THE PITFALL OF ORAL MUCOCUTANEOUS CANDIDA PARAPSILOSIS IN A CHILD WITH HIV INFECTION

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INTRODUCTION

Mucocutaneous candidiasis is one of the most common manifestations of human immunodeficiency virus (HIV) infection and is clearly related to the development of clinical cellular immunodeficiency. The occurrence of mucocutaneous candidiasis is common, with up to 90% of cases with advanced disease that develop oropharyngeal infection.[1] Candidiasis is the most common oral manifestation of pediatric HIV infection, with reported prevalences ranging between 20% and 72%.[2,3]

Over the past decade, the incidence of *Candida parapsilosis* has dramatically increased. In fact, reports indicate that *C. parapsilosis* is often the second most commonly isolated *Candida* species from blood cultures. *C. parapsilosis* was most frequently isolated in North America (14.3% of all *Candida* isolates) and Latin America (9.9%), although the frequency of isolation varied considerably within each of the five geographic locations, ranging from 0% (Indonesia) to 16.9% (Australia) in the Asia-Pacific region, from 1.3% (Slovakia) to 7.8% (Spain and Turkey) in Europe[4] However, the incidence of *C. parapsilosis* rose from 4.8% to 6.6% between 1997 and 2005.[5]

Oral lesions in HIV/AIDS indicate the progress of disease process and therefore, have prognostic significance.[6] The risk factors that influence the development of such oral manifestations include, low CD4+ T cell count, xerostomia and lack of highly active antiretroviral therapy (HAART).[7] Oral candidiasis is more common among children with low CD4 lymphocyte counts or symptomatic HIV disease than among those with normal counts or no symptoms.[3] Candidiasis has been associated with a more-rapid progression to death (median time from lesion to death, 3.4 years) than has herpes simplex virus infection (4.3 years).[8] In a study of children with vertical HIV infection, it was found that long-term survivors (more than 5 years) were significantly less likely to have histories of oral candidiasis than were children who died during infancy or early childhood.[9]

Although many skin disorders are easily recognized by simple inspection, the history and physical examination are often necessary for accurate assessment. The color, turgor, texture, temperature, and moisture of the skin should always be examined thoroughly under adequate illumination. Skin lesions should be palpated, inspected, and classified on the bases of morphology, size, color, texture, firmness, configuration, location, and distribution. One must also decide whether the changes are those of the primary lesion itself or whether the clinical pattern has been altered by a secondary factor such as infection, trauma, or therapy. If the diagnosis is not clear after a thorough examination, one or more diagnostic procedures may be indicated. [10]

C. parapsilosis are generally susceptible to all classes of antifungals.[11] Fluconazole displays predictable pharmacokinetics and an excellent tolerance profile in all groups, including the elderly and children. Fluconazole decreased the rate of mucosal infections caused by Candida. Unfortunately, there are very few pediatric treatment studies with the newer antifungal agents. Most recommendations for treating children are therefore derived from data in adults. In spite of this shortcoming, experience to date has indicated that these antimicrobials are safe and effective in younger patients.

This report presenting the first case of oral mucocutaneus candida parapsilosis in pediatric patient with HIV infection, focusing on its diagnostic approach and management.

CASE REPORT

A, 3 years 10 month old boy presented on August 13th, 2013 with crust in regio perioral since one month before admission, the boy was felt down on the road and wounded in perioral area. The wound became wider and covered by black crust around the erosions. The mother already brought him to the dermatologist, general practitioners and alternative medicine, but none of the treatments worked. The crust getting wider and thicker so the boy couldn't open his mouth, the erosion which covered by the crust caused the difficulties of breathing. Other symptoms were lost of appetite, cough and sometimes accompanied by fever. The child has no history of allergic hipersensitivity, the parents didn't know about history of allergic hipersensitivity in his family because the boy was adopted child
The past medical history revealed that the boy was diagnosed with HIV infection and lung tuberculousis at 2 years old . He had controlled to PIPI outpatient clinic and pediatrics consultant PIPI regularly followed him up. He was treated with anti retroviral and anti tuberculous drug since November 2012.

Initial physical examinations presented an alert boy and weak condition. Pulse rate was 120 beats per minute. The pulse rhythm was regular and adequate. Rospiration rate was 28 times per minute, not accompanied by respiratory distress or nasal flare. Axillar temperature was 36.5 °C. Blood pressure was 100/ 60 mmHg. The body weight was 11,6 kg, the body height was 97 cm, ideal body weight was 12 kg. The Z-score for heigh/age and weight/age were in percentile 2 (good nutritional status).

The head and neck examination revealed there was no sign of jaundice, cyanosis, dyspneu nor orbital edema. Oral mucosa and conjunctiva were pale and wet. There was erosions on the perioral covered with blackish, thickening crust which easily bleed if removed. It was itchy and when the crust had exfoliated there was pinkish erosions with irregular border underneath the crust. Chest examination was normal, symmetrical movement without chest wall retraction, or the use of

additional respiratory muscles. Wheezing and rhales were not found with vesicular breath sounds in both lung fields. Cardiac auscultation found normal sound of S1S2 and no systolic murmur nor splitting and gallops.

The abdomen was flat, there was no prominent and collateral veins obtained. Bowel sounds are normal. There was no liver enlargement. Spleen was not palpable and no other abdominal tumor.

Upper and lower extremities were well perfused, warm, dry and red. Capillary refill time less than 2 seconds. No edema was found in orbital and extremity. There were papules and pustule all over body surface, itchy and dry.

