CASE REPORTS

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Rhinofacial Conidiobolomycosis in a 16-Year-Old Girl

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ABSTRACT

Objectives: To present the case of a 16-year-old girl with progressive facial disfigurement spanning 11 months due to conidiobolomycosis.

Methods:

Design: Case Report
Setting: Tertiary Government Hospital
Patient: One

Results: A 16-year-old girl presented with a severe facial deformity of 11 months duration. The lesion started as a swelling in the right nasal vestibule, which later involved the entire nose, forehead, cheeks, upper and lower lip. A series of tissue biopsies revealed varied results -- chronic inflammation, chronic granulomatous inflammation with foreign body type giant cells, and eosinophilic granuloma—resulting in delayed provision of appropriate treatment. On the fourth biopsy using Grocott methenamine silver staining technique, septate fungal hyphae were identified. With a diagnosis of rhinofacial conidiobolomycosis, she was started on Itraconazole 100mg three times daily for eight months. Her facial swelling subsided gradually during the course of treatment and no systemic drug-related complications were observed.

Conclusion: Rhinofacial conidiobolomycosis is a rare chronic localized fungal infection that usually affects midline facial structures in immunocompetent hosts. Early detection and diagnosis, and appropriate medication can give rapid resolution. To the best of our knowledge, this may be the first documented case of rhinofacial conidiobolomycosis in the Philippines.

Keywords: *Conidiobolomycosis; Conidiobolus; fungal infection; Itraconazole, therapeutic use*

Rhinofacial conidiobolomycosis (RFC), also known as rhinoentomophthoromycosis, is a rare, chronic, subcutaneous mycoses caused by Conidiobolus.[1] The fungal infection manifests as an indolent and painless swelling in the midfacial structures and commonly originates in the nasal cavity or sinuses from which the fungus extends to involve subcutaneous tissues of the nose and the face.[1] We present a rare case of a 16-year-old girl with progressive facial disfigurement spanning 11 months due to such a fungal infection.

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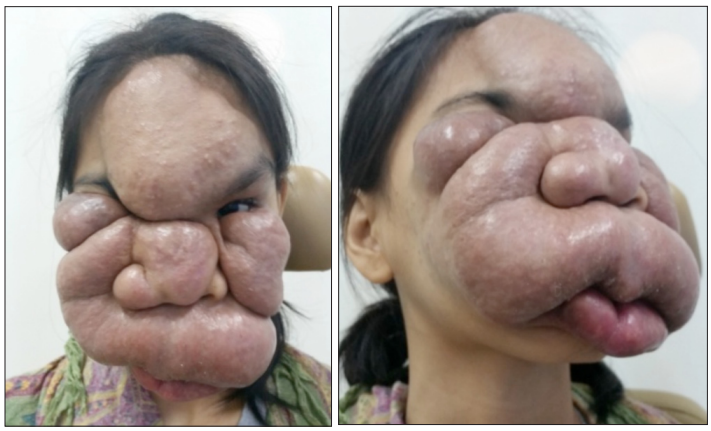
CASE REPORT

A 16-year-old girl consulted with a complaint of progressive facial swelling. *(Figure 1)* Her condition started 11 months prior to consult when she noticed a slow growing papule on her right nasal vestibule. It was firm, painless and did not bleed during manipulation. There were no associated signs and symptoms. Her past medical history was unremarkable.

After one month, she noticed progressive swelling of her right nasal cavity. Physical examination by an otorhinolaryngologist revealed an irregularly swollen right nasal vestibule and inferior turbinate. *(Figure 2)* Systemic examination was within normal limits. Contrast enhanced paranasal sinus CT scans revealed soft tissue swelling and congested right inferior turbinate. *(Figure 3)* Nasal endoscopy showed a rough nasal vestibule mass and congested right inferior turbinate. Punch biopsy of the right nasal mass only showed chronic inflammation. She was given unrecalled antibiotics for a week and intranasal steroid therapy for a month with no relief.

Seven months prior to consult, the swelling extended from the entire nasal area to the right cheek. Biopsy of the nasomaxillary swelling via gingivobuccal approach showed chronic inflammation with giant cell reaction and fibrosis. She was advised a repeat biopsy due to the inconclusive result, but refused and was lost to follow-up.

