Successful medical treatment of an *Aspergillus terreus* mycetoma of the nostril/lip in a 16-year-old Fjord pony gelding with pituitary pars intermedia dysfunction

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**Background** – Mycetoma is a chronic, proliferative lesion of cutaneous/subcutaneous tissue characterized by draining tracts and granules in the discharge caused by actinomycetes (actinomycetoma) or filamentous fungi (eumycotic mycetoma).

**Objectives** – This case report describes the unusual finding of a cutaneous mycetoma of the lateral wing of the right nostril in a gelding.

**Animal** – A 16-year-old Fjord gelding with suspected pituitary pars intermedia dysfunction (PPID) was presented for evaluation of a nonpainful, firm and raised mass involving the lateral wing of the right nostril and the lip.

**Methods and Results** – Cytological examination of the mass showed marked pyogranulomatous inflammation and histopathological examination revealed a fungal mycetoma. Fungal culture identified the causative organism as *Aspergillus terreus*, which is not known for its propensity to cause either dermal granulomas or mycetoma in domestic animals. Further investigation, including a TRH stimulation test, led to a diagnosis of PPID (Cushing’s disease), which may have led to immunosuppression of the animal and increased susceptibility to infection.

**Conclusions and Clinical importance** – The horse was treated medically with pergolide for the PPID and oral potassium iodide for the fungal infection, with good therapeutic response and no relapse after five months. Surgical debridement or excision was not performed. To the best of the authors’ knowledge, this is the first case report of a cutaneous mycetoma caused by *A. terreus* in a horse.

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**Introduction**

Mycetoma is a chronic, proliferative lesion of cutaneous/subcutaneous tissue characterized by draining tracts and granules in the discharge caused by actinomycetes (actinomycetoma) or filamentous fungi (eumycotic mycetoma). Lesions typically begin at sites of minor trauma and spread locally. The clinical manifestations vary, but lesions are usually localized and contain suppurative granulomas. The exudate usually contains granules, which vary in appearance depending on the causative agent.1 Although most reports advise surgical excision as the best option for treatment of eumycotic mycetomas, a recurrence rate of 80% is reported in humans after surgical excision alone.2,3

**Case report**

A 16-year-old Fjord gelding was presented for treatment of a mass on the right upper lip, first noticed 12 months previously, which increased significantly in size over the few months prior to presentation. Before admission, the horse received 10 days of oral trimethoprim sulfonamide therapy. Following this treatment, the mass diminished in size temporarily, then markedly increased with invasion into the lateral wing of the right nostril. No other clinical abnormalities were reported by the referring veterinarian.

On presentation, the pony was overweight, with a body score of six of nine and mild hirsutism. There was moderate hypertrophy of the right mandibular lymph node. The respiratory rate was 12 breaths per minute with no abnormalities on auscultation, but a mild inspiratory snoring noise localized to the right nostril. The mass on the right upper lip and lateral wing of the nostril measured 8 cm and was firm, raised and nonpainful (Figure 1). No overlying skin lesions or alopecia were present and no mucosal lesions were visible within the nostril. The four hooves showed mild circumferential grooves.

Differential diagnoses for the mass included neoplastic conditions and non-neoplastic nodular lesions (i.e. bacterial/fungal/parasitic granuloma, eosinophilic granuloma, cutaneous amyloidosis, haematoma, dermoid nasal cyst, idiopathic sterile granuloma or pyogranuloma).3 The major differential diagnosis for the hirsutism and overconditioning was pituitary pars intermedia dysfunction (PPID).
Haematological examination was within normal limits. Serum biochemistry revealed mild hyperglobulinaemia (41 g/L, reference range (RR) 29-30 g/L). Serum amyloid A (SAA) and fibrinogen levels were within reference ranges [SAA 1 mg/L (RR< 20 mg/L), fibrinogen 1 g/L (RR< 2 g/L)]. Endoscopy of the upper respiratory tract revealed deformation of the lateral nasal mucosa 5 cm from the nostril with a slight mucoid discharge (Figure 2). Ultrasound showed a moderately well-demarcated, poorly encapsulated, locally extensive mass within the cutaneous and subcutaneous tissue with a heterogeneous appearance (Figure 3). No fluid pockets and no foreign body could be visualized.