His initial laboratory investigations showed hemoglobin of 7.0 g/dL, leukocyte of 8,600/uL and platelet count of above 326,000/uL. Final haemostasis is normal with PPT 10.9 (11.9)s and APTT 26 (27.5) s. The serum electrolytes were in normal range with potassium 4.1 mmol/L, sodium 134 mmol/L, chloride 100 mmol/L, but low in calsium level 7.7 mg/dL with calsium corrected 8.42 mmol/L. The liver function was indicated with serum level AST 49 mg/dL and ALT 26 mg/dL, albumin level 3.1 mg/dL. The renal function was normal with BUN 6.0 mg/dL and creatinin serum 0.7 mg/dL. Hbs Ag (-), IgG/IgM toxo (–), IgG/IgM rubela (–). We diagnosed him with HIV infection stage III, chronic wound r. labialis, lung tuberculosis and pruritic papular eruption.

Picture 1 : The lession was covered by blackish, thickenning crust, some region showed pinkish lession with irregular border underneath the crust

We had given him PRC transfussion and calsium correction. He got IVFD dextrose 5% 1000cc per day. We had been inserted nasogastric tube to provide well feeding. We had boen gave empiric antibiotics due to the crust, ampicillin 500mg four times a day intravenously and gentamycin 60mg once daily intravenously. Culture of the crust and post transfussion CBC were planned.

On fourth day of admission, Laboratory examination revealed hemoglobin of 12.4 g/dL, leukocyte of 4,800/uL and platelet count of 257,000/uL. Serum electrolyte revealed sodium of 129 mmol/L, potassium of 3.6 mmol/L, chloride of 95 mmol/L and calcium of 8.4 mg/dL. We had administered vitamin K 3 mg once daily intramuscularly for three days because bleeding still occured on the exfoliated crust erosions. Metronidazole oral suspension was given 150mg three times a day to cover of anaerob bacteria.

Picture 2 : The crust were exfoliated, the bottom of crust look pink and reddish with continous bleeding.

On tenth day of admission, the crust were exfoliated, bleeding occured and there was pink and reddish lession with irregular surface at the bottom of the crust. He could open his mouth and there was pseudomembranous whitish plaques in his oral cavity and buccal

mucosae. The pseudomembrane was removed easily, revealing erythema, and minutes superficial hemorrhage at the underlying mucous. The crust swab culture revealed *Klebsiella pneumonia* (sensitive: Amikasin, Chloramphenichol, imi/mero/ertapenem). We diagnosed him with HIV infection stage III, chronic wound r. labialis, candidiasis oris, lung tuberculosis and pruritic papular eruption. Based on crust culture result the antibiotics had changed to meropenem 250mg three times a day intra venously. We also administered transamin 180mg three times a day intravenously, fluconazole 150mg once daily intravenously at first day and then maintenance 75mg once daily for three days, nystatin oral drop 1 ml three times daily to cover fungal infection. The patient was consulted to plastic surgery department for wound care, the patient had treated with mupirocin cream and debridement.

On 13th day of admission, there was no significant changes on the crusted wound, repeated culture of the wound, pathological examination and consulted to dermatology department were planned. Laboratory examination revealed hemoglobin of 14.4 g/dL, leukocyte of 11,100/uL and platelet count of above 433,000/uL, CD4 absolut 29, CD4 % 1.87 %. Because of decreasing his imunological status we had been suspected there was ARV resistance despite of his good adherence, we switched the anti retroviral to second line treatment consist of Abicavir 100mg twice a day, 3 TC 50mg twice a day and aluvia (lopinavir 150mg and rifonavin 37,5 mg) twice a day

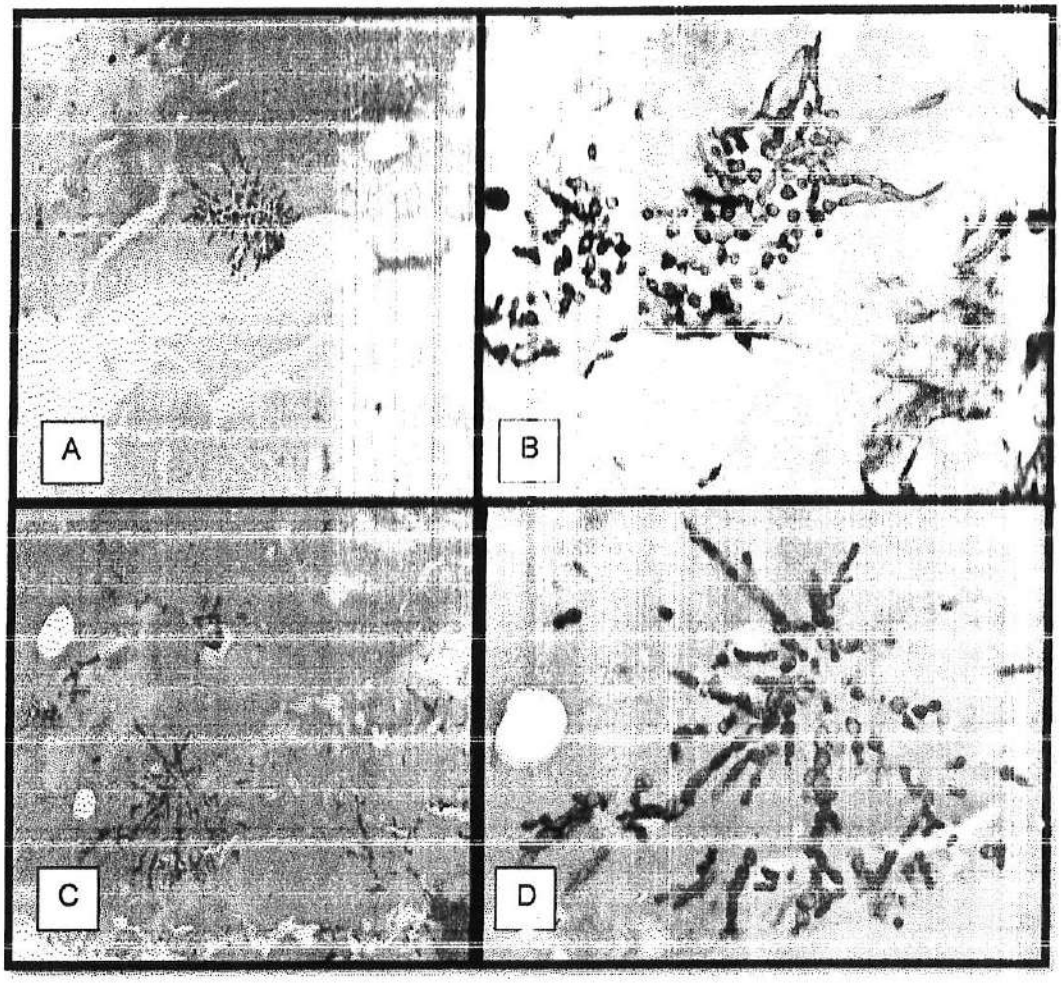
On 17th day of admission, laboratory examination revealed hemoglobin of 13.6 g/dL, leukocyte of 13,400/uL and platelet count of above 125,000 /uL,albumin level 2.6, albumin level mg/dL. The renal function was normal with BUN 9.0 mg/dL and creatinin serum 0.5 mg/dL. Faal haemostasis was normal with PPT 10.6 (12.2) and APTT 29.4 (27.9). The liver function was indicated with serum level AST 104 mg/dL and ALT 78 mg/dL.

