

## 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.

### 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.<sup>1</sup> 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.<sup>2,3</sup>

### 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).<sup>3</sup> The major differential diagnosis for the hirsutism and overconditioning was pituitary pars intermedia dysfunction (PPID).

**Abbreviations:** KI, potassium iodide; PPID, pituitary pars intermedia dysfunction; SAA, Serum amyloid A.

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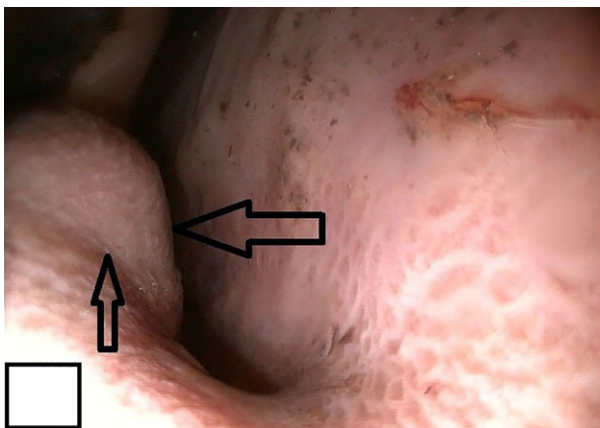
**Conflicts of interest:** No conflicts of interest have been declared.



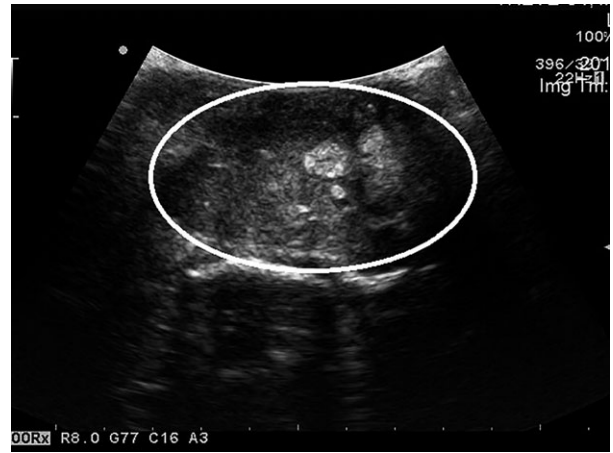
**Figure 1.** Pony with mycetoma lesion (arrows) on the right upper lip before treatment.

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



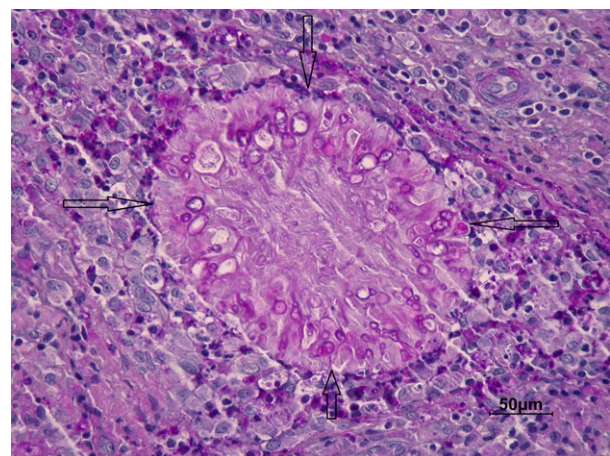
**Figure 2.** Pony with mycetoma; endoscopy image of the right ventral nasal meatus with the mass (arrows) distorting the lateral mucosal surface.



**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.

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, biserial 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.<sup>4</sup>



**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).

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,<sup>5</sup> were declined by the owner due to cost. The pony was given medical therapy with potassium iodide (KI) 30 mg/kg orally once daily (Iodure de Potassium, LDC Laboratories; Paris, France). This treatment is usually used for mycetoma due to *Sporothrix* spp., *Conidiobolus* spp., *Basidiobolus* spp., *Pseudallescheria* sp.<sup>6,7</sup> and *Phialophora* spp.<sup>1</sup> 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 5 months; however, follow-up ACTH levels were not measured.

## 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 (actinomycetoma) or fungi (eumycotic mycetoma).<sup>8</sup> Typically, lesions are characterized by tumefaction, draining tracts and grains in the discharge. Draining tracts are sometimes absent.<sup>8</sup> Usually, they are long-lasting lesions, persisting from several weeks to one and a half years.<sup>1,8</sup> 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.<sup>9</sup>

*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.<sup>10</sup> 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.<sup>11</sup> 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.<sup>12</sup> 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.<sup>13</sup> *Aspergillus terreus* is an emerging opportunistic fungus whose clinical incidence has increased in recent years.<sup>14</sup> 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.<sup>6</sup> In many cases, a combination of surgical excision and specific antifungal therapy is warranted.<sup>15</sup> 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 effect (epiphora, cough, dry seborrheic skin/coat).

Atypical infections commonly occur with PPID due to immunosuppression<sup>16</sup> 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.

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### Résumé

**Contexte** – Le mycétome est une lésion cutanée/sous-cutanée proliférative et chronique caractérisée par des fistules et des granules causés par des actinomycètes (actinomycetome) ou des champignons filamenteux (mycétome eumycotique).

**Objectifs** – Ce cas clinique décrit des données inhabituelles d'un mycétome cutané de l'aile latérale de la narine droite d'un hongre.

