Primary cutaneous facial phaeohyphomycosis due to *Verruconus gallopava* (*Ochroconus gallopava*) in an immunocompetent woman from the Sub-Himalayas – a case report and literature review

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Abstract

*Verruconus gallopava* is a melanised environmental saprophyte. Human infections of respiratory and central nervous systems occur primarily in immunocompromised subjects. Skin and subcutaneous infections are seen when disease involves multiple sites. Primary cutaneous phaeohyphomycosis is exceptional. We report a case of an immunocompetent female who had facial phaeohyphomycosis with *V. gallopava* following trauma. Lesions progressed despite antibiotic therapy. Diagnosis was established on fungal culture and she showed some favourable response to itraconazole 200 mg with terbinafine 250 mg at her second visit but was lost to follow up. No single therapeutic regimen is consistently efficacious in *V. gallopava* infections. Early laboratory confirmation is imperative to achieve success as outcome is variable even with combination of antifungal agents and surgery.

Keywords: *Verruconus gallopava*, phaeohyphomycosis, itraconazole.

Introduction

*Verruconus gallopava*, a dematiaceous fungus is an environmental saprophyte and rarely pathogenic. Organ transplant, haematological malignancies and advanced HIV infection constitute the risk factors [1-3]. Pulmonary or cerebral infections occur frequently and cutaneous and subcutaneous disease is seldom encountered [3-6]. Diagnosis may be missed due to lack of clinical suspicion. Response to systemic antifungal therapy with itraconazole (ITR), voriconazole (VOR) and amphotericin B (AMB) is unpredictable in advanced disease. We report primary cutaneous facial phaeohyphomycosis due
to *V. gallopava* showing initial response to oral ITR.

**Case Report**

A 50 years old Nepalese woman injured her right cheek with a wooden splinter following which a non-healing painful, red lesion appeared. She visited a peripheral health institution where empirical amoxicillin with clavulanic acid 625 mg T.I.D with topical antibiotics were prescribed. Dermatological consultation was taken as there was negligible response after two weeks of therapy. We saw the lady with a well to ill defined erythematous, crusted, indurated, tender plaque of 2.5X3.5 cm size over a diffuse swelling of right cheek [Fig. 1].

![Figure 1](image1.png)

**Figure 1** Erythematous, crusted, indurated, plaque of 2.5X3.5 cm size over a diffuse swelling of right cheek

Rest of skin, hair and nails were healthy. General physical examination was non-contributory, vitals were within normal range and there were no systemic features. Laboratory investigations revealed absence of diabetes, HIV infection, tuberculosis or malignancies. Considering phaeohyphomycosis provisionally, skin biopsy was subjected to histopathology which revealed a granulomatous lesion. Direct microscopy of sample revealed sparse septate hyphae.

Fungal culture on SDA with chloramphenicol grew olivaceous mould at 25°C which had a characteristic surrounding reddish brown diffusible pigment [Fig. 2].

![Figure 2](image2.png)

**Figure 2** Dark olivaceous velvety growth with surrounding reddish pigment characteristic of *Verruconus gallopava* seen on Sabouraud’s dextrose agar

Micro-slide culture showed pigmented, septate hyphae with conidigenous cells bearing characteristic brown ovoid to clavate conidia on cylindrical denticles, grouped in two and constricted at the central septum consistent with *V. gallopava* [Fig. 3].

![Figure 3](image3.png)

**Figure 3** Pigmented, septate hyphae with conidigenous cells bearing clavate conidia of *Verruconus gallopava* on cylindrical denticles constricted at the central septum (cotton blue staining, 100X).

A repeat biopsy was cultured and patient was instituted itraconazole 100mg B.D. The lesion showed minimal regression after one month therefore terbinafine 250 mg daily was added. On the next review, there was good response.
Meanwhile the fungal culture of the second biopsy also showed growth of *V. gallopava*. The identity of the isolate was confirmed at the National Culture Collection of Pathogenic Fungi (NCCPF), PGIMER, Chandigarh, as *V. gallopava* (accession number 380006). The final outcome could not be documented as patient was lost to follow up.