Repeated crust swab culture after meropenem administered on 20th day of admission, the crust swab culture revealed *Acinetobacter baumanni* (sensitive: Amikasin, Chloramphenichol, imi/ mero/ ertapenem) so meropenem 250 mg three times a day intravenously was continued.

On 24th day of admission, laboratory examination revealed hemoglobin of 11.5 g/dL, leukocyte of 6,890/uL and platelet count of above 375,000 /uL, albumin level 3 mg/dL. The liver function was indicated with serum level AST 110 mg/dL and ALT 91 mg/dL. Fluconazole therapy was stopped after fifteen days of treatment.

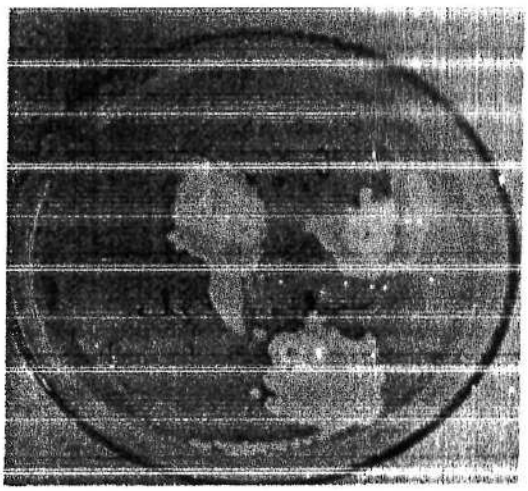
On 29th day of admission, scrapping of the erosions was done, and the pathology anatomy analysis revealed squamous cell carsinoma, by than we ask to reviewed pathology anatomy reading because the clinical prensentation did'nt match with squamous cell carsinoma. The pathology anatomy department suggested for open biopsy. We had stopped meronem therapy. Serology marker of *Herpes simplex* was planned by dermatology department and the result of Anti HSV 1 and 2 IgG/IgM were negative.

On 39th day of admission there was no significant changes on the crusted wound, fungal cultured was planned. We send exfoliated crust to microbiology laboratory to distinguish the causes, we put exfoliated crust in the jar filled with NaCl 0.9 % and then send it. . In microbiology laboratory half of the specimen were cultured. The other placed in 10% formaldehyde solution (Formalin) and then had given praffin block and the specimen has been sliced by microtom 3 micron. The microscopy examination revealed colony of candida.



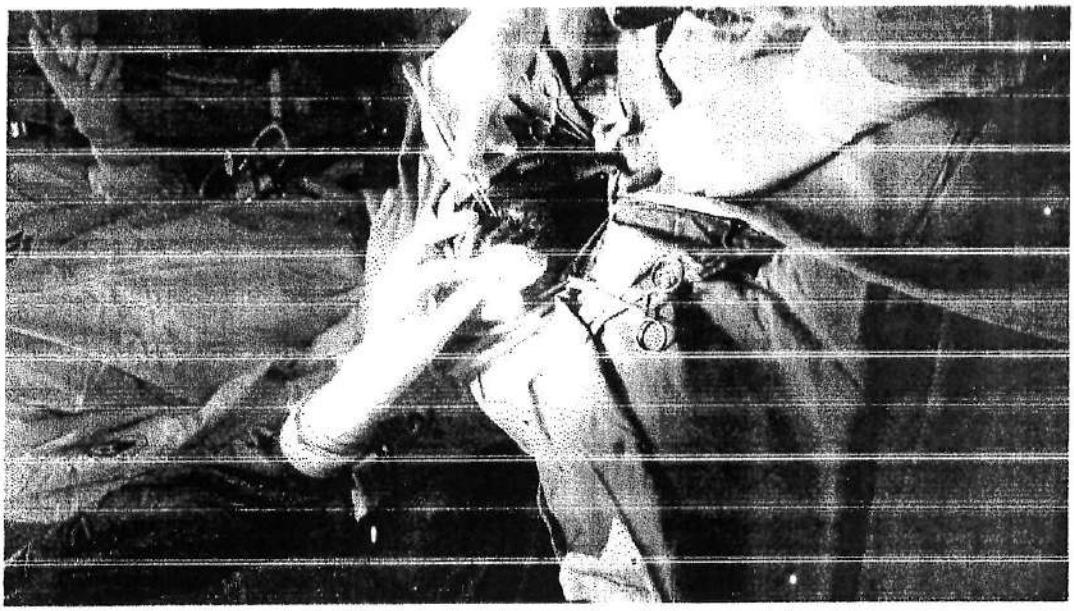
A.with GMS staining 450x B. With GMS staining 1000x
C.with PAS staining 450 x D. with PAS staining 1000 x
Picture 3 A, B, C, D ; showed yeast phase and pseudohyphal form.

