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Abstract

In the Mediterranean basin, one of the most important agents of myiasis is Oestrus ovis Linnaeus 1758 (Diptera, Oestridae).
Herein, we report a rare case of nasal myiasis with a secondary infection complication in a patient from northern Italy who had
been visiting Corsica. A healthy, 39-year-old Italian woman spent 2 weeks of vacation in Corsica in June 2018. During her stay,
she suddenly felt a foreign body inside her nose, followed by cough, pain, burning at the pharyngeal level, cephalalgia, and nasal
congestion with secretions from the nostrils. The clinical examination showed a hyperemic and irritated mucosa and endoscopic
examination of the patient's nose and right maxillary sinus revealed three tiny mobile larvae, morphologically and molecular
identified as L1 instar larvae of Oestrus ovis. The patient's infestation was probably imported from Corsica, as Mediterranean
islands are ideal geographical areas for the development of O. ovis, and the timing of infestation match with the period of O. ovis
larviposition. Although rhinomyiasis is rare, it should be considered in people returning from abroad presenting with an acuteonset
and foreign body sensation in the nose.

Keywords Nasal myiasis . Sheep bot fly . Oestrus ovis

Introduction

Myiasis is among the five most commonly reported dermatological diseases in travel medicine (Francesconi and Lupi 2012). First and second instar larvae of Diptera are the main causative agent of human myiasis and could be responsible for complications such as allergic reactions, secondary infection complications, and tissue-invasive internal-cavitary myiasis (Dunbar et al. 2008).

In theMediterranean basin, one of themost important agents of myiasis is Oestrus ovis Linnaeus 1758 (Diptera, Oestridae) (Theodorides 1996; Scala et al. 2001; Poddighe et al. 2010), a fly that exerts an obligate parasitism of the nasal and sinus cavities of small ruminants (Angulo-Valadez et al. 2008).

The disease has been reported worldwide and is caused by the females of O. ovis which deposit first-stage larvae (L1) directly in or around the nostrils of sheep and goats (Scala et al. 2001; Jacquiet and Dorchies 2002). First-stage larvae (L1) enter the nasal cavity and then migrate from the nasal septum and turbinates to the ethmoid where they molt into the second stage larvae (L2) (Angulo-Valadez et al. 2008). L2 further ascend the nasal cavity to the frontal or maxillary sinuses where they molt into third instars (L3) (Scala et al. 2002). Thereafter, L3 larvae re-enter the nasal cavity before being sneezed out by the host via the nasal mucus and then pupate under the soil within 12–24 h (Jacquiet and Dorchies 2002). Finally, when the external conditions are favorable (temperature between 20 and 30 °C), the pupa molt into an adult fly usually in a period from 30 to 34 days (Zumpt 1965).

Accidentally, O. ovis L1 larvae can be deposited in humans and be responsible for benign or severe myiasis. The most common site of human infestation is the conjunctival sac, resulting in ophthalmomyiasis (Fries et al. 2018). Other locations for infestation are the throat (Masoodi and Hosseini 2003), the nose (Lucientes et al. 1997; Einer and Ellegård 2011; Hoyer et al. 2016), and the ears (Al-Dabagh et al. 1980; White et al. 2015).

We report a rare case of nasal myiasis with a secondary infection complication in a patient from northern Italy who had been visiting Corsica.

Material and methods

A healthy, 39-year-old Italian woman spent 2 weeks of vacation in the Calanche Cliffs region of Corsica (Piana, France; Coordinates: 42° 15′ 09″ N; 8° 39′ 26″ E) in late June 2018. During her stay, on July 1, during an outdoor activity, she suddenly felt a foreign body inside her nose. This led to coughing, pain, and burning at the pharyngeal level. She started complaining of cephalalgia and nasal congestion with secretions from the nostrils. On her return, about 5 days later, she was seen by her physician who prescribed a broadspectrum antibiotic therapy on the basis of a severe rhinopharyngitis symptomatology.

The patient showed no clinical improvement after the antibiotics and was then admitted to the Otorhinolaryngology Unit of Biella Hospital, Italy, with complaints of breathing difficulties since she had come back from Corsica. The woman was not on any medication nor was she suffering from any chronic pathology and she had never worked in contact with animals.