After a period of six months, she was admitted due to rapid increase in the facial swelling, now involving the entire nasal area, forehead, cheeks, upper and lower lip. It was associated with nasal congestion, foul smelling nasal discharge and epistaxis. Due to the severity of the facial swelling she had obstructed vision and epiphora in the right eye. Repeat CT scan showed marked involvement of bilateral maxillary soft tissues and the right nasal cavity. No bony lesions or erosions were



Anterior Antero-lateral

Figure 1. Anterior and antero-lateral views showing extensive facial swelling involving the entire nose, forehead, cheeks and lips. (Photos published in full, with permission)

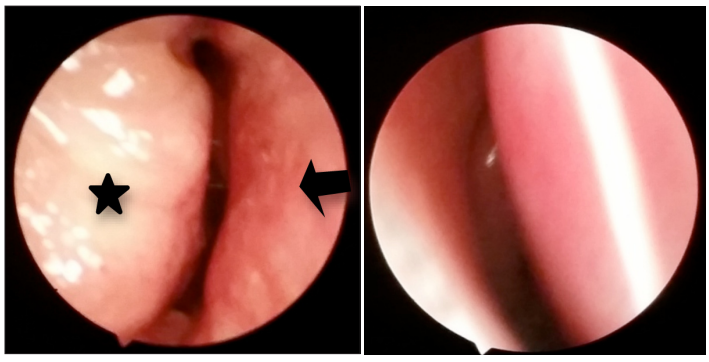


Figure 2. The right nasal cavity showed swollen inferior turbinate (star) and nasal septum (arrow). The mucosa is rough, irregular and granulomatous in appearance compared to the left nasal cavity with unremarkable findings.

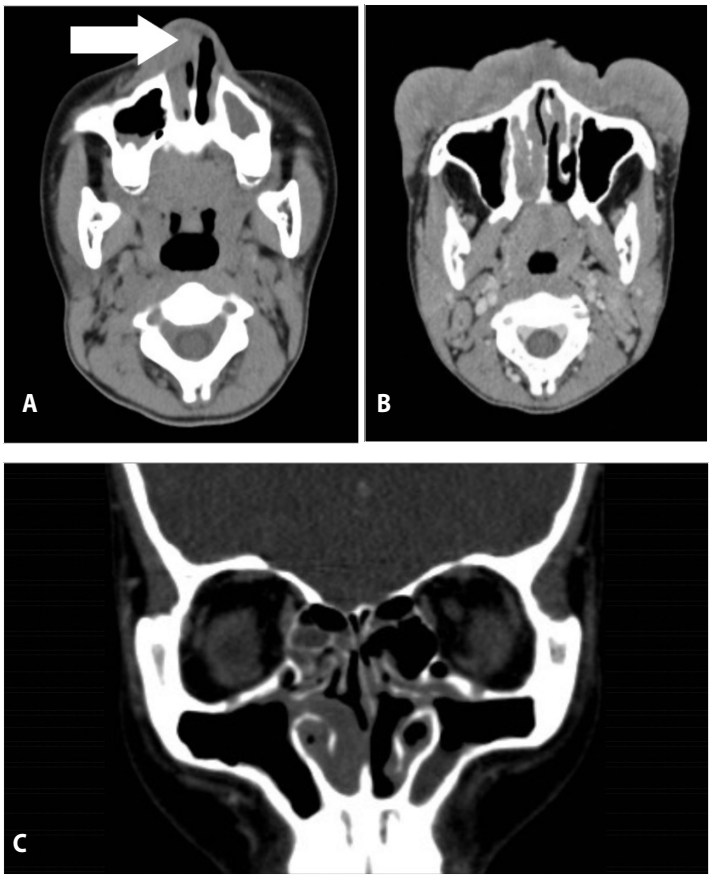
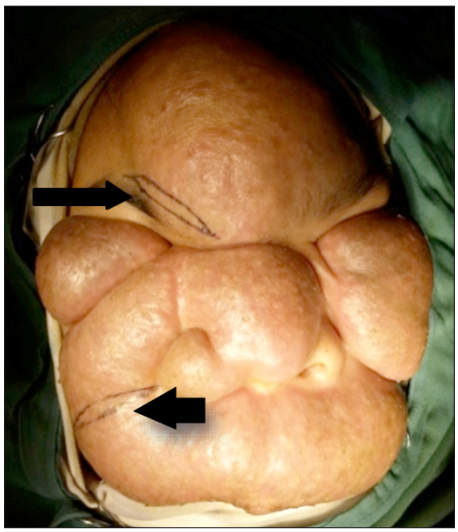