The fungal culture from exfoliated crust using reagen API 20 CaUx and processed with Vitex 2 compact revealed *Candida parapsilosis* susseptible to flucytosin, fluconazale, voriconazole, amphotericin B. We had been diagnosed him with HIV infection stage iii, periorai candidiasis parapsilosis, lung tuberculosis and pruritic papular eruption. We decided to give him micafungin intravenous injection



Picture 5: showed *C. Parapsilosis* culture on seboroud agar are white, creamy, shiny, smooth and wrinkled

100mg single dose for five days and followed by fluconazole for 10 days

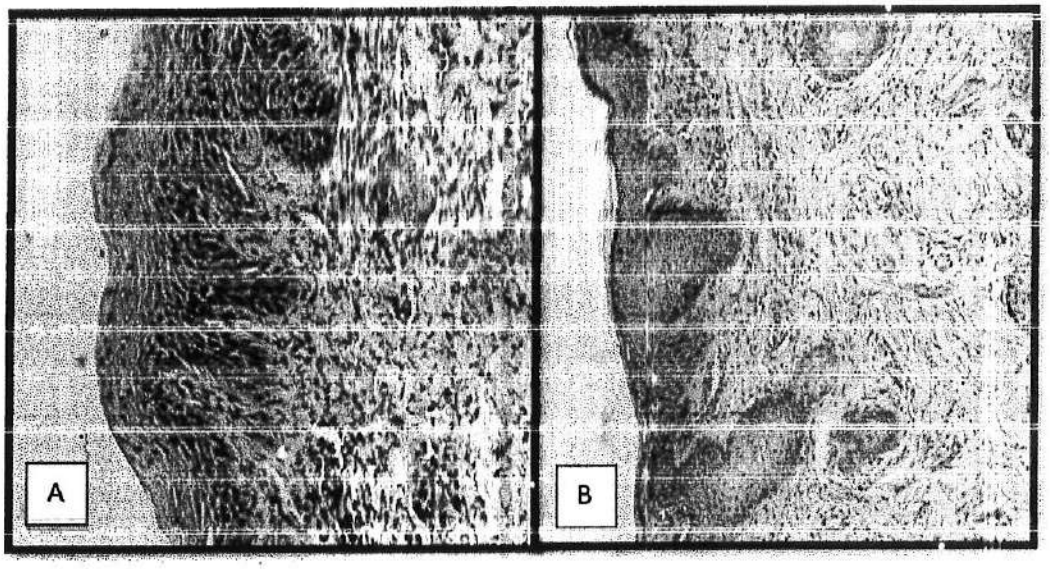


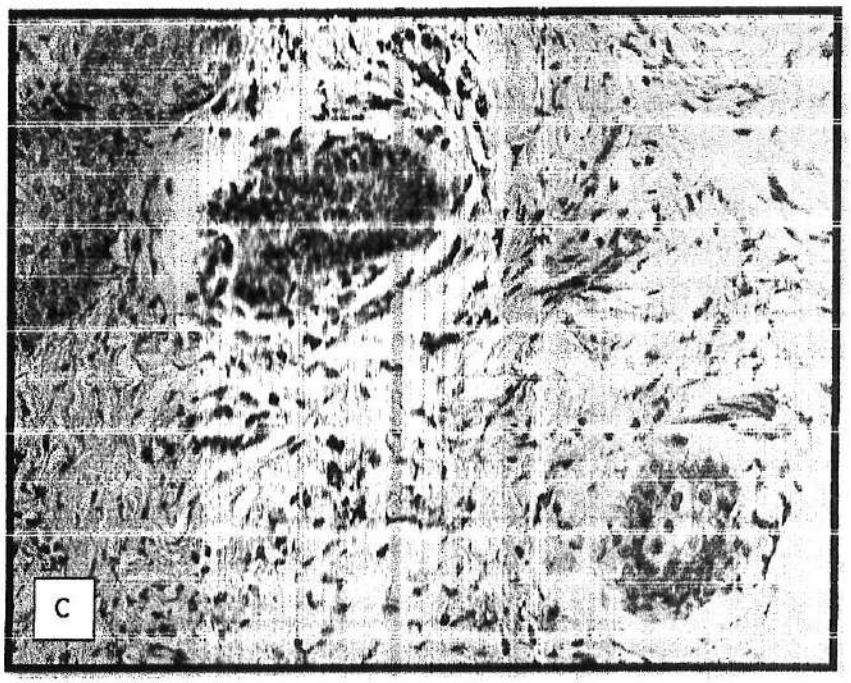
Picture 6: showed on September 27th, 2013, he had underwent open biopsy by head and neck surgery.

Picture 7; after open biopsy

On October 8th, 2013, This patient responded well to treatment with micafungin for the infection, crust was minimalized, no itchy and decrease of bleeding. From head and neck surgery suggested of normal saline for debridement and on going the topical antibiotic. Anatomy pathology of

perioral erosions was drawn no sign of *Kapossi's sarcoma* or other carsinoma but there were chronic non specific process.