The clinical examination showed a hyperemic and irritated mucosa and flexible endoscopy of the patient's nose and right maxillary sinus was performed. It revealed three tiny mobile and translucent larvae, 1 mm in size with dark heads at the level of the nasopharynx, near the Eustachian tube and in the right nasal cavity. These were promptly removed. On the following day, the patient was hospitalized and, under general anesthesia, underwent functional endoscopic sinus surgery (FESS) in order to remove larvae that were located in the nasal septum, lower and middle meatus. FESS showed a hyperemic and hypertrophic mucosa. The nasopharynx and maxillary cavities explored with optical fibers were free from parasites. The recovered larvae were sent to the parasitology laboratory for morphological identification and therefore were then sent to the Laboratory of Genetics and Immunobiochemistry of the Istituto Zooprofilattico Sperimentale del Piemonte, Liguria e Valle d'Aosta (IZSPLVA) for genetic identification using the Forensically Informative Nucleotide Sequencing (FINS) method (Bartlett and Davidson 1992). Genomic DNAwas extracted from the sample using a commercial kit based on a column method (NucleoSpin®Tissue, Macherey-Nagel, Duren, Germany), while a portion of the Cox1 gene of about 700 bp was amplified by a PCR reaction following Ward et al. (2005). Both strands were sequenced using the Sanger method on the semi-automatic sequencer ABI PRISM 3130 Genetic Analyzer (Applied Biosystems, Foster City, USA) and the sequences obtained were assembled using DNASTAR's SeqMan software package.

An examination of the patient after 2 days did not reveal any larvae and there had been a substantial improvement in nasal mucosa, despite the patient still experiencing nasal discomfort, coughing, and respiratory difficulties. The woman was therefore submitted to chest X-ray that showed a pneumonia focus in the left lung. The patient was therefore treated with antibiotics (Amoxi-clavulanato and Ciproxin), as well as with decongestants and antihistamines. No specific antiparasitic treatment was administered. The patient was discharged after 10 days.

Results

Observation at light microscopy without staining showed larvae composed of 11 metameres, each one displaying four

rows of spines (Fig. 1). The cephalic segment had two large black hooks, while the posterior segment consisted of two tubercles, each containing 10 curved spines. These features were consistent with the keys pointed out by Zumpt (1965), and the larvae were identified as L1 instar larvae of Oestrus ovis. The sequence obtained by molecular examination of larvae was compared with those deposited both in the GenBank database, and in BOLD (http://boldsystems.org). Both databases showed an identity greater than 99% with the deposited Oestrus ovis sequences (GenBank accession numbers: MG755264.1 and KR820703), with a 98% coverage of the analyzed sequence. Fromthe validation tests carried out by the lab, the result is statistically significant if the similarity value is ≥ 98%. The genetic analysis therefore confirmed the morphological identification.

Discussion

Myiasismay be caused by larvae of various Diptera species. One of the most common agents is O. ovis, which normally parasitize sheep and goats (Scala et al. 2002). Human myiasis by O. ovis is uncommon in temperate regions of the world, but they are more common in areas with a warm and humid climate. Human myiasis usually occurs from spring to early-autumn, above all in patients living in/near livestock areas. Usually, O. ovis leads to external ophthalmomyiasis (Gregory et al. 2004; Panadero-Fontán and Otranto 2015; Basmaciyan et al. 2018; D'Assumpcao et al. 2019), though nasal myiasis has been also described (Uriarte and Ell 1997; Lucientes et al. 1997; Einer and Ellegård 2011). Regarding Europe, myiasis by O. ovis is endemic in the Mediterranean basin (Rizk et al. 2017, Calışkan et al. 2014), with sporadic cases in central Europe (Delhaes et al. 2001; Weinand and Bauer 2001; Basmaciyan et al. 2018).

Due to climatic conditions and the presence of numerous sheep farms, Mediterranean islands are ideal geographical areas for the development of O. ovis (Scala et al. 2002). Pampiglione (1958) reported that 58.2% of cases of conjunctival myiasis in Italy were recorded in Sardinia, where the parasite has been recovered in 100% of the sheep flocks examined (Scala et al. 2002; Poddighe et al. 2010). A study carried out on shepherds from Sicily, reported that 80.3% of them had contracted O. ovis myiasis at least once in their lives (Pampiglione et al. 1997). The same survey reported that frequently involved sites were the pharynx (77 times), often extending to the larynx, the conjunctiva (56), the nose (32), and rarely the ear (1) (Pampiglione et al. 1997).
A similar situation was described in Corsica, where between 1990 and 1991, there were fifteen human cases in the Ajaccio Municipality (Mariotti and Vacheret 1992), the same region where the event described in the present case report probably occurred. The anamnesis and the timing of infestation, as well as the recovery of first instar larvae of O. ovis (which indicates quite a recent infestation) suggest that the patient most likely became infected during her trip to Corsica, whereas she normally lives in Biella (Piedmont, Italy).
In the last 20 years, seven sporadic cases of O. ovis have been reported in humans in continental Italy, all with ocular involvement, among which a case in Perugia (Crotti et al. 2005), three cases in the province of La Spezia (Dono et al. 2005), a case in Ravenna's LidoAdriano (Rivasi et al. 2009),

one in the city of Bari (Otranto et al. 2009), and another in the city of Florence (Zammarchi et al. 2014).