Figure 3. A. Paranasal sinus CT-scan with contrast in axial view (December 2013) showing a diffuse thickening of the soft tissue with heterogenous enhancement in the right nasal cavity (arrow). There is also a congested turbinate and bilateral maxillary sinusitis. **B.** Craniofacial CT scan with contrast (August 2014) showing a heterogeneously enhancing soft tissue thickening over the entire maxilla (white arrow) in axial view; and right inferior turbinate (white arrow) in **C.** coronal view; no bony lytic lesions were noted.

noted. *(Figure 3)* Repeat biopsy in two different sites, right glabellar and nasolabial area, both revealed eosinophilic granuloma. *(Figure 4)* Fungal culture on blood agar and bacterial cultures were also negative. Laboratory work-ups were unremarkable except for elevated eosinophil count. She was discharged with an impression of an inflammatory reaction and prescribed Cefuroxime 500mg capsule three times a day for 1 week, again without relief.

After one month due to the persistent facial swelling, a repeat biopsy from the contralateral side of the forehead was sent to another institution for additional immunostaining, bacterial and fungal studies. Tumor immunohistochemistry of CD1a and Langerin were negative for Langerhans cells while CD68 and CD163 stains were positive for histiocytes. Histochemistry revealed dermal mycosis with septate fungal hyphae using Grocott methenamine silver staining technique. *(Figure 5)* Considering the clinical features and histopathology report, a diagnosis of rhinofacial conidiobolomycosis was established.

She was treated with Itraconazole 100mg tablet three times a day for eight months with good response. The facial swelling showed marked improvement with significant reduction in extent and softening consistency of the swelling. *(Figure 6)*



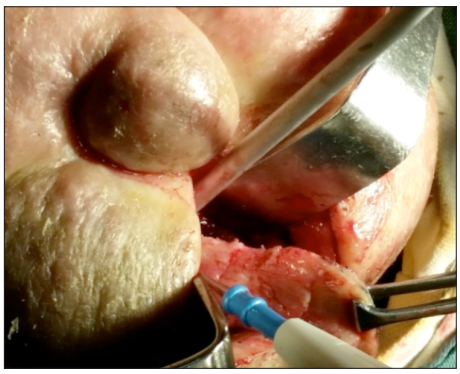
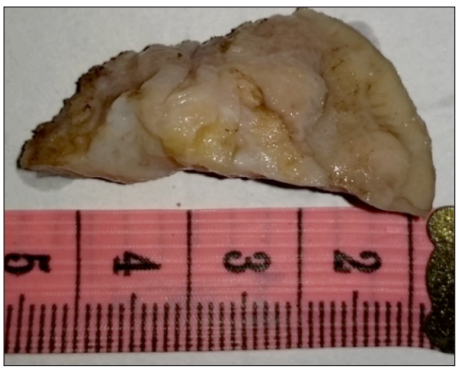
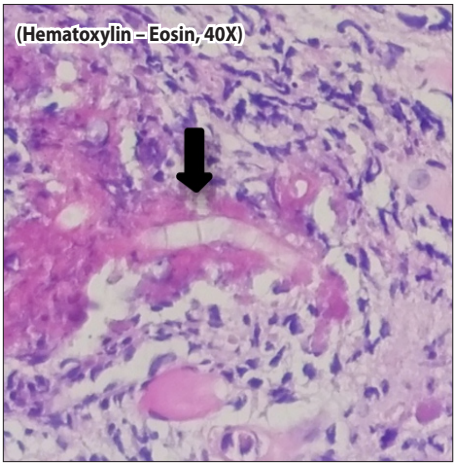


Figure 4. Incision biopsy from two different sites. (Top) glabellar (thin black arrow) and nasolabial area (thick black arrow). (Above) Actual nasolabial biopsy.