Deep biopsies were performed with sedation and local anaesthetic, and submitted for histopathological examination and fungal culture. Histopathological results showed normal epidermis with pilosebaceous follicles and large amorphous aggregates composed of tight clusters of large, bulbous, thick-walled, colourless (hyaline) fungal elements in the deep dermis. These were intermingled with numerous neutrophils, histiocytes, macrophages, lymphocytes and plasma cells. Organisms were strongly positive staining with periodic acid Schiff stain (Figure 4). Bacterial culture was not performed; fungal culture was positive after 6 days on enriched medium, revealing a pure culture. The macroscopic features of the colonies were fluffy and cinnamon brown. Microscopically, the observation of accessory conidia and long conidiophores finished by spherical, biseriate vesicles enabled the identification of *Aspergillus terreus*.

The basal ACTH level was elevated at 51.9 pg/mL (RR< 35 pg/mL for autumn/winter interval). After TRH stimulation ACTH was 100 pg/mL (RR< 90 pg/mL), which was suggestive of PPID. The ACTH response curve to TRH stimulation in February in the Northern Hemisphere is generally lower than other months, but a peak of 100 pg/mL at 10 min was shown to be 100% sensitive and specific for PPID.4

Figure 1. Pony with mycetoma lesion (arrows) on the right upper lip before treatment.

Figure 2. Pony with mycetoma; endoscopy image of the right ventral nasal meatus with the mass (arrows) distorting the lateral mucosal surface.

Figure 3. Pony with mycetoma; ultrasound image showing a moderately well-demarcated, poorly encapsulated, locally extensive mass within the cutaneous and subcutaneous tissue of the right nostril with heterogeneous appearance.

Figure 4. Pony with mycetoma; photomicrograph of mucosal biopsy showing large, amorphous fungal aggregate (arrows) composed of tight clusters of large, clear, bulbous fungal elements (grain or granule) (periodic acid Schiff stain, x400).

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Due to the location and size of the lesion and the infiltrative aspect, surgical excision was ruled out. Specific antifungal therapy such as fluconazole/voriconazole, which are good options for systemic treatment due to excellent bioavailability after oral administration, were declined by the owner due to cost. The pony was given medical therapy with potassium iodide (KI) 30 mg/kg orally once daily (loducre de Potassium, LDC Laboratories; Paris, France). This treatment is usually used for mycetoma due to Sporothrix spp., Conidiobolus spp., Basidiobolus spp., Pseudallescheria spp., and Phialophora spp. The pony also received pergolide mesylate 1 mg orally once daily (Prascend, Boehringer Ingelheim; Paris, France) to treat the PPID, and the owners were advised to continue lifelong treatment. The mass had resolved when the pony was examined after 4 weeks of treatment with KI; the treatment was continued for an additional 2 weeks. Five months after treatment, no recurrence had occurred. No other clinical changes had occurred, apart from a mild improvement in hirsutism at 2 weeks. 

Discussion

Mycetomas are rare, chronic pyogranulomatous infections of the skin and subcutaneous tissues wherein the organism is present in tissues as granules/grains, and are caused by actinomycetes (actinomyctoma) or fungi (eumycotic mycetoma). Typically, lesions are characterized by tumefaction, draining tracts and grains in the discharge. Draining tracts are sometimes absent. Usually, they are long-lasting lesions, persisting from several weeks to one and a half years. The lesions are usually only successfully managed with a combination of surgical debridement or excision, followed by aggressive medical therapy. In this case, medical therapy alone was sufficient to give long-term remission of the lesion. The antifungal therapy was combined with pergolide treatment to reduce the immunosuppressive effect of the PPID, which was likely one of the primary reasons for the formation of this unusual mycetoma lesion in this pony.

