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RESEARCH ARTICLE

PRIMARY CUTANEOUS ASPERGILLOSIS IN A 13-YEAR-OLD BOY WITH BONE MARROW APLASIA: CASE REPORT

Raounak Lhamel, Ayad Ghanam, Abdeladim Babakhouya, Maria Rkain and Noufissa Benajiba
Department of Pediatrics, Mohammed VI University Hospital, Oujda, Morocco.

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Abstract

Cutaneous aspergillosisis a rare condition, and while rare in immunocompetent individuals, it predominantly affects immunosuppressed patients, particularly those with hematological-oncological disorders within the pediatric demographic. Herein, we present a 13-year-old boy under follow-up for bone marrow aplasia. The child developed long-lasting fever and papulous and ulcerous indurated skin lesions on his whole body. Blood count showed agranulocytosis with neutrophils count of 10/µl. Thoracic, abdominal and pelvic Computed Tomography (CT) scan has revealed bilateral alveolar syndrome in the lungs. Skin biopsy revealed cutaneous aspergillosis. Despite treatment, the boy's condition did not improve, and he passed away 2 weeks following his hospital admission because of septic shock. Cutaneous aspergillosis is due to Aspergillus flavus and A. fumigatus, for primary and secondary (invasive) cases, respectively. The rapid progression of this disease from the initial cutaneous infectious region necessitates prompt medical intervention to avoid increasing the risk of mortality. This condition typically manifests after the fungus is directly inoculated through skin contact with contiguous infected areas or via hematogenous spread from a remote mycotic site to the skin.

Introduction:-

After Candida albicans, Aspergillus spp. ranks as the second most prevalent cause of fungal infections in humans, particularly leading to high mortality among immunocompromised individuals, especially neonates [1,2]. Aspergillus species are known to lead to severe infections and is especially dreaded in neonatal intensive care units [2]. The most commonly affected organs include thecentral nervous system,lungs, and paranasal sinuses [1,2]. Primary cutaneous aspergillosis (PCA) is an uncommon manifestation typically linked to immunodeficiency due to hematologic disorders. The fungus can infect the skin through two main routes: colonization by airborne Aspergillus conidia on traumatized skin or through non-sterile medical devices. It is crucial to aggressively treat cutaneous infections to avert the development of systemic infections [2]. The diagnosis is often confirmed postmortem, as it typically leads to disseminated infections.

Our work highlights a case of PCA in a 13-year-old boy diagnosed with bone marrow aplasia.

Corresponding Author:- Raounak Lhamel
Address:- Department of Pediatrics, Mohammed VI University Hospital, Oujda, Morocco.

Case presentation:
We report a 13-year-old patient, with a history of bone marrow aplasia, who exhibited prolonged fever with widespread skin lesions. Upon admission, the clinical examination revealed a fever of 39.5°C, a normal heart rate of 84 beats per minute and a high respiratory rate of 31 breaths per minute. The arterial blood pressure was normal at 110/75mmHg. Dermatological examination revealed multiple skin lesions present on the face, all four limbs, and the trunk. The skin lesions were of varying ages of development, ranging from inflammatory, indurated papules to lesions that were ulcerated with a blackish base, mimicking the appearance of ecthyma gangrenosum (Figure 1 and 2)

Complete blood count revealed agranulocytosis with a neutrophil count of 10/µl. The Hemoglobin level was low at 5g/dL. The platelet level was also low at 3000/µl. A microbiological sample was taken from the cutaneous lesions, and the patient was placed on empirical antibiotic therapy with Ceftazidime, Ciprofloxacin, and Amikacin, yet the fever persisted, and microbiology results revealed no specific germs. A thoraco-abdomino-pelvic CT scan was performed and revealed bilateral alveolar syndrome in the lungs, initially suspecting tuberculosis or pneumocystis. Antitubercular drugs and Cotrimoxazole were also started in our patient. A skin biopsy revealed cutaneous aspergillosis. The histology and mycological study were suggestive of aspergillosis since dichotomous branching, septate hyphae, branching at an angle less than 45°have been identified in Hematoxylin and eosin, and in Grocott stained slides (Figures 3 and 4)

The therapy with amphotericin B and fluconazole was started. Despite treatment, the boy's condition did not improve, and he passed away 2 weeks following his hospital admission because of septic shock.