**Sujet** – Un hongre Fjord de 16 ans suspecté de PPID (pituitary pars intermedia dysfunction) a été présenté pour examen d'une masse alopecique, ferme, non douloureuse évoluant au niveau de l'aile de la narine droite et de la lèvre.

**Méthodes et résultats** – L'examen cytologique de la masse a révélé une inflammation pyogranulomateuse et l'examen histopathologique a révélé un mycétome fongique. Une culture fongique a identifié *Aspergillus terreus* comme l'organisme responsable bien qu'il ne soit pas reconnu comme pouvant entraîner des granulomes ou des mycétomes chez l'animal domestique. Des tests supplémentaires comprenant un test de stimulation TRH a mené au diagnostic de PPID (maladie de Cushing) qui peut entraîner une immunosuppression et une augmentation de la susceptibilité aux infections.

**Conclusions et importance clinique** – Le cheval a été traité avec succès médicamenteusement pour le PPID avec du pergolide et de l'iodure de potassium avec une bonne réponse thérapeutique et aucune rechute après cinq mois. Un débridement chirurgical ou une exérèse n'a pas été réalisée. A la connaissance des auteurs, ceci est le premier cas de mycétome cutané dû à *A. terreus* chez un cheval.

### Resumen

**Introducción** – Mycetoma es una lesión crónica proliferativa de tejido cutáneo/subcutáneo caracterizada por drenajes y gránulos en el exudado causado por actinomicetos (actinomicetoma) u hongos filamentosos (micetoma eumicótico).

**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 Fjordo 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 fúngico. El cultivo fúngico 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 podía 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 (Actinomycetom) oder filamentöse 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, derben und erhabenen Masse, die den lateralen Nasenflügel und die Lippe betraf, vorgestellt.

**Methoden und Ergebnisse** – Die zytologische Untersuchung der Masse zeigte eine deutliche pyogranulomatöse Entzündung und die histopathologische Untersuchung zeigte ein Mycetom. Die Pilzkultur identifizierte den verursachenden Organismus als *Aspergillus terreus*, der nicht bekannt ist für eine Neigung, entweder dermale Granulome oder Mycetome bei Haustieren zu verursachen. Eine weitere Untersuchung, die einen TRH Stimulationstest beinhaltete, führte zur Diagnose von PPID (Morbus cushing), welcher zur Immunsupprimierung des Tieres und zu einer erhöhten Empfindlichkeit für eine Infektion geführt haben könnte.

**Schlussfolgerungen und klinische Bedeutung** – Die PPID des Pferdes wurde medizinisch erfolgreich mit Pergolid und Kaliumbromid *per os* behandelt. Es bestand eine gute therapeutische Reaktion und kein Wiederauftreten nach fünf Monaten. Es wurde kein chirurgisches Debridement oder eine Exzision durchgeführt. Nach bestem Wissen der Autoren handelt es sich hierbei um den ersten Fallbericht eines kutanen Mycetoms, welches durch *A. terreus* bei einem Pferd verursacht worden war.

#### 要約

**背景** – 菌腫は、放線菌(放線菌腫)または糸状真菌(真菌性菌腫)によって引き起こされる瘻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菌腫の所見を記述する。

**供与動物** – 下垂体中間部の機能障害(PPID)が疑われた16歳のフィヨルド・ホースの去勢雄が、右鼻孔の外側翼と口唇を巻き込む、痛みを伴わない、固く隆起した腫瘤の評価のために来院した。

**方法と結果** – 腫瘤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は真菌性菌腫が明らかになった。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菌腫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、このことが患者の免疫抑制および易感染性傾向をもたらした可能性がある。

**結論および臨床的な重要性** – 患馬は経口ヨウ化カリウム、およびPPIDに対してはペルゴリドにて治療され、良好な治療反応を示した。5ヶ月後までに再発は認められなかった。外科的な搔爬や切除は行われなかった。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菌腫の最初の症例報告である。

#### 摘要

**背景** – 足菌腫是一种皮肤/皮下组织的慢性、增生性病変,以放线菌(放线菌性足菌腫)和丝状真菌(真菌性足菌腫)引起的窦道和带颗粒的分泌物为特征。

**目的** – 报告一不常见病例,一只去势马右侧鼻腔侧翼上发现一处皮肤足菌腫。

**动物** – 一只疑似患有垂体中间部功能障碍(PPID)的16岁峡湾马,对其右侧鼻孔和嘴唇侧翼上的无痛性、坚实且凸起的团块进行评估。

**方法和结果** – 团块的细胞学检查结果显示出明显的脓性肉芽肿性炎症,组织病理学检查发现真菌性足菌腫病,真菌培养鉴定发现病原微生物为土曲霉。目前,对该菌在家畜上引发真皮肉芽肿或足菌腫的易感性并不清楚。进一步调查包括TRH刺激试验,用于诊断PPID(库兴氏病),该病可能导致动物的免疫抑制并增加感染风险。

**结论和临床意义** – 使用培高利特,该马匹的PPID获得成功治疗,同时服用碘化钾,取得良好疗效,五个月之后并无复发。本病例未进行手术清创或切除。根据作者的了解,这是第一例由土曲霉引起的马皮肤足菌腫病例。

#### Resumo

**Contexto** – O micetoma é uma lesão cutânea/subcutânea crônica, proliferativa 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 imunossupressão no animal, aumentando a sua suscetibilidade à infecção.

**Conclusões e importância clínica** – O cavalo foi tratado com pergolida 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*.