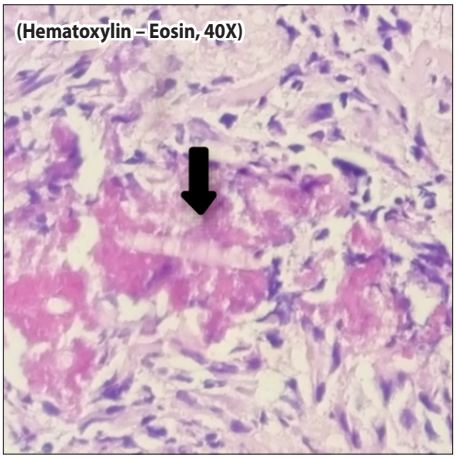


Figure 5. White to tan rubbery glabellar mass measuring 2x3x5cm. Histopathological sections of the glabellar mass (Hematoxylin & Eosin, 40x magnification) showing a mixed granuloma with numerous neutrophils. Note: Splendor-Hoeppli phenomenon characterized by the presence of thin walled septated hyphae (black arrow) characteristically enveloped by an eosinophilic sheath.

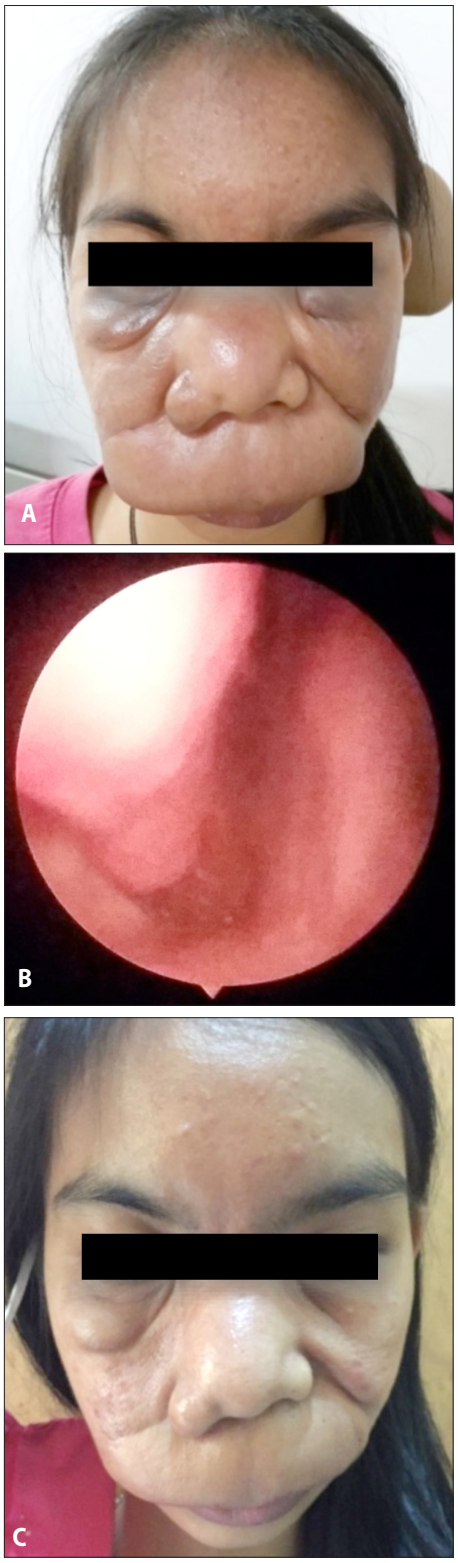


Figure 6. Clinical findings after 1 month of Itraconazole treatment. **A.** Reduction of facial swelling of the forehead, nose, cheeks and lips. **B.** Decreased swelling and smoothening of the inferior turbinate. **C.** Post-treatment for 8 months. The swelling has decreased and there is smoothening of the skin.

DISCUSSION

Rhinofacial conidiobolomycosis is a chronic, progressive, indolent fungal infection which involves granulomatous changes in the subcutaneous tissue.[1] These granulomatous changes eventually lead to a progressive swelling of the subdermal area. Rhinofacial conidiobolomycosis presents as a painless swelling over the midline of the face and usually affects middle-aged men in tropical countries like Africa and South-East Asia.[1] In this case, it occurred in a healthy young girl with no associated risk factors and an unremarkable past medical history. Compared to other types of fungal infections, conidiobolomycosis most commonly occurs as a chronic infection in otherwise healthy hosts.[2]