The most common agents of eumycotic mycetoma in horses belong to the Scedosporium/Pseudallescheria complex and Madurella genera (i.e. Madurella mycetomatis); however, Curvularia verruculosa, Phialophora oxyspora, and Aspergillus spp. have also been occasionally detected. Aspergillus species do not generally cause mycetomas in humans or animals. Infections caused by Aspergillus species are more commonly seen in the respiratory tract of immunocompromised individuals or in those on prolonged antibiotic therapy. Although Aspergillus species are mentioned as possible causal organisms of mycetoma lesions, only one well-documented case of Aspergillus (A. versicolor) infection of the skin of horses has been reported. To the best of our knowledge, this is the first case report of a cutaneous mycetoma caused by Aspergillus terreus in a horse.

Aspergillus terreus is a saprophytic, ubiquitous fungus found in dust, forage and wood. Members of this species are diverse in their colonial morphology, and can grow as bright orange colonies or colonies that appear as various shades of cinnamon brown, with colony appearance ranging from velvety, heavily sporulating colonies to fluffy, poorly sporulating phenotypes. Aspergillus terreus is an emerging opportunistic fungus whose clinical incidence has increased in recent years. Definitive diagnosis is best achieved by skin biopsy and special stains to identify fungi, but culture is required for species differentiation.

Different treatment modalities have been advocated for fungal granulomas, such as immunotherapy, antifungal chemotherapy and surgery. In many cases, a combination of surgical excision and specific antifungal therapy is warranted. Specific antifungal treatment was considered, but was not implemented due to financial constraints. It is possible that surgical debridement with specific antifungal therapy may have led to a faster resolution of the lesion. The pony received initially 4 weeks oral KI treatment, which resolved the lesion without any adverse effects (ephipora, cough, dry seborrheic skin coat).

Atypical infections commonly occur with PPID due to immunosuppression and this may have been a contributing factor to the development of mycetoma in this horse. The concurrent treatment with pergolide mesylate to control the PPID and limit the immunosuppressive effects of the disease may have contributed to the success of the conservative treatment method used.

References

Resumen

Contexto – Le miyctomo es una lesión cutánea/subcutánea proliferativa y chronique caracterizada por drenajes y gránulos en el exudado causado por actinomicetos (actinomycetoma) o hongos filamentosos (micetoma eumycotico).

Objetivos – Este artículo describe un caso poco habitual de un micetoma cutáneo en el ala lateral de la fosa nasal derecha en un caballo macho castrado.

Animal – Se presentó un caballo macho castrado de 16 años de raza del Fjord con sospecha de disfunción de la pars intermedia de la pituitaria (PPID) para la evaluación de una masa no dolorosa, firme y elevada que afectaba el ala lateral de la fosa nasal derecha y el labio.

Métodos y resultados – El examen citológico de la masa mostró marcada inflamación piogranulomatosa y el examen histopatológico reveló un micetoma fungico. El cultivo fungico identificó el organismo causal como Aspergillus terreus, que no es conocido por ser propenso a causar granulomas dérmicos o micetomas en animales domésticos. Investigaciones adicionales, incluyendo una prueba de estimulación con TRH, llevaron a un diagnóstico de PPID (enfermedad de Cushing), que podría haber causado inmunosupresión del animal y una susceptibilidad aumentada a la infección.

Conclusiones e importancia clínica – El caballo fue tratado con éxito con pergolida para la PPID y yoduro de potasio oral, con buena respuesta terapéutica y sin recaídas después de cinco meses. No se realizó debridamiento quirúrgico o excisión. A nuestro entender basado en evaluación de la literatura, este es el primer caso de un micetoma cutáneo causado por A. terreus en un caballo.

