Radiographic Findings in Hyperimmunoglobulin E Syndrome

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ABSTRACT

The aim of this study is to demonstrate the spectrum of radiologic findings of hyperimmunoglobulin E (hyper-IgE) syndrome that is relatively rare in adults. We describe the imaging findings of this rare disease in five patients. The study group consisted of 4 men and 1 woman. The final diagnosis was made according to laboratory findings in all cases. We detected lung involvement in 3 cases, paranasal sinus involvement in 4 cases and vascular involvement in 1 case. Soft tissues were involved in 5 cases. Bone involvement was demonstrated in 3 patients. The most frequent radiologic finding was widespread infectious involvement of soft tissues, bones and neighboring structures such as bursae and tendons and respiratory system.

Key Words: Hyperimmunoglobulin E syndrome, Respiratory system, Musculoskeletal system, Vascular system, Radiographic findings.

Turk J Haematol 2002;19(4): 465-472

Received: *17.01.2002* ***Accepted:*** *26.03.2002*

INTRODUCTION

Hyper-IgE syndrome is a rare immunodeficiency disease of infancy and childhood. It is rarely seen in adults. It frequently involves upper and lower respiratory tract and musculoskeletal system[1-3]. Imaging findings with the laboratory findings are of great value in the diagnosis of this rare syndrome. The level of immunoglobulin E (IgE) is increased at least 10 times of normal. Marked eosinophilia and the defective chemotactic features of neutrophils are the other associated laboratory findings[1]. But the diagnosis is generally delayed due to lack of familiarity of radiologist to this rare disease. In this paper we tried to present the computed tomography (CT) and magnetic resonance imaging (MRI) findings of this rare syndrome that have not been reported previously to the best of our knowledge.

CASE REPORTS

Case 1

A 15-year-old girl presented with pain and swelling in her legs. She had severe cough. Physical examination showed decreased respiratory sounds. It was learned that she had multiple attacks of lung infections before. Lung CT showed a large cavitary focus at the

right apical segment and hematogeneous focuses widespread throughout the lungs (Figures 1a,1b). Microbiologic examination revealed *Staphylococcus aureus* at the sputum. During the medical therapy, the lesion at the right apical segment gave formation of a pneumatocele and resultant pneumothorax occurred (Figure 1c). Axial CT section through the legs showed severe involvement in cutaneous and subcutaneous tissues. The thickness of the subcutaneous and cutaneous tissues was increased and detected as hypodense with streaky appearance (Figure 1d). In some areas extensive fluid collections and abscess formation due to infectious involvement of underlying tissues were seen. Infectious involvement of soft tissues in this case was close to the knee joints extending to the ankles bilaterally. Laboratory tests showed increased level of IgE (2000 IU) and eosinophil in blood (40%). Based on the radiologic and laboratory findings, the diagnosis of hyper-IgE syndrome was made.

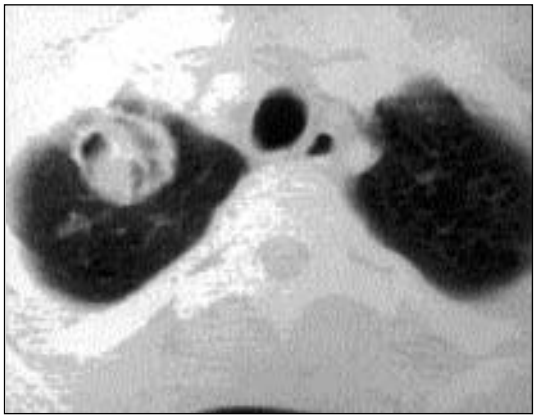

Figure 1a. A-15-year-old girl with hyper IgE syndrome. Axial CT section in width window shows a cavitary lesion due to Staphylococcus aureus infection at the upper apical segment of right lung.

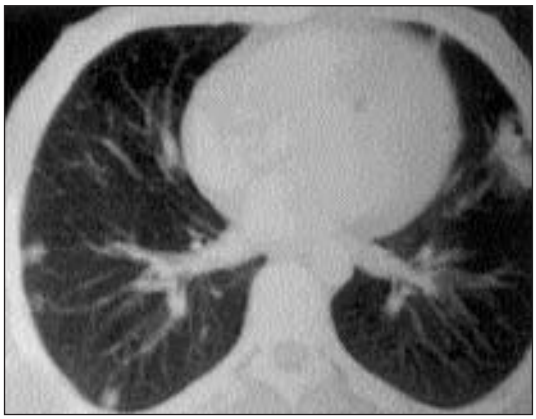

Figure 1b. A-15-year-old girl with hyper IgE syndrome. On the lower section, multiple hematogenous focuses are demonstrated.

