Muscular and Hepatosplenic candidiasis in a patient with acute myeloblastic leukemia: A Case Report and literature review

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Abstract

Soft tissue candidiasis is an opportunistic infection that occurs in immunocompromised patients and must always be diagnosed and treated as soon as possible. In this case report, the patient is a 14-year-old boy with acute myeloid leukemia M3-type who presented with numerous soft tissue and hepatosplenic candidal abscesses.

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Authors' contributions

Amirreza Jahanshahi: Interpreted the patient's images

Sanam Nami: Preparation and interpretation of Candida albicans slides and cultures

Abbas Ali Hosein Pour Feizi: interpreted the laboratory data and evaluated the patient's course

Samin Alihosseini: Interpreted the patient's images, prepared the first draft, edited the images

Mehran Jaberinezhad: prepared the first draft, Conducted a literature review

Mirsaeed Abdollahi: prepared the first draft, revised the manuscript, Conducted a literature review

Faezeh Rahimi: Interpreted the patient's images, Conducted a literature review

Masih Falahatian: Interpreted the patient's images, revised the manuscript, edited the images

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Abstract

Soft tissue candidiasis is an opportunistic infection that occurs in immunocompromised patients and must always be diagnosed and treated as soon as possible. In this case report, the patient is a 14-year-old boy with acute myeloid leukemia M3-type who presented with numerous soft tissue and hepatosplenic candidal abscesses.

Keywords: Candida albicans, muscular abscess, hepatosplenic candidiasis, acute myeloid leukemia, magnetic resonance imaging, case report

Key Clinical Message

Muscular and subcutaneous candidiasis is a rare entity in immunocompromised patients, but it should be kept in mind when we see multiple cystic soft tissue masses in addition to target-shaped hepatosplenic lesions in neutropenic patients. US and MRI are useful imaging modalities for the diagnosis and follow-up of these patients.

Background

Candida infections are rare in immunocompetent patients. However, it has considerable importance and prevalence in immunocompromised patients such as transplant and cancer patients [1]. Patients with cancer are at higher risk of candidiasis mainly due to chemotherapy-induced suppression of innate and adaptive immune cells as well as disruption of epithelial barriers [2].

The manifestations are usually categorized into mucocutaneous or invasive forms. Typical presentations of mucocutaneous form can be seen as paronychia, intertrigo, thrush, vulvovaginitis, and esophageal candidiasis. Candidemia is the most easily recognized manifestation of invasive candidiasis, but it can involve virtually any anatomic site and cause widespread visceral dissemination [3]. However, subcutaneous and intra-muscular candidal abscess formation is very rare, even in immunocompromised patients, and can be seen as case reports in the literature [4]. According to our knowledge, this is a rare case of concurrent hepatosplenic candidiasis and Candida albicans muscular abscess in a person with AML type M3.

Case Presentation

The patient is a 14 years old boy who presented with signs of epistaxis and fatigue from three months ago. Laboratory data showed severe pancytopenia. Considering the risk of spontaneous hemorrhage, he was immediately transferred to the tertiary center for comprehensive care. Subsequent investigations through bone marrow biopsy and flow cytometry were consistent with the diagnosis of acute myeloid leukemia (AML) M3 type. The patient received appropriate therapy first with daunorubicin and ATRA and later with Arsenic trioxide. He then presented to the hospital three months later with numerous bulging subcutaneous masses on his buttocks, thighs, calves, and plantar surface of his feet. Similar lesions, albeit fewer, were observed in the back and upper extremities.

Ultrasonography was done, and multiple thick-walled cystic lesions containing some internal echogenic material were seen in the subcutaneous tissue and within muscular compartments of lower extremities with peripheral vascularity on Doppler ultrasound, suggestive of abscess formation. Multiple target-shaped and hypoechoic lesions were also observed in the liver and spleen (Figure 1). Magnetic resonance imaging(MRI) of the lower extremities was performed and showed numerous iso- to hyper-signal on T1 and hyper-signal on T2-weighted oval lesions with hypo-signal rim within different muscles of the lower extremities and also in subcutaneous tissue. The almost diffuse hypo-signal intensity of bone marrow of the bilateral tibia and fibula on the T1-weighted sequence was also seen due to leukemic infiltration (Figure 2). Subsequent needle aspiration of muscular lesions under ultrasound guidance was performed, and cytopathology and culture reports were consistent with abscess formation due to *Candida Albicans* (Figure 3). Brain MRI also was performed and showed subdural hematoma in the right frontoparietal convexity(due to low platelet level). A chest x-ray didn't show any abnormality.