**Table:** Cases of *Verruconus gallopava* infection reported in literature

| No. | Year/Ref | Sex | Age | Site involved | Predisposition | Therapy | Outcome |
|-----|----------|-----|-----|---------------|----------------|---------|---------|
| 1   | Dixon et al, 1986, USA [25] | ND | ND | Lung | ND | ND | ND |
| 2   | Fukushima et al, 1986, Japan [2] | F | 58 | Subcutaneous abscess | AML | 5-FC | Survived |
| 3   | Ferrani et al, 1990, USA [15] | M | 62 | Lungs, liver, kidney, brain | CLL | None | Died |
| 4   | Sides et al, 1991, ND [13] | M | ND | Lung | IC | ND | ND |
| 5   | Sides et al, 1991, South Africa [13] | ND | ND | Lung | Coal mine worker | ND | ND |
| 6   | Sides et al, 1991, South Africa [13] | ND | ND | Lung | Coal mine worker | ND | ND |
| 7   | Sides et al, 1991, USA [13] | ND | ND | Lung | IC | ND | ND |
| 8   | Sides et al, 1991, USA [13] | ND | ND | Brain | IC | ND | ND |
| 9   | Sides et al, 1991, USA [13] | M | 47 | Lung | Cardiovascular disease | ND | ND |
| 10  | Sides et al, 1991, USA [13] | M | 60 | Brain | Lymphoma, nocardiosis | Craniotomy, AMB, 5-FC, fluconazole | Died |
| 11  | Mancini et al, 1992, USA [26] | M | 30 | Pulmonary nodule | SOT (heart) | AMB | Survived |
| 12  | Smith et al, 1993, ND [27] | M | 46 | Cerebral abscess | SOT (heart) | None | Died |
| 13  | Vukmir et al, 1994, USA [28] | M | 68 | Cerebral abscess | SOT (liver) | AMB, 5FC, ITR | Survived |
| 14  | Kralovic et al, 1995, USA [29] | M | 63 | Lung, brain, disseminated | SOT (liver) | AMB, ITR, surgery | Died |
| 15  | Rossmann et al, 1996, USA [30] | M | 59 | Brain | SOT (liver) | AMB | Died |
| 16  | Bonham et al, 1996, USA [31] | ND | ND | Brain | SOT (liver) | ND | Survived |
| 17  | Jenney et al, 1998, Australia [32] | M | 58 | Pulmonary nodule | SOT (heart), diabetes | AMB, ITR | Survived |
| 18  | Horre et al, 1999, UK [12] | ND | ND | Systemic | AIDS | ND | ND |
| 19  | Horre et al, 1999, Australia [12] | ND | ND | Systemic | ND | ND | ND |
| 20  | Horre et al, 1999, USA [12] | ND | ND | Brain | Diabetes mellitus | ND | ND |
| 21  | Horre et al, 1999, ND [12] | M | 48 | Lung | SOT, HIV positive | ND | ND |
| 22  | Horre et al, 1999, Australia [12] | ND | ND | Lung | ND | ND | ND |
| 23  | Horre et al, 1999, USA [12] | ND | ND | Lung | SOT | ND | ND |
| 24  | Burns et al, 2000, Canada [21] | F | 58 | Lung, skin | SOT (lung) | AMB, ITR | Survived |
| 25  | Odell et al, 2000, USA [7] | M | 38 | Multiple lung abscess | Wood pulp worker | Surgery (lobection), ITR | Survived |
| 26  | Bowyer et al, 2000, UK [17] | M | 69 | Eye (endophthalmitis) | CLL | AMB intravitreal, ITC, fluconazole | Died |
| 27  | Mazur et al, 2001, USA [33] | F | 32 | Lung, shoulder abscess, brain abscess | SOT (lung), diabetes | AMB, SFC, ITR, surgery | Survived |
| 28  | Malani et al, 2001, USA [5] | M | 32 | Lung, brain, thyroid | SOT (kidney), diabetes | AMB, ITR, FCZ | Died |
| 29  | Zhao et al, 2002, China [18] | M | 68 | Lung | Pemphigus | AMB, ITR | Survived |
| 30  | Wang et al, 2003, China [4] | M | 13 | Disseminated, brain, lung, spleen | SOT (kidney) | AMB, ITR, VOR | Died |
| 31  | Bravo et al, 2004, USA [23] | M | 72 | Lung | Alcohol abuse, MAC infection lung | ITR | Survived |
| 32  | Fukushima et al, 2005, Japan [16] | F | 66 | Brain, lung, femoral mass | CLL | AMB, 5-FC, ITR, Itrbina-fine | Died |
| 33  | Ohori et al, 2006, USA [19] | M | 54 | Systemic | SOT (heart) | ND | Died |
Discussion