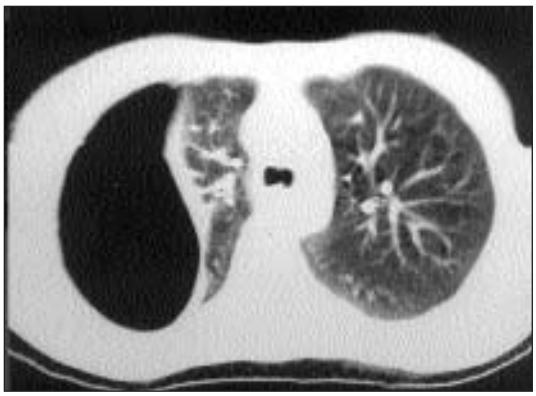

Figure 1c. A-15-year-old girl with hyper IgE syndrome. Axial CT section shows pneumothorax due to rupture of pneumatoceles to the pleural cavity during medication.

Case 2

A 21-year-old man admitted with purulent, sometimes bloody, nose secretions and severe headache. He also complained purulent secretions from the swelling

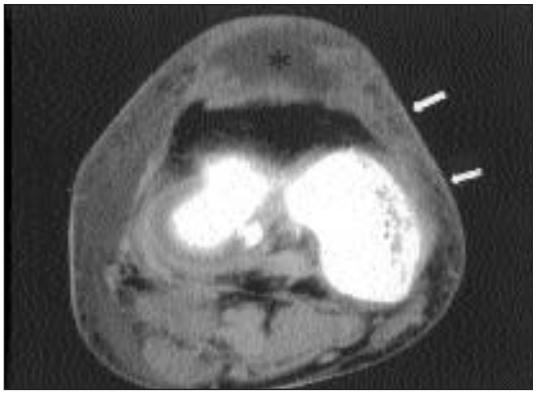

Figure 1d. A-15-year-old girl with hyper IgE syndrome. Axial contrast-enhanced CT section through the right knee joint shows thickening of the cutaneous and subcutaneous tissues and increased density of fatty tissue with streaky, irregular enhancement (arrows). Note the fluid collection in cutaneous and subcutaneous tissue with low density (asterisk).

lesions of his arms and legs. Physical examination showed widespread involvement in extremities and fistula formations with purulent secretions. Microbiologic analysis showed *Staphylococcus aureus*. Coronal paranasal sinus CT sections showed prominent mucoperiosteal thickening and loss of normal aeration of the sinuses (Figure 2a). On axial CT sections through the arms and legs, prominent thickening and fluid collections deep to the subcutaneous tissue and fistula tracts to skin were demonstrated (Figure 2b). The levels of IgE was 3200 IU, eosinophil count was 26%.

Case 3

A 27-year-old man presented with the complaints of fever, swelling, redness and pain in his arms and legs. He had coughing and dispnea. The temperature was 39°C. Physical examination showed tenderness with motion in his upper and lower extremities. The extremities were swollen and red. The respiratory sounds were decreased especially at the right lung. Coronal paranasal sinus CT revealed mucoperiosteal thickening in maxillary and sphenoid sinuses. Axial CT section through the lungs showed right middle lobe consolidation. Widespread cutaneous, subcutaneous, muscle infection was demonstrated in the extremities. The infectious involvement extended to acromioclavicular and knee joints and subacromial-subdeltoid bursae (Figures 3a,3b,3c). The infectious involvement in cutaneous and subcutaneous tissues was detected as decreased signal intensity on T1-weighted MR images and increased intensity on T2-weighted MR images. The thickness of these tissues also increased. The lesions showed marked contrast enhancement after gadolinium injection. Laboratory test revealed elevated levels of IgE (3000 IU) and defective chemotactic function in neutrophils.