So, antifungal therapy with intravenous Amphotericin-B was given to him for two weeks and then step-down therapy with oral fluconazole was started. After three months of anti-fungal treatment with oral fluconazole along with chemotherapy, the patient was evaluated again clinically and by imaging modalities including ultrasonography and MRI. He felt generally well and bulging subcutaneous lesions in the back, upper extremities, and thighs disappeared or shrinkage, compared with pre-treatment physical examination. Although MRI showed almost complete resolution of bone marrow leukemic infiltration, many of the leg abscesses still persisted without change, and some of the lesions coalesced together. Fortunately, Some leg abscesses changed to non-enhancing signal void small foci in post-treatment MRI due to calcification, which was confirmed on the targeted ultrasound. Also, the complete resolution of hepatic lesions and calcification of splenic lesions was seen in ultrasonography (Figure 4).

Due to the persistence of abscess on the buttocks and plantar surface of the feet, which impaired the patient's walking and sitting ability, surgical incision was also performed. Post-surgical pathology was reported as granulation tissue with focal abscess formation with complete resolution of candida infection.

Discussion

Among AML subtypes, M3 is usually considered highly curable[5]; however, treatment introduces new complications to the scene, mainly because of the induction of immunosuppression. Opportunistic Infections and particularly fungal infections such as candidiasis are one of these complications. It is well known that an increase in the fungal load, a compromised mucosal surface, and a lowered host immune response are all necessary for the disease to manifest. Other risk factors can also contribute to this process, namely the presence of indwelling catheters and recent surgical and percutaneous interventions [3]. Candida species orig-

inating from intestinal microbial flora typically spread through blood circulation and cause macro nodular skin lesions. Organisms may spread to other organs, especially the liver, spleen, and kidneys[6].

Ultrasonography remains a useful tool for detecting and monitoring candidiasis lesions; however, candidal lesions may be undetectable in imaging before neutrophil count recovery, especially in chronic disseminated candidiasis (CDC). Manifestations of imaging depend on the stage of the disease, but the most frequent ultrasound pattern in the liver and spleen is several small hypoechoic lesions. Four dominant patterns of hepatosplenic involvement have been described. The earliest pattern is composed of a peripheral hypoechoic zone that correlates with fibrosis, with a second hyperechoic zone composed of inflammatory cells. The central hypoechoic nidus relates to necrotic fungal elements. This pattern is called "wheel within a wheel." The second pattern is called "bull's eye," or target pattern, with a peripheral hypoechoic halo encircling a central echogenic core. The third and most common pattern is seen as multiple hypoechoic lesions that can be seen in conjunction with the other three patterns. The fourth pattern, manifesting as echogenic foci, usually is seen at the late stages of the disease and correlates microscopically with central fibrosis or calcifications, or both [7].

MRI seems to be superior to computed tomography(CT) scan and ultrasonography in identifying hepatosplenic and musculoskeletal lesions associated with candidiasis. In a patient with acute hepatosplenic or soft tissue candidiasis, lesions on MRI are round, measured <1 cm in diameter, markedly hyper-intense on T2-weighted images and show restriction on diffusion-weighted imaging(DWI). At the chronic stage, especially with antifungal treatment, a hypo-signal rim surrounding the primary lesions and a non-enhancing center on contrast images are seen, which is consistent with the necrotic core seen on histologic examination. When the lesions are calcified, they appear hyperdense on CT scan and low signal on MRI [8-10].

There aren't many studies that provide imaging results of subcutaneous and intramuscular candidal abscesses. We discovered a few case reports in the literature that contained imaging data such as CT or MRI (Table. 1). When dealing with an AML patient who has various cutaneous, muscular, and hepatosplenic lesions, we must evaluate a variety of differential diagnoses, including chloroma, multifocal bacterial abscess, tuberculoma, cysticercosis, and hydatidosis, in addition to systemic candidiasis.

Chloromas or myeloid sarcomas are comprised of immature myeloid cells, most often leukemic blasts[11]. It is characterized by an extramedullary tumoral lesion which can readily be diagnosed by ultrasonography or CT scan and biopsy [12]. The numbers of these lesions are lower than candidal lesions usually. MRI presents it as iso to hypo-signal on T1 and mildly hyper-signal on T2 weighted images. They have vascularity in Doppler ultrasound and show enhancement after contrast injection in CT scan and MRI [13]. Bone and periosteum is the most common site of involvement, but any tissue can be affected, such as skin, orbit, paranasal sinuses, and central nervous system [14, 15]. Moreover, chloroma is more prevalent in AML M2, M4, and M5 subtypes, not M3 [16].