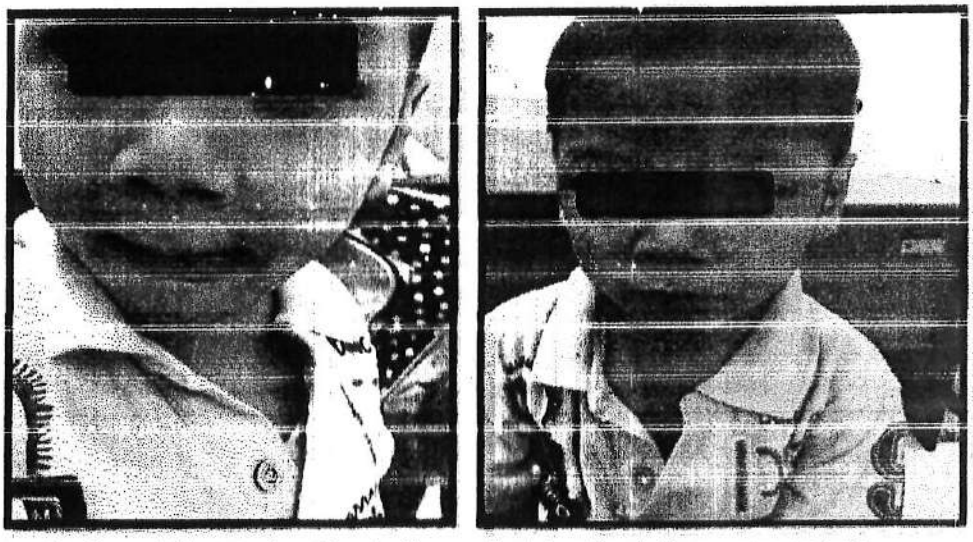




Picture 8: A. PAS staining 40x
B. PAS staining 100x
C. PAS staining 200x

Anatomy pathology of perioral erosions was drawn no sign of *Kapossi's sarcoma* or other carsinoma.

There was acanthosis, longer rete ridge on epidermis region. On the dermis showed infiltration of limfosit, histiosit,some of neutrofil and dilated vascular.



Picture 9; showed the crust getting better and minimalized, there was macula hipopigmentation noted.

On October 16th, 2013 , there was macula hipopigmentation noted, there was no itchy and no bleeding anymore, the crust had eliminated. Laboratory examination revealed hemoglobin of 10.8 g/dL, leukocyte of 10,420 /uL and platelet count of above 369.600 /uL,albumin level 3.5 mg/dL. The renal function was normal with BUN 12 mg/dL and creatinin serum 0.7 mg/dL. The liver function was normal indicated with serum level AST 64 mg/dL and ALT 56 mg/dL. Serum electrolyte revealed sodium of 140 mmol/L, potassium of 4.3 mmol/L, chloride of 105 mmol/L and calcium of 9,1 mg/dL. On October 24th, 2013, the patient discharge from the hospital, being in good health.

DISCUSSION

In this case, A, 3 years 10 month old boy presented with crust in regio perioral, the crust getting wider and thicker so the boy couldn't open his mouth, the erosions which covered by crust had been caused the difficulties of breathing. Other symptoms are lost of appetite, cough and sometimes accompanied by fever. There was no history of allergic hipersensitivity. In facing a child with HIV infection and manifestation of perioral lession, one should think about predisposition infection that may be associated with his imunological status. From the inspection there were erosion on the perioral covered with blackish, thickening crust which easily bleed if removed. It was itchy and when the crust had exfoliated there were pinkish erosions with irregular border underneath the crust.

Skin lession was divided into two group. Primary lession and secondary lession. In our patient there were crust and erosion which had been classified to secondary lession. Primary lesions are classified as macules, papules, patches, plaques, nodules, tumors, vesicles, bullae, pustules, wheals, and cysts. Primary lesions may change into secondary lesions, or secondary lesions may develop over time where no primary lesion existed. Primary lesions are usually more helpful for diagnostic purposes than secondary lesions. Secondary lesions include scales, ulcers, erosions, excoriations, fissures, crusts, and scars. Erosions involve focal loss of the epidermis, and they heal without scarring. Crusts consist of matted, retained accumulations of blood, serum, pus, and epithelial debris on the surface of a weeping lesion.[12]

The perioral lession in HIV patient can caused by many condition such as viral infection, bacterial infection, fungal infection and malignancy. There were diagnostic procedures had been indicated for finding the primary causes.

Direct smear / Potassium hydroxide (KOH) examination is used for suspected fungal infections of skin, hair and nails. Scrapings (using a scalpel blade) from a scaly lesion are placed on a clean glass slide. Place

scrapings on a glass slide. Apply a few drops of 10–20% KOH. Apply a cover slip. Heat the slide to facilitate dissolution of the cell walls or allow the slide to sit for 15–20 min without heating. If 20% KOH in dimethylsulfoxide (DMSO) is used, heating is unnecessary. KOH can also be formulated in ink-based preparations which darken the hyphae for easier identification. Examine microscopically at 10× or 20× power with the condenser in the lowest position. Demonstration of hyphae or spores confirms the diagnosis of *Tinea*. Oral lesions suspected of *Candida* can be scraped in a similar fashion to demonstrate the typical pseudohyphae or budding yeast forms.

Fungal cultures confirm a diagnosis of *tinea capitis, tinea corporis* or *onychomycosis*. Using appropriate fungal culture media (Sabouraud's agar, Mycosel agar) allows for identification of fungal species.

Bacterial cultures of the purulent material from representative lesions are swabbed with a soft sterile swab, inserted into the appropriate tube and sent to the laboratory.

Skin biopsy is carried out for routine histopathologic or immunofluorescence examination. Topical anesthetic can be applied to the skin prior to biopsy to reduce the pain of the needle stick for local anesthesia. Punch biopsies or elliptical biopsies should demonstrate all three levels of the cutis (epidermis, dermis and subcutaneous fat). Shave biopsies (saucerization) may be indicated for more superficial lesions.[13]. Punch biopsy is a simple, relatively painless procedure and usually provides adequate tissue for examination if the appropriate lesion is sampled. The selection of a fresh, well-developed primary lesion is extremely important to obtain an accurate diagnosis. The site of the biopsy should have relatively low risk for damage to underlying dermal structures. The skin is anesthetized by application of EMLA cream and/or intradermal injection of 1-2% lidocaine (Xylocaine), with or without epinephrine, with a 27- or 30-gauge needle after cleansing of the site. A punch, 3 or 4 mm in diameter, is pressed firmly against the skin and rotated until it skin to the proper depth. All three layers (epidermis, dermis, subcutis) should be

contained in the plug. The plug should be lifted gently with forceps or extracted with a needle and separated from the underlying tissue with an iris scissors. Bleeding abates with firm pressure and with suturing. The biopsy specimen should be placed in 10% formaldehyde solution (Formalin) for appropriate processing.[11] Biopsy is best done by a physician who is trained in the knowledge of which areas are best biopsied and what histology is expected. Immunofluorescence may be indicated for certain connective tissue disorders or bullous diseases and requires special transport media.