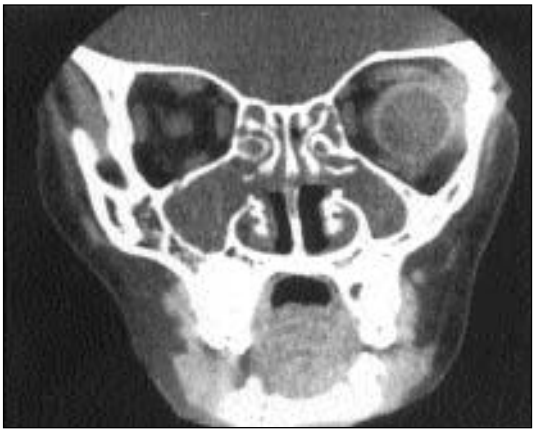

Figure 2a. A-21-year-old man with the involvement of upper respiratory system and soft tissues. Coronal CT section of paranasal sinuses shows mucosal thickening of the bilateral maxillary and ethmoid sinuses.

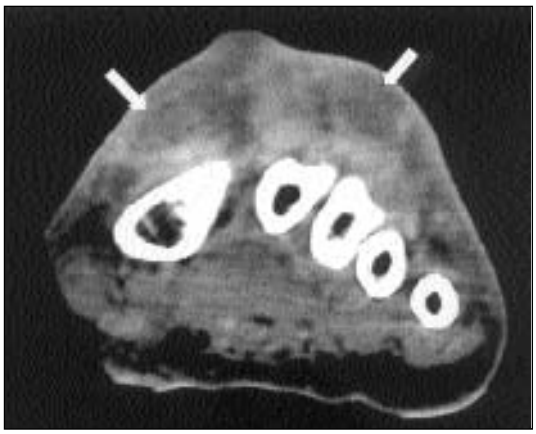

Figure 2b. A-21-year-old man with the involvement of upper respiratory system and soft tissues. Axial CT section through the elbow shows hypodense fluid collections in the cutaneous tissue (arrows) and abscess formation in the muscle (asterisk).

Case 4

A 26-year-old man presented with the signs of widespread pain and tenderness in his extremities buttocks and restriction in movement for 15 days. He had chronic cough and heavy sputum with foul odor for 1 year. He had also a history of recurrent lung infections and allergy for 5 years. On physical examination extremities were swollen and red. There was an excessive pain at the lateral side of the left ankle on palpation. Paranasal sinus CT revealed pansinusitis. High-resolution CT sections through the mediobasale segment of right lower lobe showed extensive bronchiectatic changes (Figure 4a). MRI sections through the buttocks showed hypointense abscess formation within the gluteus maximus muscles. Lesions showed ring like contrast enhancement after intravenous (IV) gadolinium injection (Figure 4b). Axial MRI sections through the left ankle showed infectious involvement at the lateral side of the ankle with increased thickness in cutaneous and subcutaneous tissue and decreased intensity. The

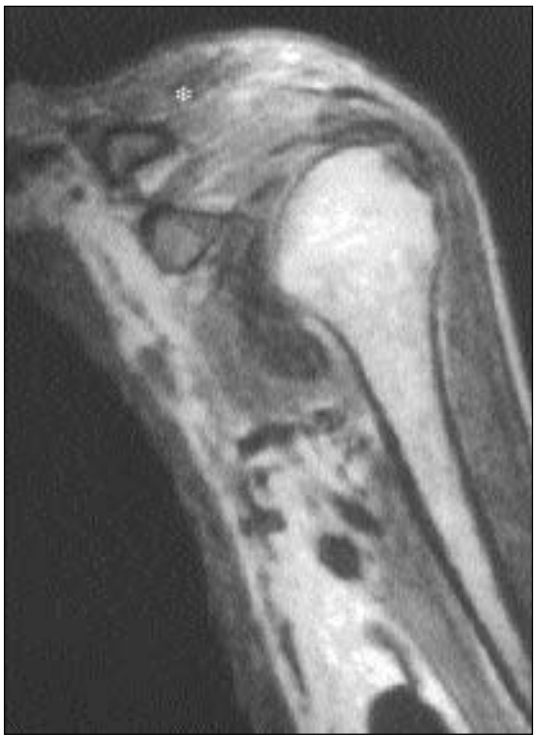

Figure 3a. A-27-year-old man with soft tissue, joint, bursae involvement. On T1-weighted coronal shoulder MR section, the cutaneous and subcutaneous tissues show increased thickness and decreased signal on the superior aspect of the joint (asterisk).