Multifocal bacterial abscesses can occur in immunocompromised patients. Septic emboli can be primarily found in the lungs, especially in AML patients with port-catheter [17]. However, culture and gram staining of blood and aspirated fluid of abscess returned negative for our patient; his chest x-ray was also normal. Moreover, Bacterial abscesses don't show the typical "bull's eye" ultrasound pattern mentioned before.

Extra-pulmonary tuberculosis should always be considered as a differential diagnosis of multiple subcutaneous and hepatosplenic masses in an immunocompromised patient, even though it's a rare finding[18]. These abscesses are often observed in the chest wall and spine. The limb is a very uncommon location of involvement[19]. They are often secondary to ruptured necrotic lymph nodes, tuberculous osteomyelitis, or arthritis[20]. Culture and Acid-fast staining of blood and aspirated fluid of abscess were also negative.

Cysticercosis is a kind of endemic parasitic disease that is a very rare entity in our country. The central nervous system and skeletal muscles are humans' most commonly affected tissues. In ultrasonography, the scolex is seen inside the lesion, which may be calcified. When the lesions are cystic, they have similar characteristics to fluid on both CT and MRI, but when these lesions calcify, they appear as hyperdense foci parallel to muscle fibers on CT, giving a characteristic appearance called "rice-grain" calcification [21]. This

disease is not related to the host's immunity state [22].

Soft tissue and skeletal muscle hydatid cyst is a very rare condition and is usually secondary. They can occur in the lower extremities, trunk, neck, or legs. Pectoralis major, Sartorius, quadriceps, and gluteus muscles can be involved. It usually appears as a focal multi-vesicular cystic lesion in the muscle(s) that can invade the adjacent bone [23]. They have a characteristic appearance on ultrasound, CT scan, and T2 weighted sequence of MRI as a cystic lesion with serpentine undulant membranes called "water lily sign" or "serpentine sign" in the liver, spleen, and other regions[24].

Soft tissue mycetoma due to maduramycosis or other fungal infections usually occurs in the foot and in endemic areas. Mycetoma is a kind of chronic inflammation of soft tissue caused by fungi or actinomycetes. They appear as multiple, small, round T2 hyperintense lesions with central hypointense foci in MRI. Central hypointense foci are mycetoma grains in pathology called "dot in a circle sign," which is specific for this entity [25, 26]. One of our patient's lesions had a similar appearance in MRI (Figure 2C). Although the "dot in a circle" sign is a characteristic sign of mycetoma, the accumulation of candida hyphae can cause hypointense signal areas in both T2 and T1 weighted images in MRI [27].

Conclusion

In conclusion, we presented an AML M3 patient with a multifocal muscular and hepatosplenic abscess caused by Candida albicans, shown in ultrasound and MRI and proved by pathology. He was treated with medical and surgical methods successfully. Also, we reviewed the literature about imaging manifestations of a few similar cases and finally discussed imaging features of musculoskeletal candidiasis and its differential diagnosis.

List of abbreviations:

AML *:* Acute Myeloid Leukemia

CDC: Chronic Disseminated Candidiasis

CT : Computed Tomography

DWI: Diffusion Weighted Imaging

IHC: Immunohistochemistry

MRI : Magnetic Resonance Imaging

PAS: Periodic Acid Schiff

US: Ultrasonography

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Table 1. Cases of subcutaneous and muscular abscesses caused by *Candida albicans* published in the literature

Author (Year)	**Sex/age**	**Risk Factors for Candida Infection**	**Underlying Medical Condition**	**Localization**	**Imaging findings (Ultra-sound, CT, MRI)**	**Treatment**	**Sur-gery**
Nelp [28] (1963)	17/ F	Poorly controlled diabetes mellitus, Daily injection of insulin	diabetes mellitus,	thighs	–	Nitrofurazone gauze in abscesses cavities	+
Mochizuki et al. [29] (1988)	59/ M	2-month hospitaliza-tion (bedridden)	subarachnoid hemorrhage, intracranial surgery (4 times)	Left Knee (3x11 cm subcuta-neous abscess)	–	Miconazole, Amphotericin-B	-
Manfredi et al. [30] (1997)	36/ M	Progressive HIV-related immuno-compromise, IV-drug abuser, peripheral sensory neuropathy, advanced liver cirrhosis, chronic HBV infection (treated with zidovudine (500 mg daily) for 6 months)	AIDS	right upper thoracic wall (5 cm)	Chest X-ray and an ultrasono-graphic examination confirmed an isolated sub-cutaneous abscess	oral itraconazole	–
Tuon et al. [31] (2006)	32/M	Tuberculosis	gastrointestinal surgery, short bowel syndrome	Skin abscess	-	fluconazole	+