Phaeohyphomycosis encompasses infections due to melanised fungi and *Verruconus gallopava* is rarely encountered. The nomenclature of *Verruconus gallopava* has evolved from *Diplorhinotrichum gallopavum, Dactylaria gallopava* to the genus *Scolecobasidium* [7]. In 1983, de Hoog classified it under *Ochroconus* and recently it is christened as *Verruconus gallopava* [7-9]. It is an environmental fungus occurring in soil, decaying vegetation and hot springs [7,10]. It has caused epidemic encephalitis in birds [11]. Only 59 human infections are scripted in world literature primarily from the USA, Australia, China, Canada, Japan, New Zealand and India [Table 1]. In the review of the demographic profile of 46 cases, male to female ratio was 3.2:1. Majority, 73.3% (33/45) acquired infection in their fifties and no case was reported in children below ten years [Table 1]. Poverty of immunity

| Case | Gender | Age | Site | Disease | Treatment | Outcome |
|------|--------|-----|------|---------|-----------|---------|
| 34   | M      | 79  | Lung | Pneumoconiosis | ND | ND |
| 35   | M      | 68  | Lung | ND | ND | ND |
| 36   | ND     | ND  | Lung | ND | ND | ND |
| 37   | M      | 83  | Lung | ND | ND | ND |
| 38   | M      | 28  | Lung, brain, hip, joint | Advanced HIV | VOR, caspofungin | died |
| 39   | F      | 79  | Lung | I/C (previous basal cell carcinoma and surgically cured melanoma) | VOR | survived |
| 40   | F      | 64  | Lung | SOT(kidney) | AMB, VOR, fluconazole | survived |
| 41   | M      | 60  | Lung | SOT (kidney) | ITR | survived |
| 42   | M      | 50  | Lung | SOT (liver) | VOR | survived |
| 43   | ND     | ND  | Lung | SOT (kidney) | ND | ND |
| 44   | M      | 58  | Peritoneum | SOT(heart) | VOR | survived |
| 45   | M      | 53  | Lung, spine | SOT(kidney) | AMB, VOR | died |
| 46   | M      | 54  | Lungs | SOT(B/L lungs) | AMB, VOR | survived |
| 47   | M      | 66  | Lung | SOT(lung) | VOR | survived |
| 48   | F      | 57  | Lung | SOT (lung) | VOR | survived |
| 49   | F      | 60  | Lung | SOT(heart) | ITR | survived |
| 50   | M      | 57  | Lung | SOT(B/L lungs) | Lobectomy, ITR | died |
| 51   | M      | 58  | Lung | SOT (lung) | AMB, ITR | survived |
| 52   | M      | 67  | Brain | SOT (liver) | AMB, ITR | died |
| 53   | M      | 69  | Brain | SOT (liver) | AMB, ITR | survived |
| 54   | M      | 53  | Lung, spine, abscesses | SOT (kidney) | Surgical drainage, AMB, VOR | survived |
| 55   | M      | 55  | ND | SOT (lung) | ITR | survived |
| 56   | M      | 34  | Lung | Chronic granulomatous disease, on therapy - AMB, 5-FC, Interferon for Aspergillosis | ITR, VOR pneumonectomy, po saconazole | survived |
| 57   | M      | 55  | Lung, subcutaneous, brain, peritoneum | SOT(heart), diabetes | VOR | died |
| 58   | M      | 55  | Skin, hyperkeratotic plaques | I/C, Gardner | ITR, terbinafine | died |
| 59   | F      | 30  | Allergic fungal rhinosinusitis | I/C, agricultural worker | Surgery, steroids and topical antibiotics | survived |
| 60   | F      | 50  | Facial skin | Manual labourer | ITR, terbinafine | died |