The northernmost finding of sheep bot fly larvae in Italy was a nasal myiasis in a dog from Milan (Zanzani et al. 2016). The same authors reported O. ovis infestation in small ruminants from three provinces located to the north of Milan (Bergamo, Varese, and Brescia) (Zanzani et al. 2016). Many authors have tried to hypothesize how the spreading outside the area of center-southern Italy occurred. The possible explanation for the case acquired in the center of Florence is the transport of animals and parasites (adult female fly) from the countryside (Zammarchi et a l . 2014) . Likewise, 4 cases of ophthalmomyiasis occurred in the Marseille metropolis (South France) during a 4-week period, which corresponds exactly to the time and location of la Transhumance, a large-scale event with gathering of huge sheep flocks that had passed through many towns near Marseille (Bonzon et al. 2013).

Other cases of myiasis from returning tourists have been reported, namely, in two British males, returning from holidays in Spain (Uriarte and Ell 1997) and from Morocco (Smillie et al. 2010). Another case report deals with a nasal and ophthalmomyiasis in a Swedish man who had spent a week on a Greek Island (Einer and Ellegård 2011). Finally, a French woman from northern France was infested while on holidays in the southern part of the country (Miramas) (Delhaes et al. 2001).

The clinical cases (all external ophthalmomyiasis) described in Corsica by Mariotti and Vacheret (1992) were all recorded between May and July, the same period in which the adult O. ovis fly, according to the chronobiology of the diptera already described in the Mediterranean islands (Scala et al. 2002; Mula et al. 2013). Host-searching and larvipositing of O. ovis are visually guided. The antennae of adult O. ovis female flies also have several types of olfactory sensilla that can detect several synthetic odor compounds (Poddighe et al. 2010). These mechanisms seem to be fundamental in host targeting (small ruminants) and human infection seems to highlight a failure in this process, or that the fly detects some smells and flavors (e.g., emanations from human skin, sweating, perfumes) that can obfuscate their senses. Some authors reported that repeated infections near swimming pools could be related to the use of sunscreen creams (Uriarte and Ell 1997; Vasallo Matilla 1991).

Besides O. ovis, several species of Diptera are involved in human myiasis, e.g., Rhinoestrus purpureus, Pharyngomyia picta, Cephenemyia ulrichii, Gedolstia häsleri, but also Gasterophilus intestinalis and Dermatobia hominis (Mariotti and Vacheret 1992; Mula et al. 2013; Panadero-Fontán and Otranto 2015). The differential diagnosis is based on the morphology of the first instar larvae, particularly the cephalic and last segment. Morphological characteristics of O. ovis larvae are relatively typical, but specific expertise is required; hence, a molecular diagnosis is preferable (Otranto et al. 2004).

The first reports of human nasal myiasis by O. ovis described first-stage larvae and concluded that development to second and third stage larvae was not possible outside the normal host (i.e., sheep and goats) (Quesada et al. 1990; Macdonald et al. 1999). However, more recent surveys seem to indicate that it is possible for larvae to develop into the second (Uriarte and Ell 1997; Einer and Ellegård 2011) and even third stage, within humans (Lucientes et al. 1997). Even though the infection described in this case report occurred in a healthy patient, rhinomyiasis is more common in patients with

atopic rhinitis, malignancy, or chronic infection.

The first reported case of human nasal myiasis with third stage O. ovis larvae was an autochthonous infestation in an immunodeficiency virus positive, urban, English man (Badia and Lund 1994). The second case, reported by Uriarte and Ell (1997), occurred in an asthmatic patient that had been taking prednisolone, and the authors stated that the resultant immunosuppression may have facilitated the transformation of the migrating larvae within the host.

Subsequently, many cases have been reported in nonimmunocompromised hosts, also with development of larvae at second (Einer and Ellegård 2011) and third stage (Lucientes et al. 1997; Delhaes et al. 2001), confirming that larval O. ovis infestation can occur and develop until L3 stage even in a healthy person. Nasal myiasis can cause extensive necrosis, sloughing, and destruction of intranasal tissue, including septal or palatal perforation. Hence, the larvae must be completely removed to prevent severe sequelae (Dunbar et al. 2008).

There is no consensus regarding a standard treatment for nasal myiasis. Published treatments include nasal irrigation with weak solutions of chloroform, nasal packing with chloroform and turpentine, and manual removal of larvae. Antiparasitic treatments (e.g., ivermectin) in conjunction with endoscopic removal and saline irrigation demonstrated a good efficacy and minor side effects (White et al. 2015). In our experience, early detection and mechanical removal of larvae are essential for the prognosis of patients with myiasis. In the treatment of myiasis, local and systemic antibiotics can be combined to avoid superinfection. In the present case, the pneumonia could have been due to involuntary inhalation of some instar larvae, as already described for other Diptera myiasis (McMahon and Bunch 1989), and was resolved with antibiotics. In conclusion, although rhinomyiasis is rare, it should be considered in people returning from abroad presenting with an acute-onset, unilateral foreign body sensation in the nose. An increased awareness of this condition among physicians is the key for a timely diagnosis and effective clinical management.

Compliance with ethical standards

Conflict of interest The authors declare that there is no conflict of interest.

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