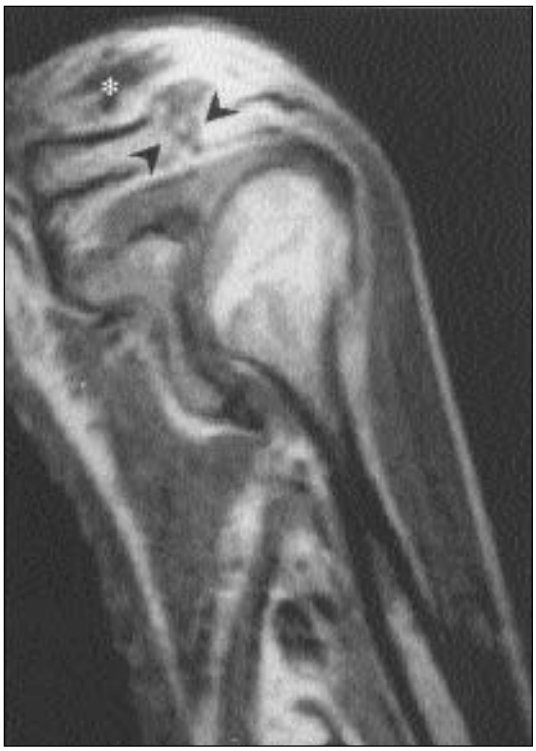

Figure 3b. A-27-year-old man with soft tissue, joint, bursae involvement. Coronal, contrast enhanced T1-weighted image shows contrast enhancement in the subcutaneous tissue. Note the hypointense abscess formation in subcutaneous tissue with peripheral enhancement (asterisk). Note the extending of infectious process to the acromioclavicular joint (arrowheads).

infectious process extended to ankle joint. T2-weighted MR sections showed increased intensity within the joint due to infectious involvement. There was also increased intensity surrounding the peroneus brevis and longus tendons due to tendinitis (Figure 4c). Axial CT sections through the upper and midpelvis showed abscess formation and infectious involvement in iliopsoas muscle. The infectious process extended to left iliac wing and sacrum. Left iliac wing showed periostitis just near the infectious process in the muscle (Figure 4d). At upper and lower sections to this point osteomyelitis and sequestrum formation were observed (Figure 4e). The level of IgE was found 3500 IU. The eosinophil count was 30%.

Case 5

A-46-year-old man admitted with purulent secretion from the cutaneous tissues. It is learned that his arms and legs began to swell 15 days ago. He had pain and tenderness during palpation and movements. He had no history of allergy and lung infection before. Axial CT sections through mid-abdomen showed abscess formation within the psoas muscles bilaterally (Figure 5a). Increased thickness and decreased density due to infectious involvement of cutaneous and subcutaneous tissues were observed widespread throughout the all four extremities especially prominent near the joints. The infectious process extended to the neighboring bone tissue in foot. The infectious involvement in cuneiform bone in the right foot showed decreased signal intensity on T1-weighted MR image and increased signal intensity on T2-weighted MR image. The lesion showed contrast enhancement after IV gadolinium injection. At the 5th day of hospitalization, progressive swelling was detected at the dorsal surface of the right foot. Ultrasound examination showed an anechoic lesi-

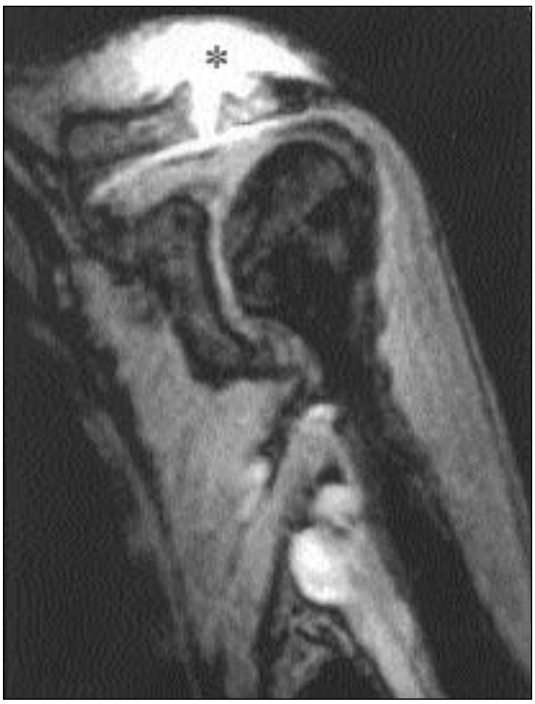

Figure 3c. A-27-year-old man with soft tissue, joint, bursae involvement. Coronal T2-weighted MR image shows high signal intensity in cutaneous, subcutaneous tissue (asterisk) and acromioclavicular joint. Note also hyperintense fluid in subacromial subdeltoid bursae.