Footnote: F female; M male; AML acute myeloid leukaemia; CLL chronic lymphatic leukaemia; I/C Immuno competent; B/L bilateral; 5-FC 5 fluorocytocine; SOT solid organ transplant; AIDS acquired immunodeficiency syndrome; ITR itraconazole; VOR voriconazole; AMB amphotericin B; ND not determined.
was predisposing factor in 80% cases. Solid organ transplant was reported as risk factor in 52.5% cases and other conditions included diabetes, HIV/AIDS, lymphoma and haematological malignancy. Cardiovascular accident, pemphigus, pneumoconiosis, chronic granulomatous disease and steroid therapy were antecedent in few cases.

*V. gallopava* is a pneumotrophic and neurotropic fungus. The inhaled fungal spores establish granulomatous reaction in the respiratory tract. Early asymptomatic infection followed by cavitary or non-cavitary lesions and abscesses develop in lungs and if suspected and detected then is amenable to treatment associated with a good clinical response. Literature reveals 50% cases having only pulmonary involvement [Table 1]. More often respiratory infection remains unabated and *Verruconus* sp. spreads to the central nervous system due to its neurotropism causing cerebral infection or abscess. Joint, kidney, thyroid, spine and liver are affected in cases when multiple system involvement is present.

Secondary cutaneous and subcutaneous lesions have been described in subjects having *Verruconus* sp. infection of lung or brain with leukaemia, solid organ transplant and diabetes. Primary cutaneous phaeohyphomycosis is rare, recognised in one Immunocompetent case. The present case is second in this regard having localized primary cutaneous lesion following trauma and repeat isolation of *Verruconus gallopava* confirmed at NCCPF, PGIMER, Chandigarh established diagnosis. Systemic fungal invasion by *V. gallopava* accounts for high mortality of 46-80%.

A variety of treatment regimens have been tried based on clinical experiences but optimal therapy remains ambiguous. The antifungal prescriptions employed frequently include ITR, AMB and VOR. ITR is consistently potent and flucytosine reasonably effective especially when toxicity of AMB is a concern. VOR is a useful alternative with potent antifungal activity and broad spectrum against black fungi. It has an advantage of maintenance of therapeutic serum levels and effective concentration in the CSF and tissue. AMB is advocated in life-threatening phaeohyphomycosis when benefits are weighed against toxicity.

Experience of treating cutaneous phaeohyphomycosis due to *Verruconus* is inconstant. Patients with secondary cutaneous or subcutaneous affliction along with involvement of other body sites treated with 5-FC, AMB and ITR recovered whereas a patient given VOR succumbed to infection. The only reported case of primary skin condition was managed on oral terbinafine 250 mg daily, ITR 200 mg twice daily for four months followed by parenteral AMB. The outcome was not encouraging as initial healing process was interrupted probably due to secondary systemic spread of fungal infection and septicemic shock. It is difficult to comment on final outcome of the present case as was lost to follow up. Year wise distribution of *Verruconus gallopava* cases reported in literature showing age, sex, site involvement, predisposing factors, therapy and outcome shown in table 1.
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