients a trauma history was found (1,4,9,24). Our case was a 57 year old male with an OF located in his left groin which occurred following an angiography procedure, this patient had also undergone bilateral inguinal hernia repair as well as angiography. In our case the trauma history was postulated as an etiological factor like the case of Daroca et al. (8).

Montgomery and Meis had studied the immunohistochemical profile of 53 NF cases (4). They had reported that in addition to the more commonly recognized fibroblastic and myofibroblastic features; a fibrohistiocytic differentiation was exhibited by NF cases (4). They had found that SMA, muscle specific actin and vimentin had been expressed but desmin and S-100 protein had not been expressed by NF cases. Our immunohistochemical profile in our cases of NF, PF, OF and ABC of ST are similar as the findings of Montgomery and Meis (4). In our cases rather than presented MO case, SMA and vimentin were strongly expressed. Mac-387 was focally expressed in histiocytes. Neither desmin nor S-100 protein expression was detected. Additionally, these lesions were found collagen rich in Masson's trichrome stain. Presented MO case was also collagen rich in Masson's Trichrome and immunohistochemically S-100 protein expression was found in chondroid areas but SMA, desmin and Mac-387 were negative. Sarangarajan and Dehner (6) had reported that in cases of cranial and extra-cranial fasciitis including NF of childhood; vimentin and SMA were expressed. Desmin was not expressed in their cases. These immunohistochemical findings were also similar to the findings of our cases and the cases of Montgomery and Meis (4).

These reactive, pseudosarcomatous soft tissue lesions are very infrequent and challenging entities. Even though their names are different, either their clinical behavior, morphological or immunohistochemical findings are close to each other. A history of trauma is the most popular suggested etiological factor that triggers this reactive process. Although recent cytogenetic studies have demonstrated clonal chromosomal aberrations in some NF cases which raise the possibility that NF may be in fact neoplastic rather than reactive in origin (24); Koizumi et al. had recently demonstrated polyclonal cellular expansion by HUMARA-MSP assay in NF (25). This recent

Table 3: Aneurysmal bone cyst of soft tissue cases

Patient	Author	Age (year)	Sex	Location
1	Salm et al. (19)	32	Male	Thigh
2	"	45	Female	Abdominal wall
3	Amir et al. (12)	15	Female	Left groin
4	Petrik et al. (17)	7	Male	Left common carotid artery
5	Rodriguez-Peralto et al. (19)	20	Female	Left shoulder
6	Lopez-Barea et al. (13)	57	Female	Left arm
7	Shannon et al. (20)	29	Female	Left retroclavicular region
8	Nielsen et al. (15)	8	Male	Right shoulder
9	"	29	Female	Right groin
10	"	37	Female	Upper arm
11	"	28	Male	Left deltoid
12	"	30	Female	Thigh
13	Ajilogba et al. (23)	12	Female	Lateral aspect of the left thigh
14	Wang et al. (24)	21	Male	Right gluteus medius
15	Presented case	23	Female	Left groin

finding showed NF is obviously a reactive process (25). However some questions still remain:

What factors are responsible for allowing the development of NF or OF in one patient and MO in another patient following an episode of trauma?

2. The mineralization of organic matrix of bone in normal physiological conditions is well-known but what are the factors that allow the formation of heterotopic bone after a trauma in these reparative benign processes in some patients and not in others?

In order to clarify these questions, further studies of both clinicopathologic and genetic analysis in larger series of these different reactive processes are needed. In order to ensure these larger series for further studies, more cases of these rare entities must be added to the literature.

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