Rhinofacial conidiobolomycosis is caused by the saprophytic fungus *Conodiobolus coronatus or Conidiobolus incongruous,* under the class Zygomycetes, order *Entomophthorale*.[3] The causative fungus is thick-walled with short hyphae that grow at temperatures between 30^{O}C and 37^{O}C.[4] Although the causative agents were not successfully grown and isolated in this case, specific laboratory tests such as Grocott methenamine silver staining technique aided identification of the fungal pathogen with septate hyphae. The mode of transmission is nose-picking which causes traumatic inoculation of the nasal mucosa with contaminated dust or soil containing the spores.[5]

Two genera of zygomycetes exist, *Basidiobolus* and *Conidiobolus.* In *Conidiobolus* infection, the nasal mucosa below the inferior turbinate is commonly affected and appears as a uniform, progressive nasal swelling forming a midfacial deformity. In *Basidiobolus* infection, the limb and limb girdle are predominantly affected.[6] The initial presentation in the patient was nasal swelling limited to the nasal cavity, specifically the vestibule and inferior turbinate. Eventually the swelling progressed and it involved the entire nasal dorsum, cheeks, forehead and lips leading to a severe facial deformity.

The most common presentation of RFC is characterized by chronic, indolent and localized swelling of the nose, paranasal sinuses, cheeks, and upper lips.[7] Clinically, the extent of involvement can be divided into three phases. In phase I, involvement is limited to the nasal cavity, paranasal sinuses, and pharynx. In phase II, infection extends to the surrounding subcutaneous tissues causing facial swelling with involvement of the lips. In phase III, the muscles, bones, and viscera are affected.[3] Due to failure of early identification of the causative agent and inadequate follow-up with her physician, the infection eventually progressed to phase II involving her entire face.

The diagnosis of RFC is both clinical and histopathological. A history of nose-picking and physical findings of midfacial swelling should trigger a high index of suspicion. Histological examinations are

essential for confirmation of the diagnosis. *Conidiobolus coronatus* may grow on Sabouraud's dextrose agar but this medium was not utilized for the initial biopsy specimens. Having said that, fungal cultures may be negative in more than 85% of cases.[3] Condiobolomycosis infection is characterized histopathologically by the presence of septate hyphae surrounded by an eosinophilic halo, the so-called Splendore-Hoeppli phenomenon.[8] *(Figure 5)*

In this case, adding to the difficulty in establishing such diagnosis were the initial histopathological results of chronic inflammatory granulomatous cellular infiltrates composed of lymphocytes, epithelioid cells, giant cells, histiocytes and rich eosinophils which can be seen in various disease entities. The identification of the Splendore-Hoeppli phenomenon together with the clinical presentation of midfacial swelling established RFC as the diagnosis. Rhinofacial conidiobolomycosis should be included in the differential diagnoses of healthy patients who present with nasal symptoms and painless midfacial swelling.[11]

The treatment of RFC has not been well established because the disease is infrequently reported and studied. Although a number of antifungals have been used and reported as effective, there is still lack of evidence to determine the antifungal of choice, its dosage and duration.[3] Daily high-dose antifungal therapy and months of continuous treatment are required for successful management, and this may sometimes be difficult due to poor compliance resulting from adverse effects and drug cost.[9] Our patient was treated with Itraconazole 100mg three times a day for a period of eight months. Besides its excellent antifungal activity, Itraconazole also has anti-tumorigenic effects, inhibits angiogenesis, and plays a role in controlling inflammation and swelling in fungal infection.[10] We noted good response to therapy as shown by a progressive decrease in facial swelling and smoothening of the skin. *(Figure 6)*

Rhinofacial conidiobolomycosis is an endemic condition in Asia but may be under reported due to lack of clinical suspicion and mycological facilities in hospitals. A number of RFC cases have been reported and publications are limited to case reports. To the best of our knowledge, this case is the 62nd reported in Asia and the first in the Philippines based on a 2015 case report and literature review of Conidiobolomycosis in Asia.[12] We found no previous local reports in a search of The Cochrane Library, Wiley Online Library, HERDIN, Philippine E-Journals, Philippine Journals Online, and Google Scholar, using the keywords *rhinofacial swelling, Conidiobolomycosis,* and *Philippines*.

In summary, rhinofacial conidiobolomycosis is a rare chronic localized fungal infection that usually affects midline facial structures in immunocompetent hosts. Early detection and diagnosis, and appropriate medication can give rapid resolution. To the best of our knowledge, this may be the first documented case of rhinofacial conidiobolomycosis in the Philippines.

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