Polymerase chain reaction provides a highly sensitive test for viral genomes. First, nucleic acid is extracted from the patient material to be analyzed. Any RNA virus genome present in the material is transcribed into DNA by reverse transcriptase. This DNA, as well as the DNA of the DNA viruses, is then replicated in vitro with a DNA polymerase as follows: after the DNA double strand has been separated by applying heat, two synthetic oligonucleotides are added that are complementary to the two ends of the viral genome segment being looked for and can hybridize to it accordingly. The adjacent DNA (toward each 50 end) is then copied with an added polymerase, whereby the oligonucleotides act as primers. The new and old strands are once again separated by heat and the reaction is started over again. Running several such cycles amplifies the original viral DNA by a factor of many thousands. Beginning with the second generation, the newly synthesized DNA strands show a uniform, defined length and are therefore detectable by means of gel electrophoresis. The specificity of the reaction is verified by checking the sequences of these DNA strands by means of hybridization or sequencing. The amplification and detection systems in use today for many viruses are increasingly commercially available, and in some cases are also designed to provide quantitative data on the "viral load." If a viral infection induces humoral immunity, the resulting antibodies can be used in a serodiagnosis. When interpreting the serological data, one is confronted by the problem of deciding whether the observed reactions indicate a fresh, current infection

or earlier contact with the virus in question. Detection of IgM (without IgG) proves the presence of a fresh primary infection. IgM is now usually detected by specific serum against human IgM in the so-called capture test, an EIA. To test for IgM alone, a blood specimen must be obtained very early in the infection cycle. Concurrent detection of IgG and IgM in blood sampled some what later in the course of the disease would also indicate a fresh infection. It could, however, also indicate a reactivated latent infection or an anamnestic reaction (i.e., a nonspecific increase in antibodies in reaction to a nonrelated infection), since IgM can also be produced in both of these cases. A fourfold increase in the IgG titer within 10–14 days early on in the course of the infection or a drop of the same dimensions later in the course would also be confirmation.[14]

After the diagnostic procedure had been done, several causes of the perioral lession of the HIV patient commonly identified (table1)

Table 1. Differential diagnosis of oral ulcers in individuals with HIVinfection

Viral infections
• *Herpes simplex virus*
• *Cytomegalovirus*
• *Varicella zooster virus*
Bacterial infections
• Ulcerative periodontal disease (gingivitis or periodontitis)
• Necrotizing ulcerative stomatitis
• *Mycobacterium tuberculosis*
• *Mycobacterium avium-intracellulare* complex
Fungal infections
• *Cryptococcus neoformans*
• *Histoplasma capsulatum*
• *Aspergillus*
Neoplastic conditions
• *Kaposi's sarcoma*
• *Non-Hodgkin's lymphoma*
Medications
• Zalcitabine (dideoxycytidine)
• Foscarnet
Other conditions
• Granulocytopenia
• Aphthous ulcers

From : Mark W, Kline M.D. Oral manifestations of pediatric Human Immunodeficiency Virus Infection: A Review of the literature. Pediatrics. 1996;3:380-8

Oral manifestations are observed commonly in children with human immunodeficiency virus (HIV) infection. It has been estimated that oral lesions develop in one third of HIV-infected as the primary or initial manifestation of HIV infection.[15] The perioral erosions that had given clinical picture of crust and erosion were classified for several group of causes :

Viral Infection

Human immunodeficiency virus infected children are prone to opportunistic viral infections in the oral mucosa, mainly from the *Herpesviridae* family members such as herpes simplex virus (HSV), the *cytomegalovirus* (CMV) and *Epstein-Barr virus* (EBV), all of which are important etiologic agents of morbidity.[16] In this patient laboratory examination for Anti HSV 1 dan 2 IgG/M were negative

***Herpes simplex Virus* (HSV)**

Ulcerative lesions recorded in the current study include, herpes simplex, aphthous ulcers and non-specific ulcers. Chronic persistent infection with *Herpes simplex virus* (HSV-1) is common in patients with HIV infection. Lesions may appear as grouped blisters that rupture, crust, and heal in 7 to 10 days. Once severely immunosuppressed, HIV-infected individuals often experience chronic lesions that continue to expand and form large, painful ulcers and crusted erosions which are 2 to 10 cm or larger. The viral genome codes for about 90 proteins, categorized as "immediate early" (regulatory functions), "early" (DNA synthesis), and "late" (structural) proteins. Herpes simplex viruses are classified in types 1 and 2, which differ both serologically and biologically (host-cell spectrum, replication temperature). Initial infection with herpes simplex type 1 usually occurs in early childhood. The portal of entry is normally the oral mucosa ("oral type") and the infection usually manifests as a gingivostomatitis. The viruses then wander along axons into the CNS, where they persist in a latent state in the trigeminal (Gasseri) ganglion.