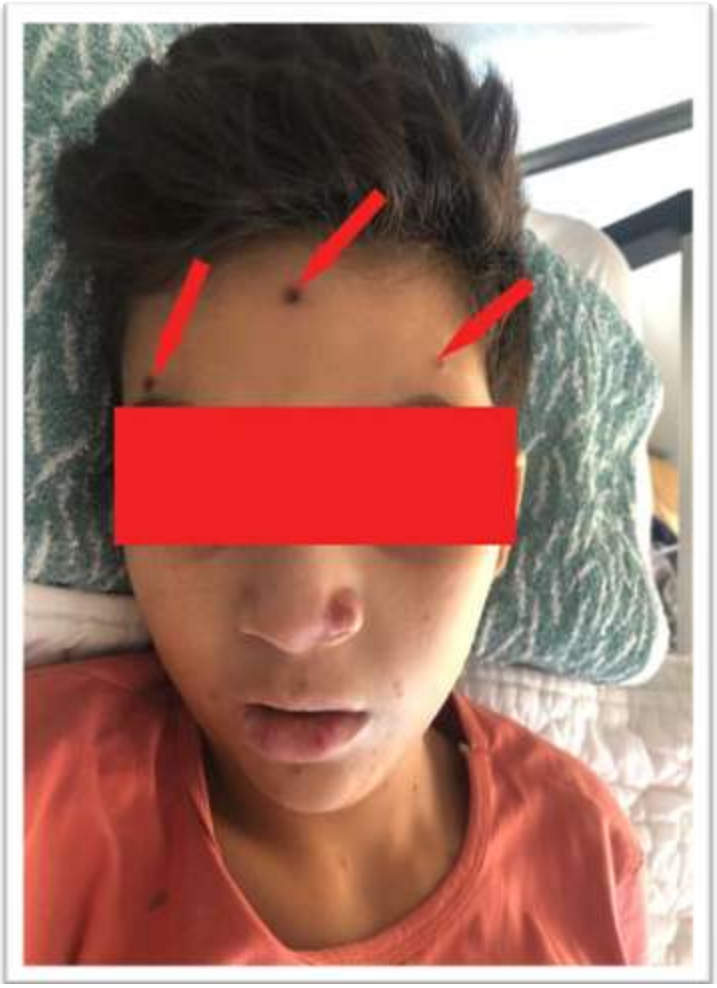

Figure 1:- Figure showing skin lesions on the face of the patient. They were of varying ages of development (Red arrows).

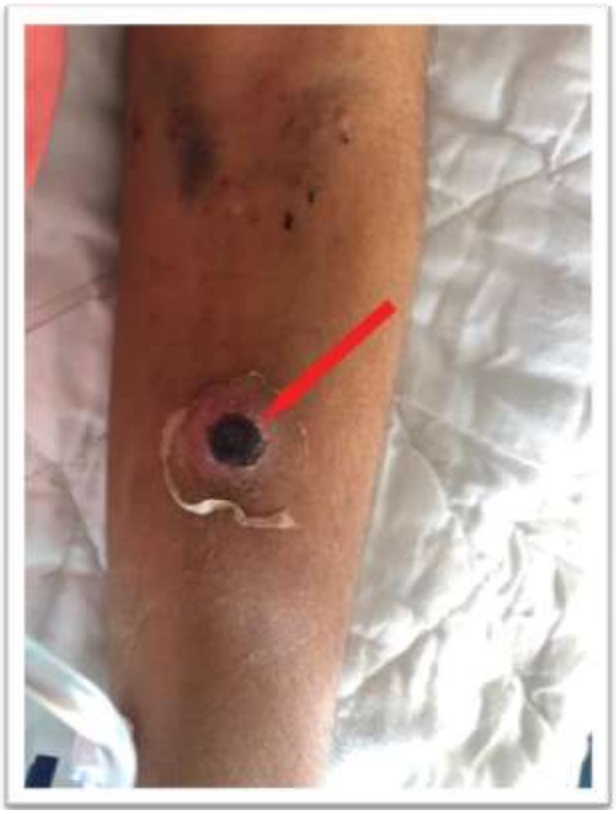

Figure 2:- Figure showing a necrotic lesion on the forearm of the patient simulating the appearance of ecthyma gangrenosum (Red arrow).