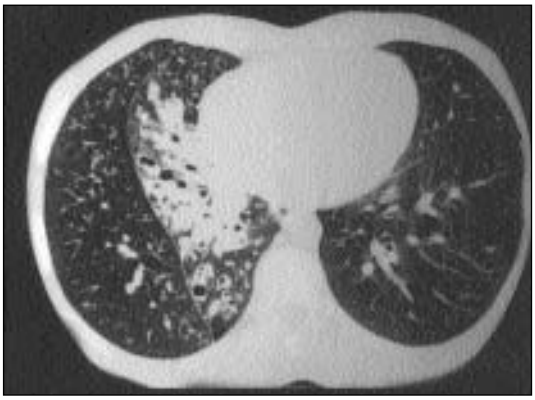

Figure 4a. A-26-year-old man with lung, soft tissue, bone and tendon involvement. High resolution CT section shows bronchiectasis at the mediobasale segment of the right lung due to recurrent infections.

on at the dorsal surface of the foot. Color Doppler imaging revealed vascular signals within the lesion. The spectral evaluation showed swirling pattern due to "to-

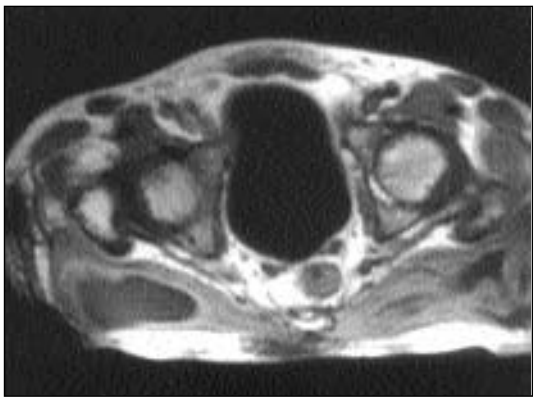

Figure 4b. A-26-year-old man with lung, soft tissue, bone and tendon involvement. Contrast-enhanced, axial T1-weighted MR image through the gluteus muscles shows hypodense mass lesions with ring enhancement at gluteus maximus muscles.

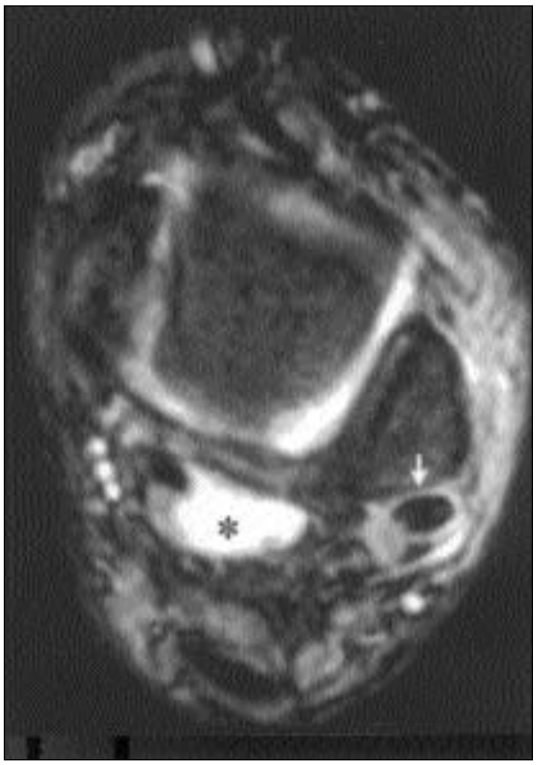

Figure 4c. A-26-year-old man with lung, soft tissue, bone and tendon involvement. Axial T2-weighted MR image of left ankle shows increased thickness and increased signal intensity in cutaneous and subcutaneous tissues. Note also thickening and increased signal intensity in the tendons of perenous brevis and longus due to spreading of infectious process neigbouring tissues (white arrow). Note also synovial cyst as increased signal intensity protruding posterior to the joint (asterisk).