Florescu et al. [32] (2010)	50/M	Immunosuppression (Mycophenolate mofetil 1.5 g twice a day, prednisone 5 mg/d and a day, prednisone 5 mg/d	Cardiac transplant recipient, on trimethoprim/sulfamethoxazole treatment for cerebral nocardiosis	subcutaneous abscesses of legs	**MRI**: cellulites and a medial fluid collection (4* 1.5cm) **CT**: large (5*3*7 cm) multiloculated fluid collection in the posterior leg	Moxifloxacin, Fluconazole; trimethoprim/sulfamethoxazol	–
Buchanan et al. [33] (2013)	55/M	central catheter placement	gunshot wounds	neck	**CT**: multiseptated abscess of the left lower neck and left supraclavicular region	anidulafungin	+
Kakeya et al. [34] (2014)	50/ M	Immunosuppression (40 mg/day of hydrocortisone, 0.5 mg/day of dexamethasone)	Right adrenalectomy, daily corticosteroid replacement, Cushing's syndrome, pulmonary cryptococcosis	subcutaneous abscesses of legs	**MRI**: rounded fluid-collection signal in the soft tissue of the legs	Fluconazole	+

Musa et al. [35] (2014)	67/M	diabetes mellitus	-	retropharyngeal region	**Lateral neck x-ray**: widening of soft tissue of prevertebral area with area of lucency indicating air content **CT**: ill-defined thin rim-enhancing hypodense collection	oral Fluconazole	+
Peker et al. [36] (2015)	68/ M	diabetes mellitus	buccal-space infection	left cheek	**Panoramic radio-graph**: extensive bone loss between the teeth related with buccal abscess **MRI**: fluid accumula-tion compatible with an abscess located in the area of masticatory muscle structures reaching the left infraorbital region	Amphotericin-B and oral fluconazole	–

Messina et al. [37] (2015)	42/M	Immunosuppression	HIV-seropositive	right chest wall	**Ultrasound**: heterogeneous mass with irregular contours with echogenic stippling and hypo echoic area in intimate contact with the muscular plane **CT**: liquid collection in relation to the anterior chest wall with air bubbles	Fluconazole	+
Kothari et al. [38] (2016)	42/ M	Chemotherapy (darubicin, cytarabine and cytarabine), neutropenic	acute myeloid leukemia	arms, chest, back and legs, spleen	**CT**: splenomegaly and multiple hypodense nodules **FDG PET:** splenomegaly with diffuse uptake in the spleen	Micafungin, voriconazole	–
Amita et al. [39] (2017)	60/ M	diabetes mellitus	tuberculosis	right forearm	-	Intravenous antifungal drug	–
Yi et al. [40] (2019)	60/ M	myelosuppressive chemotherapy	acute granulomonocytic leukemia	subcutaneous abscess of calves, splenic abscess	**CT**: multiple hypodense lesions in the spleen **MRI**: multiple subcutaneous abscesses in the calves	Amphotericin-B flucytosine	–

Sung et al. [41] (2021)	57/ F	type 2 diabetes mellitus	blunt eyelid trauma with self-administered acupuncture	facial candidal abscess	**CT**: soft tissue swelling in the left periorbital area	fluconazole	+
Yoshihara et al. [42] (2022)	42/ F	Hashimoto's disease	Laparoscopic cholecystectomy 9 months prior to admission	lower left rib in the anterior chest wall	**Contrast-enhanced CT:** the fluid density area around the lower left side of rib (6.5 cm in diameter)	Micafungin, fluconazole	+
Current study (2023)	14/M	acute myeloid leukemia M3 type (Treated with daunorubicin, ATRA and later with Arsenic trioxide)	acute myeloid leukemia M3 type	arms, buttocks, thighs, calves, and plantar surface of feet	**Ultrasonography:** multiple thick walled cystic lesions containing some internal echogenic material, Multiple target shaped and some hypoechoic lesions were also observed in liver and spleen **MRI:** numerous iso to hyper signal on T1 and hyper signal on T2 weighted oval lesions with hyposignal rim within different muscles	Liposphotericin-B and Fluconazole	+

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