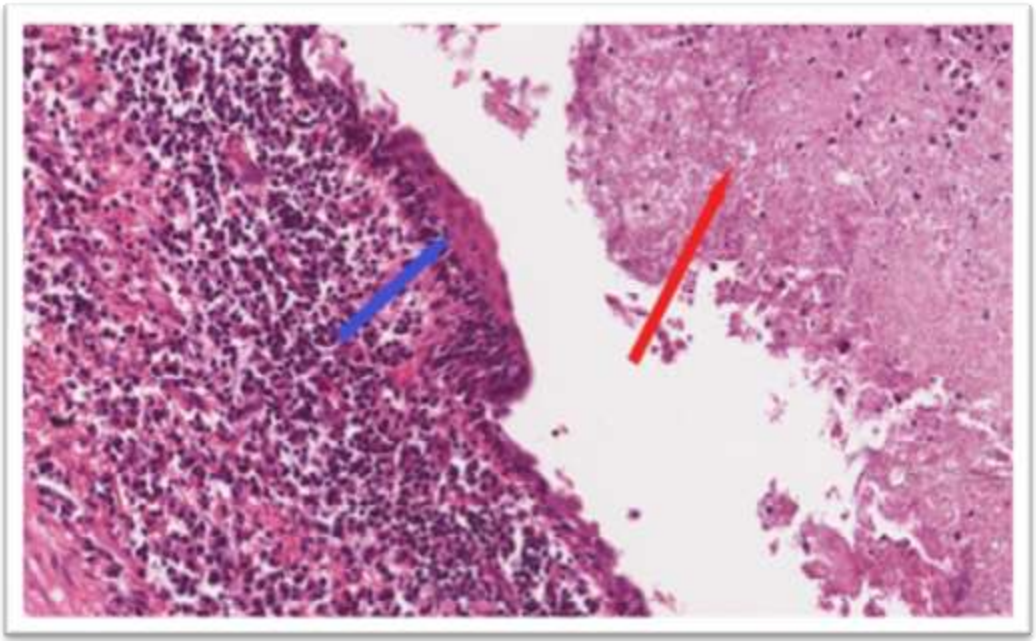

Figure 3:- Microphotography revealing presence of dichotomous branching, septate hyphae (Red arrow), branching at an acute angle in proximity to skin (Blue arrow) (H&E stain; 200X).

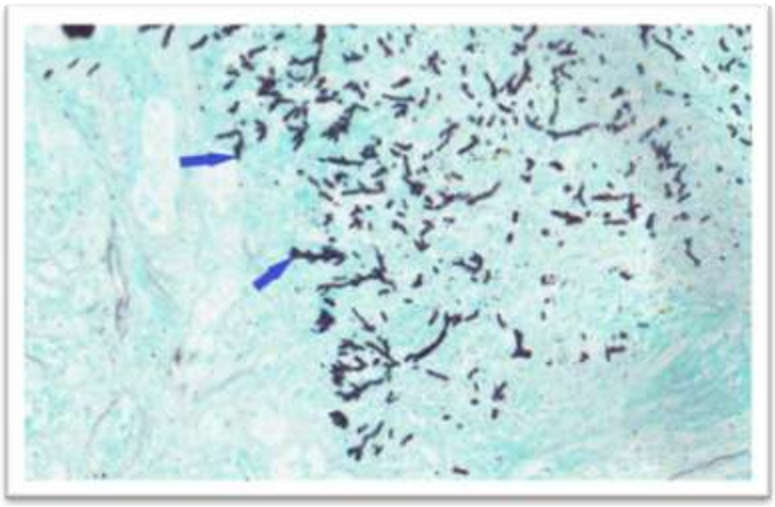

Figure 4:- Microphotography showing positivity of the observed septate hyphae to Grocott stain (Blue Arrow). (Grocott stain, 100X).