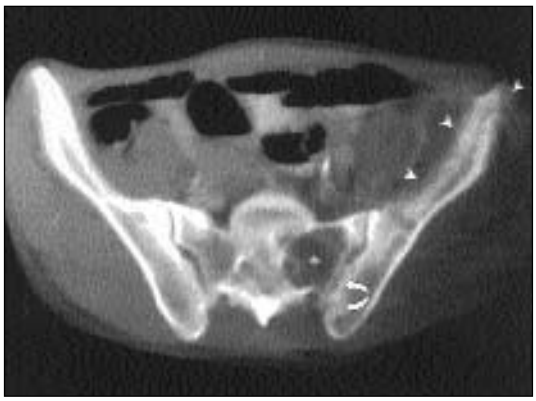

Figure 4d. A-26-year-old man with lung, soft tissue, bone and tendon involvement. Axial CT section through the iliac wings shows contiguous spread of infectious process in the left iliacus muscle to the left iliac wing and note the formation of periostitis neighboring iliac wing (arrowheads). Contiguous spread of infection to sacrum is seen as a lytic lesion (asterisk). Left sacroiliac joint is seen as narrowed comparing right site and note also subchondral sclerosis due to infectious spread (curved arrow).

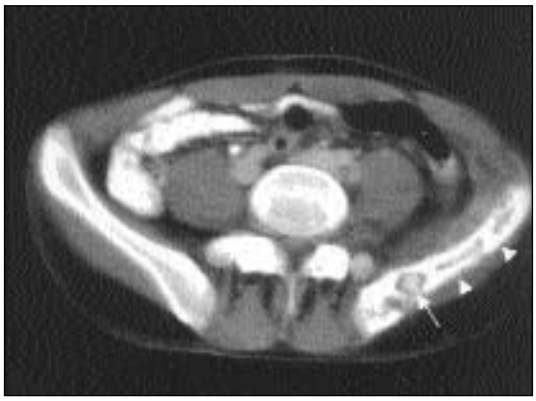

Figure 4e. A-26-year-old man with lung, soft tissue, bone and tendon involvement. Axial CT section through the upper margins of iliac wings shows periostitis (arrowheads) and hyperdense sequestreum formation (arrow) in the medulla.

and-fro" flow within the neck of the pseudoaneurysm (Figure 5b). Pseudoaneurysm showed decreased signal intensity in MR sections (Figure 5b,-e). The levels of IgE was 4000 IU, eosinophil count was 25%.

DISCUSSION

Hyper-IgE syndrome is a rare disease. It most often occurs during infancy and early adulthood. But there have been several reported cases during adulthood[1,4,5]. Autosomal dominant transmission of the hyper-IgE syndrome was found, but with variable expressivity[6]. The most important and diagnostic laboratory results are the elevated levels of the IgE. The levels are generally ten times of normal (greater than 2000 IU/mL). Marked eosinophilia is the other laboratory manifestation. Deficits in the mitogen and chemotaxis responses of neutrophils are also seen.

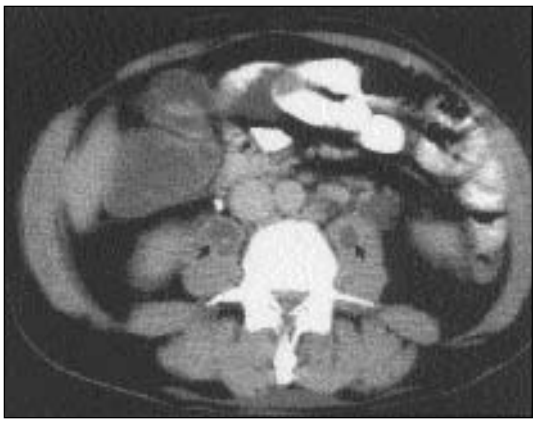

Figure 5a. A-46-year-old man with soft tissue, bone, deep muscle and vessel involvement. Axial CT section shows bilateral hypodense psoas abscesses (arrows).

The most commonly seen clinical presentation is the widespread infectious involvement of the cutaneous and subcutaneous tissues as in our cases. The infectious involvement of these tissues can be detected as increased thickness both CT and MRI. The density of these tissues decreases in CT. Infected cutaneous and subcutaneous tissues showed decreased signal intensity on T1-weighted MR images, increased signal intensity on T2-weighted MR images. The lesions show contrast enhancement with streaky appearances on both CT and MR images.

The infectious extension to neighboring tendons, bursae and joints can be best detected by MRI due to higher contrast resolution. Tenosynovitis or synovial inflammation of tendon sheaths may occur in hyper-IgE syndrome. Adjacent infectious focuses may spread contiguously to the tendon sheath. Hyperintense fluid collection in the tendon sheath on T2-weighted MR images and contrast enhancement of the tendon sheath are indicative of inflammation.