Zusammenfassung

Hintergrund – Das Mycetom ist eine chronische, proliferative Veränderung von kutanem/subkutanem Gewebe, welches durch Fistelgänge und Granula im Ausfluss, die durch Actinomyceten (Actinomycetoma) oder filamente Pilze (eumykotisches Mycetom) verursacht werden, charakterisiert ist.

Ziele – Dieser Fallbericht beschreibt den ungewöhnlichen Befund eines kutanen Mycetoms am rechten lateralen Nasenflügel eines Wallachs.

Tier – Ein 16 Jahre alter Fjordwallach mit Verdacht auf eine Dysfunktion der Pars intermedia der Hypophyse (PPID) wurde zur Untersuchung einer nicht schmerzhaften, derbe und erhabenen Masse, die den lateralen Nasenflügel und die Lippe betraf, vorgestellt.


**要約**

背景 – 真菌症は、放線菌(放線菌腫)または糸状真菌(真菌性腫瘍)によって引き起こされる細管および肉芽腫を特徴とする皮膚/皮下組織の慢性の増殖性病変である。

目的 – 本症例報告では、フィヨルド・ホースの去勢馬の右鼻孔の外側翼に認められた非一般的な皮膚腫瘍の所見を記述する。

供試動物 – 不動の中心間の機能障害(PPID)が疑われた16歳のフィヨルド・ホースの去勢馬が、右鼻孔の外側翼と口唇を巻き込む、痛みを伴わない、固く隆起した腫瘍の評価のために来院した。

方法と結果 – 腫瘍の細胞診検査では顕著な化膿性肉芽腫性の炎症が認められ、病理組織学的検査で真菌性腫瘍が明らかになった。真菌の培養検査によって、原因菌は*Aspergillus terreus*と同定された。*Aspergillus terreus*が家畜の真皮に肉芽腫や腫瘍を引き起こすことはこれまで報告されていない。TRH刺激試験を含む更なる検査により、PPID(クッシング病)が診断され、これがこの病態の免疫抑制および易感性傾向をもたらした可能性がある。

結論および臨床的意義 – 本症例の症例報告は、通常の治療法として小切開や放射線療法が行われなかった。著者らの知る限りでは、これは*A. terreus*によって引き起こされた馬の皮膚の真菌性腫瘍の最初の症例報告である。

**Resumo**

Contexto – O micetoma é uma lesão cutânea/subcutânea crônica, prolífера e caracterizada por tratos fistulosos com secreção contendo grânulos, causados por actinomicetos (actinomicetoma) ou fungos filamentosos (micetoma eumicótico).

Objetivos – Este relato de caso descreve um achado raro de um micetoma cutâneo na face lateral da narina direita de um cavalo.

Animal – Um equino macho castrado, da raça Fjord com suspeita de disfunção pituitária da pars intermedia (PPID) foi apresentado para avaliação de uma massa firme, elevada e não dolorosa envolvendo a face lateral da narina direita.

Métodos e resultados – Exame citológico da massa revelou inflamação piogranulomatosa e a histopatologia revelou um micetoma fúngico. A cultura fúngica identificou *Aspergillus terreus* como o agente causador. Este não é conhecido pela sua probabilidade de causar granulomas dérmicos ou micetomas em animais domésticos. Investigação posterior, incluindo teste de estimulação por TRH, levou ao diagnóstico de PPID (síndrome de Cushing), que pode ter causado imuonoospressão no animal, aumentando a sua suscetibilidade à infecção.

Conclusões e importância clínica – O cavalo foi tratado com pergolida para para a PPID e iodeto de potássio por via oral, com boa resposta terapêutica e sem recidiva após cinco meses. Debridamento cirúrgico e excisão não foram realizados. De acordo com o conhecimento dos autores, este é o primeiro relato de caso de micetoma cutâneo em equinos causado por *A. terreus*.