Discussion:-

Cutaneous aspergillosis is classified into two types: primary and secondary. Primary cutaneous aspergillosis often originates from direct implantation of the Aspergillus species into the skin, typically due to trauma [3–5]. Additionally, literature describes another mechanism known as "by contiguity," where the fungus may spread to the skin or mucosa from an adjacent cavity, such as the maxillary or paranasal sinuses [6, 7].

This type of aspergillosis is common in patients with catheters, those who have experienced trauma from arm boards, burns, or from contaminated dressings. Additionally, cases have been documented where airborne fungal spores in neonatal ICUs during construction renovations lead to infection [8-11].Conversely, secondary cutaneous aspergillosis arises from a disseminated infection [1]. PCA, or primary cutaneous aspergillosis, is most commonly induced by species such as Aspergillus flavus, A. ustus, A. terreus, and A. niger. Primary cutaneous aspergillosis affects children of all ages without favoring any gender. Due to its rarity and underreporting, the exact incidence of this infection is not established [3]. This infection is restricted to the skin and exhibits nonspecific clinical features that may appear on any part of the body.

Typical sites include areas around catheter insertions, venoclysis sites, nasogastric tube sites, and places where adhesive materials or long-term fixation devices are used. Commonly, lesions are located on the soles,palms, torso, arms, and the legs[3, 4].The affected areas may initially appear as erythematous and indurated macules, papules, plaques, or hemorrhagic bullae. These may evolve into necrotic ulcers topped with black eschar. While uncommon, the presence of nodules and pustular lesions has also been documented [12,13].

In our patient, the lesion were initially in form of papules and transformed progressively into ulcerated inflamed lesions. In neonates, typically, the skin manifestations initially appear as cellulitis, rapidly evolving into necrotic ulcers characterized by black eschars [8]. According to research, pustules were also observed in a number of affected patients [8]. In some instances, during a mycological analysis, hyphae are visible under direct microscopic examination [14]. The diagnosis of PCA is typically confirmed through a biopsy and culture.

It should be noted that in pediatric patients, both laboratory and clinical examinations may yield normal results which do not rule out systemic aspergillosis.

In contrast to adults, radiographic signs such as "halo" sign, infiltrates, the air crescent sign (Monod’s sign), or cavitationsare rare in the pediatric group and are especially uncommon in neutropenic patients [15].On the other hand, it is crucial to acknowledge that the 1-3 β-D glucan identification test using the wall exoantigen is not exclusive to detecting Aspergillus spp., as it may also detect other pathogens such as Fusarium spp., Candida spp.,Pseudomonas aeruginosa, Pneumocystis jiroveciand sometimes Cryptococcus neoformans during infections [7,

16, 17]. Furthermore, false positives may occur when patients receive immunoglobulin therapy or albumin infusions during hemodialysis [17].

Tahir et al. reported on an immunocompetent female who developed multiple ulcers in her perineumand axillae, likely contracting the infection through contaminated palm oil used in her research.

The infection was probably inoculated when she shaved these areas with razor blades. The patient achieved full recovery following surgical intervention of the wounds [18].

Neonatal afflictions have also been reported in the literature .Stock et al. [19] reported necrotic lesions located on the back, perineum, and axillae skin of a premature neonate, where Aspergillus fumigatus was identified. The contamination was traced back to a non-sterile, disposable glove infected with Aspergillus fumigatus, which likely caused the neonate's skin infection[19].In premature infants, primary cutaneous aspergillosis is rarely reported, with literature reviews revealing only a handful of cases within the past two decades in this particular demographic [2].

Similarly, Anderson et al. [20] reported a case involving a child with acute myeloid leukemia who exhibited two asymptomatic erythematous and geometric dermal plaques on his right forearm.

These skin plaques developed at the site where tapes were used to secure an arm board for intravenous access. Aspergillus niger was isolated from the culture. The lesions swiftly improved following systemic antifungal treatment[20].

Systemic antifungal medications such as amphotericin B and itraconazole are employed to treat aspergillosis. The approach to treating primary cutaneous fungal infections remains debatable, with both medical and surgical methods being applied[21].

Conclusion:-

In patients with weakened immune systems presenting with atypical skin lesions, infectious diseases should be considered. For accurate pathogen identification, obtaining multiple samples through biopsy and cultures may be necessary. The use of sterile, single-use devices is highly recommended for these patients.

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