S3 Text: Differential diagnoses of the rhinomaxillary bony changes indicative of leprosy that were observed in KD271.

The most relevant differential diagnoses of the rhinomaxillary skeletal lesions indicative of leprosy that were observed in KD271 are bacterial granulomatous infections other than leprosy (e.g., treponematoses, tuberculosis, and actinomycosis), systemic fungal infections (e.g., aspergillosis and mucormycosis), and sarcoidosis [1-4].

From the four medical conditions collectively referred to as treponematoses, pinta, bejel, yaws, and syphilis, the three latter ones can affect the bones in their advanced stages [1,4-6]. Bejel, yaws, and syphilis are caused by three different subspecies of the bacterium Treponema pallidum [6-7]. As pinta never involves the skeleton [1,4-6], it can be ruled out as a diagnostic option in KD271. Bejel and yaws are limited to particular geographical regions of the world: arid, subtropical and humid, tropical areas, respectively [1,4-5,8]. Therefore, both bejel and yaws can be excluded in the differential diagnosis of KD271. Acquired syphilis tends to affect the bones of the skull vault and of the rhinomaxillary region of the face in its tertiary stage [1,4-5]. In the latter area, the nasal bones (not observable in our case), the bony nasal septum, the maxillary palatine process, the nasal conchae, and the lateral walls of the maxillary sinuses are the most frequently involved sites, whereas the anterior nasal spine and the maxillary alveolar process are usually spared [4-5,9-10]. Although acquired syphilis cannot be completely rejected as a diagnostic option in KD271, as the earliest identified cases of the disease from the present-day territory of Hungary derive from the end of the 15th century CE [11], it is unlikely that acquired syphilis resulted in the development of the bony changes observed in the rhinomaxillary region of the face of KD271. Tuberculosis, caused by members of the Mycobacterium tuberculosis complex, is primarily a pulmonary disease; nevertheless, it can affect any part of the human body, including the skin [1-2,4,12]. Tuberculosis of the facial skin and soft tissues, facial lupus vulgaris, is a rare extra-pulmonary manifestation of the disease [12-14]. Although long-standing facial lupus vulgaris can result in secondary involvement of the underlying bone, the maxillary alveolar process is rarely affected by tuberculosis [2,10]. Actinomycosis, caused by Actinomyces spp., is a rare medical condition, and actinomycotic involvement of the skeleton is even more uncommon [1,4-5,15-16]. In the skull, the mandible (unchanged in our case) presents the most frequently affected site, whereas the maxilla is an extremely rare localisation of actinomycosis [1,4-5,16]. Based on their localisation preference and rarity, facial lupus vulgaris and actinomycosis seem to be less likely to be responsible for the formation of the bony changes detected in the rhinomaxillary region of the face of KD271.
Aspergillosis due to Aspergillus spp. is a sporadic systemic fungal infection with worldwide distribution that can occasionally affect the skeleton [1,17-19]. If the skull is involved in aspergillosis, the nasal cavity, and the paranasal sinuses and their walls are primarily affected with eventual extension of the infection into the orbits (not changed in our case) [1,17,19]. Similar to aspergillosis, mucormycosis is a rare systemic infection with worldwide distribution that is caused by fungi belonging to the Mucoraceae family of the Mucorales order [1,17]. In the most common form of the disease, rhinocerebral mucormycosis, the infection can extend into the bones [1,17,19-21]. It spreads in the nasal cavity and paranasal sinuses with subsequent development of sinusitis; from here, the disease frequently progresses into the orbits (not in our case) [1,17,19-21]. In mucormycosis, usually only one of the maxillary sinuses is affected with consequent perforation of the corresponding maxillary palatine process [1,17,19]. Based on the above, aspergillosis and mucormycosis can be excluded in the differential diagnosis of KD271.

Sarcoidosis is an uncommon systemic granulomatous disease of unknown aetiology that generally occurs in adults between 25 and 40 years of age and appears to have a predilection for individuals of African descent [17,19,22-24]. Sarcoidosis rarely (~1%) affects the nasal mucosa and consequently the bones of the rhinomaxillary region of the face [12,17,25]. When it does, the nasal bones (not observable in our case) are the primary site of involvement, whereas the anterior nasal spine and the maxilla are not typical localisations of the disease [2,19]. Considering the racial predilection, age and localisation preference, and rarity of sarcoidosis, this medical condition can be ruled out with high certainty as a diagnostic option in KD271.

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