Direct detection of the viruses under an electron microscope is only practicable if the specimen contains large numbers of viruses, which in practice will normally only be the case in blister contents. The virus can also be detected directly in patient specimens using immunofluorescence or in-situ hybridization, but the material must contain virus-infected cells, i.e., blister contents are not as suitable here as in electron microscopy and virus isolation. Serological investigation results in HSV lack significance due to the high level of general contamination in the population.[13]

Internal malignancies

Internal malignancies may find cutaneous expression by several mechanisms. Cutaneous metastases may present as firm any cutaneous site, including the scalp. Distinctive paraneoplastic reaction patterns may result in sometimes striking rashes. genetic syndromes have increased malignancy risk that may be suggested initially by cutaneous signs.[10]
Anatomy pathology of perioral lession was drawn no sign of *Kapossi's sarcoma* or other carsinoma. Although *squamous cell carcinomas* usually develop on sun exposed skin, it can occur anywhere on the body, including inside the mouth, on the anus, and on the genitals in both men and women. The appearance of the primary tumours can vary, but the most common forms include:

o A firm, red nodule on the face, lower lip, ears, neck, hands or arms, that may bleed sometimes

o A flat lesion with a scaly crust on the face, ears, neck, hands or arms

o A new ulceration or raised area on a pre-existing scar or ulcer

o An ulcer or flat, white patch inside the mouth

o A red, raised patch or ulcerated sore on or in the anus or on the genitals

Squamous cell carcinomas are usually slow growing and can be difficult to spot, especially when it appears on skin that has other signs of sun damage, such as changes in pigmentation, loss of elasticity and wrinkling. It can also be mistaken for actinic keratoses, rough, scaly, dark brown or pink patches that appear after years of sun exposure. A small number of

actinic keratoses eventually develop into squamous cell carcinomas. Squamous cell carcinomas typically appear as a persistent thick, rough, scaly patch that can bleed if bumped. They often look like warts and sometimes appear as open sores with a raised border and a crusted surface over an elevated pebbly base.[17]

Bacterial infection

We've done swab culture twice and revealed different bacteriological causes. First result revealed *Klebseilla pneumonia* and second result revealed *Acinetobacter baumanni.* There were no significance changes for the perioral lession after antibiotics treatment.

Chronic wound pathogenic biofilms are host-pathogen environments that colonize and exist as a cohabitation of many bacterial species. These bacterial populations cooperate to promote their own survival and the chronic nature of the infection. Few studies have performed extensive surveys of the bacterial populations that occur within different types of chronic wound biofilms. There are specific major populations of bacteria that were evident in the biofilms of all chronic wound types, including *Staphylococcus, Pseudomonas, Peptoniphilus, Enterobacter, Stenotrophomonas, Finegoldia*, and *Serratia* spp. Each of the wound types reveals marked differences in bacterial populations, such as pressure ulcers in which 62% of the populations were identified as obligate anaerobes. There were also populations of bacteria that were identified but not recognized as wound pathogens, such as *Abiotrophia para-adiacens* and *Rhodopseudomonas* spp. Results of molecular analyses were also compared to those obtained using traditional culture-based diagnostics. Only in one wound type did culture methods correctly identify the primary bacterial population indicating the need for improved diagnostic.[18]

. Fungal species have gained considerable importance as opportunistic pathogens of immunocompromised individuals, particularly those infected with human immunodeficiency virus (HIV).[19] In our patient

there were erosion covered with blackish crust. The microscopy examination revealed colony of candida. There were some fungal infection with clinical picture of blackish crust :

Mucormycosis

Acute, rapidly progressive, fatal disease occurring in immunosuppressed patients caused by opportunistic fungi. Cutaneous mucormycosis:

1. Superficial: gradual onset with slow progression, associated with the use of contaminated adhesive tape; no vascular or deep tissue involvement.
2. Gangrenous: progresses rapidly with painful ulcers and eschars; vascular invasion with hematogenous spread common; poor prognosis, usually occurs in the setting of skin trauma (e.g. IM injection, open fracture, insect bites, motor vehicle accidents) in patients with an underlying predisposing condition

    a. Premature infants: associated with contaminated adhesive tape use or wooden tongue depressors for limb splinting; very grave prognosis in this setting

    b. Older children with underlying myeloproliferative disease.[20]

Aspergillus (Aspergillosis)

Aspergilloses are most frequently caused by *Aspergillus fumigatus* and *A. flavus*. *A. niger, A. nidulans*, and *A. terreus* are found less often. Aspergilli are ubiquitous in nature. They are found in large numbers on rotting plants. Morphology and culture. Aspergillus is recognized in tissue preparations, exudates and sputum by the filamentous, septate hyphae, which are approximately 3–4 lm wide with Y-shaped branchings.

Aspergillus grows rapidly, inmycelial form, on many of the mediums commonly used in clinical microbiology. Sabouraud agar is suitable for selective culturing. The main portal of entry for this pathogen is the bronchial system, but the organism can also invade the body through injuries in the skin or mucosa.[20]

The fungal culture using reagen API 20 CaUx and processed with Vitex 2 compact revealed candida parapsilosis susseptible to flucytosin, fluconazole, voriconazole, amphotericin B. We had been diagnosed him with HIV infection stage III, perioral candidiasis parapsilosis, lung tuberculosis and pruritic papular eruption. We decided to give him micafungin intravenous injection 100mg single dose for five days because we had been given him fluconazole for fifteenth days but there was no significance changes of the perioral lession.

Candidiasis has considerable clinical significance in the prognosis of HIV infection and as an indicator of the non-effectiveness of antiretroviral treatment. In the present study, the investigation of factors associated with the time patients are free of oral candidiasis revealed the following independent predictors of the disease: moderate to severe immunodepression, anemia, malnutrition and hospitalization. Moreover, the use of antiretroviral therapy (monotherapy, dual therapy or triple therapy/HAART) proved to be an independent protection factor.[21] In the present study, anemia was a predictor of oral candidiasis, as the time free of this disease was greater in children without anemia. Different clinical presentations of oral candidiasis, especially the mucocutaneous and angular forms, have previously been associated with anemia.[22]