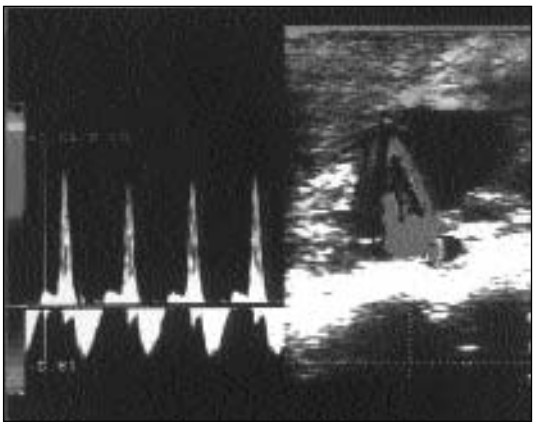

Figure 5b. A-46-year-old man with soft tissue, bone, deep muscle and vessel involvement. Color Doppler image shows typical swirling pattern of flow in the dorsal aspect of the dorsalis pedis artery. Spectral analysis shows to and fro flow in the neck of the aneurysm.

Bursitis can also be seen due to infectious spread of adjacent focuses. Most commonly affected bursae are superficially located bursae such as olecranon and prepatellar, infrapatellar subdeltoid bursae. Bursitis appears on MR imaging as a fluid collection in the anatomical location of the involved bursae, with typical low signal intensity on T1-weighted and high signal intensity on T2-weighted images.

Soft tissue abscess appears as collection of fluid, which is low-signal intensity on T1-weighted image (isointense to muscle) and high signal intensity on T2-weighted images with ring-like contrast enhancement. The infection can spread to the muscles near superficial seated soft tissue infection.

The skeletal manifestations of hyper-IgE syndrome are osteoporosis, spontaneous osteoporotic bone fractures and osteomyelitis and arthritis[1,3,7,8]. In most of the cases, osteomyelitis (and septic arthritis) arises from a contiguous source such as soft tissue infections. Periosteal bone formation is the initial radiologic manifestation of osteomyelitis. With further accumulation of pus, subperiosteal resorption of bone and cortical disruption ensue. Infection then may spread in the marrow, producing lytic osseous defects on the radiographies. The infectious agent that causes osteomyelitis is generally *S. aureus*.

The sinuses and airways (including lungs) are frequently infected. The plain radiographies or paranasal sinus CT can reveal the pathology in the sinuses. Pulmonary involvement may be in various manifestations. The pulmonary imaging features consist of recurrent alveolar lung infections, pneumatoceles, abscesses, and occasionally pneumothorax[5,9,10]. Bacteria of which commonly infects these patients are *S. aureus* and *Haemophilus influenzae*. *S. pneumoniae* and gram-negative rods are seen in some cases[3]. Recurrent pulmonary infection can cause bronchiectasis.

The involvement of the vascular system is extremely rare in hyper-IgE syndrome. Only one case was reported in the literature[11]. A bronchial artery pseudoaneurysm was detected in a-2-year-old girl presenting with the symptoms of sever hemoptysis. The development of pseudoaneurysm in hyper-IgE syndrome can be explained by the spreading of infectious process to the wall of the blood vessels. Perivascular infectious involvement of the vessel wall leads to degeneration and occlusion of the vaso vasorum with the formation of vasculitis. Occlusion of the vaso vasorum leads to transmural necrosis in the wall of the arteries. Ultimately perforation of the vessel wall can occur, and pseudoaneurysm formation follows. On CDI, pseudoaneurysm shows typical swirling pattern of flow within the pseudoaneurysm. On spectral analysis “to-and-fro” flow is demonstrated at the neck of the pseudoaneurysm. Pseudoaneurysms can be seen as signal void on T1-weighted MR images.

CONCLUSION

Delay in the diagnosis of hyper-IgE syndrome is frequent and may be due not only to nonspecific clinical manifestation of the disease, but also lack of familiarity of the radiologist and other clinicians with this rare syndrome. The most common reported manifestation of hyper-IgE syndrome is the infectious involvement of the soft tissues, upper and lower respiratory tract. The infection in cutaneous and subcutaneous tissues may spread to neighboring tendons, bursae, bones and joints. Vascular system is less frequently involved. CT and MR imaging with typical laboratory findings provide important information that may be helpful for initiating early and correct therapeutic approach.

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