Candida parapsilosis is typically a commensal of human skin, and its pathogenicity is limited by intact integument. *C. Parapsilosis* is notorious for its capacity to grow in total parenteral nutrition and to form biofilms on catheters and other implanted devices, for nosocomial spread by hand carriage, and for persistence in the hospital environment.[5] *C. parapsilosis* cells display oval, round, or cylindrical shapes. When grown on Sabouraud dextrose agar, colonies of *C. Parapsilosis* are white, creamy, shiny, and smooth or wrinkled. Unlike *C. albicans* and *C. tropicalis*, which can exist in multiple morphogenetic forms, *C. parapsilosis* does not form true hyphae and exists in either a yeast phase or a pseudohyphal form. Pseudohyphae have been observed on cornmeal agar and can be identified by light microscopy.[23] *C. parapsilosis* is not an

obligate human pathogen, having been isolated from nonhuman sources such as domestic animals, insects, soil, and marine environments.[24]

C. parapsilosis is also a normal human commensal, and it is one of the fungi most frequently isolated from the subungal space of human hands. Its transient colonization of human integument is the basis of much debate as to whether or not *C. parapsilosis* is a pathogen or bystander in certain infections. The increase in the frequency of *C. parapsilosis* infections has been attributed to a variety of risk factors, including the organism's selective growth capabilities in hyperalimentation solutions and its affinity for intravascular devices and prosthetic materials. Immunocompromised individuals such as AIDS patients and surgical patients, particularly those having surgery of the gastrointestinal tract, are at high risk for infection with *C. parapsilosis*. Additionally, patients requiring prolonged use of a central venous catheter or indwelling device, such as cancer patients, are at increased risk for infection with *C. parapsilosis*. Prolonged used of an intravenous catheter for antibiotic administration has also been associated with *C. Parapsilosis*.[5]

The incidence of *C. Parapsilosis* rose from 4.8% between 1997 and 2000 to 6.6% between 2001 and 2005. Higher rates of *C. parapsilosis* isolation were obtained in a study involving 5,346 clinical *Candida* isolates from 91 medical centers between 2001 and 2006, where it accounted for significant percentages of *Candida* species in the Asia-Pacific regions (15.97%), Latin America (18.62%), Europe (10.63%), and North America (14.04%).[25] The increase in the frequency of *C. parapsilosis* infections has been attributed to a variety of risk factors, including the organism's selective growth capabilities in hyperalimentation solutions and its affinity for intravascular devices and prosthetic materials. *C. parapsilosis* fungemia can lead to seeding of tissues, resulting in deep-seated infections, and has a mortality rate ranging from 4% to 45%.[5]

There is currently no consensus on the treatment of invasive *C. parapsilosis* diseases, although the therapeutic approach typically includes

the extraction of any removable foreign bodies and the administration of a systemic antifungal. The high incidence of mucosal and deep seated forms of candidiasis has resulted in the use of systemic antifungal agents, especially fluconazole and itraconazole. Fluconazole displays an excellent profile of tolerance in the range of doses recommended in invasive candidiasis. Side effects do occur especially with doses >400 mg/day. They have been reported to occur more often in those with the human immunodeficiency virus (HIV). Safety and tolerability have been also clearly assessed in the paediatric population, mirroring the excellent profile of tolerance observed in adult population.[5]

Echinocandins are the newest class of antifungal agents, and echinocandins currently available in the United States include caspofungin, micafungin, and anidulafungin. These drugs interfere with cell wall synthesis by inhibiting (1, 3) D-glucan synthase, an enzyme that forms glucan polymers, the major component of the fungal cell wall.[26]

Echinocandins can fail during treatments of *C. parapsilosis* bloodstream infections in which the MICs for the echinocandin used are low (0.25µg/ml). Also, "breakthrough" infections with *C. parapsilosis* have occurred in individuals receiving echinocandins for other indications.[27] In fact, at concentrations above the MIC for echinocandins, these drugs can paradoxically promote the growth of some isolates of *C. parapsilosis* and other *Candida* species in vitro.

Another part of treatment for our patient that very important was the management of HIV infection. Laboratory examination revealed that his imunologically status had been in severe imunodefficiency. Because of decreasing his imunological status we had suspected there was ARV resistance despite of his good adherence, we switched the anti retroviral to second line treatment consist of Abicavir 100mg twice a day, 3 TC 50mg twice a day and aluvia (lopinavir 150mg and rifonavin 37,5 mg) twice a day .

Survival free of disease was closely linked to the degree of immunodepression, as risk increased with the exacerbation of immune system impairment. This association has been described in previous cohorts of children throughout the world.[28,29] Treatment guidelines for initial therapy for human immunodeficiency virus type 1 (HIV-1) infection recommend the use of two nucleoside reverse-transcriptase inhibitors (NRTIs) with a nonnucleoside reverse-transcriptase inhibitor or a ritonavir-boosted protease inhibitor.[30] The advent of HAART had reduced the mortality and morbidity rates in HIV positive individuals. This is due to the reduction of HIV viral load and consequent recovery of immune system.[31] Patients receiving HAART are protected to some extent against, candidiasis, salivary gland disease, *Kaposi's sarcoma*, and oral hairy leukoplakia. The prevalence of all oral lesions has decreased by more than 30% since the introduction of HAART. However, the prevalence of HIV salivary gland disease has seen a slight increase in its incidence, while, the incidence of some lesions like oral candidiasis, aphthous ulcers, and Kaposi's sarcoma has remained the same.[32]

Summary

A case report of 3 years 10 month old boy with HIV infection stage III and perioral candidiasis parapsilosis has been reported.

We've done swab culture twice and revealed different bacteriological causes. First result revealed *Klebseilla pneumonia* and second result revealed *Acinetobacter baumanni*. There were no significance changes for the perioral erosions after antibiotics treatment.

Anatomy pathology of perioral lession was drawn no sign of Kapossi's sarcoma or other carsinoma. The fungal culture using reagen API 20 CaUx and processed with Vitex 2 compact revealed candida parapsilosis susseptible to flucytosin, fluconazole, voriconazole, amphotericin B. We decided to give him micafungin intravenous injection 100mg single dose for five days and then followed with fluconazole oral.

The patient discharge from the hospital, being in good health. There was macula hipopigmentation noted, no itchy and no bleeding anymore, the crust had eliminated.

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