OLGU SUNUMU CASE REPORT

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Pai Syndrome: A Case Report and a Literature Review

Pai Sendromu: Bir Olgu Sunumu ve Literatür Taraması

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ABSTRACT Pai syndrome (PS) is a rare regional developmental defect of the face, mainly characterized by the variable association of midline cleft of the upper lip (MCL), facial cutaneous lipomas, midanterior alveolar process and nasal polyps and intracranial (pericallosal) lipomas. Its entire clinical spectrum is still poorly delineated and the etiology remains unknown. Very few cases of Pai syndrome diagnosed prenatally have been described. Pai syndrome is usually diagnosed at birth. Differential diagnoses include Loeys-Dietz syndrome, Oculocerebrocutaneous syndrome, frontonasal dysplasia and Goldenhar syndrome, along with chromosomal anomalies. In this case report 4-year-old female patient with nasal and pericallosal lipoma is presented and the clinical and radiological features of Pai syndrome were discussed with the literature review.

Keywords: Pai syndrome; nasal lipoma; corpus callosum agenesis

ÖZET Pai sendromu (PS), yüzün nadir görülen bir bölgesel gelişimsel kusuru olup, esas olarak nazal polipler olmak üzere dudak yarığı, fasiyal deri lipomları, midanterior alveoler proses polipleri ve intrakraniyal (perikallosal) lipomların kombinasyonları ile karakterizedir. Tüm klinik spektrumu yetersiz bir şekilde tanımlanmıştır ve etiyolojisi bilinmemektedir. Doğum öncesi tanı konulan çok az sayıda Pai sendromu vakası tanımlanmıştır. Pai sendromu genellikle doğumda teşhis edilir. Ayırıcı tanılar arasında kromozomal anomalilerin yanı sıra Loeys-Dietz sendromu, okuloserebrokutanöz sendrom, frontonasal displazi ve Goldenhar sendromu sayılabilir. Bu yazıda nazal ve perikallosal lipomlu 4 yaşında bir hasta sunuldu ve Pai sendromunun klinik ve radyolojik özellikleri literatür eşliğinde tartışıldı.

Anahtar Kelimeler: Pai sendromu; nazal lipom; corpus kallozum agenezisi

Pai syndrome (PS) is a developmental disorder characterized by a median cleft of the upper lip, midline polyps of the facial skin, and nasal and pericallosal lipomas. This congenital disease was first described in 1987, and to the best of our knowledge, 60 cases have been reported in literature to date, although the etiology remains unknown.[1,2] Diagnosis of PS is established from the presence of one or more of the diagnostic criteria in addition to a nasal lipoma. Magnetic resonance imaging (MRI) is helpful in the identification of pericallosal lipomas and abnormal structures of the third ventricle. Since the mentioned pathologies may lead to

problems in respiration, alimentation or speech, early surgical intervention should be the treatment of choice.[2,3]

The clinical findings and treatment of a 4-year-old female patient are discussed in this case report, with references to relevant literature.

CASE REPORT

A 4-year-old female patient presented to our clinic with complaints of a lump to the nose. The lump, which protruded from the patient's left nostril, had been present since birth, but had increased in size gradually as she grew. The patient had experienced constant nasal obstruction, made worse with upper respiratory tract infections. The parents of the patient said that her situation had started to affect her psychological wellbeing, and that she had started to pull and play with the lump. Prior to referral, the pediatrics department of another hospital had carried out a detailed examination and had detected hypoplasia of the corpus callosum and a midline pericallosal lipoma.

A physical examination revealed a 1.5 cm soft mass protruding from the left vestibule which caused obstruction of the left septal mucosa and a filled nasal passage (Figure 1). Magnetic resonance imaging revealed dysplasia of the anterior part of the corpus callosum, as well as the presence of a lipoma measuring 42x16 mm in superior pericallosal region, displacing the anterior pericallosal artery. In addition, a nasal lipoma was detected anteriorly in the left nasal cavity measuring 18x8 mm, extending externally and impeding airflow (Figure 2a, b).

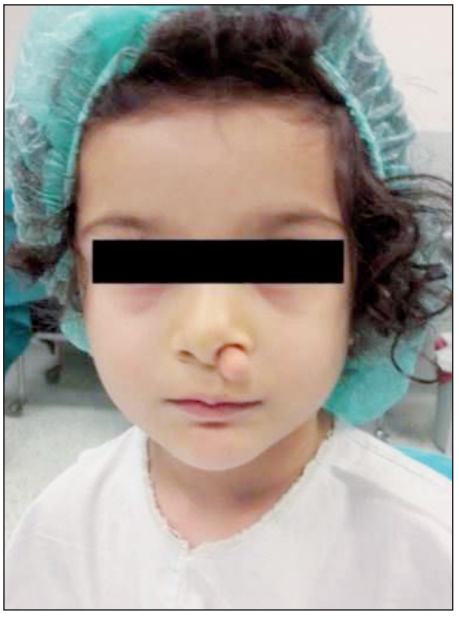

FIGURE 1: 1.5 cm soft mass protruding from the left vestibule causing a obstruction sensation in the left septal mucosa and filling the nasal passage.

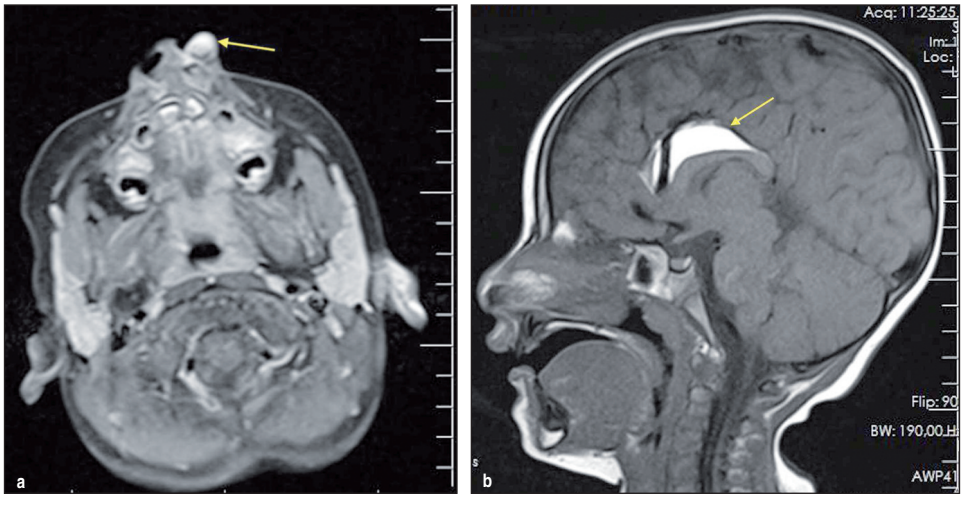

FIGURE 2: a) Axial MRI showing an 18 x 8 mm lipoma in the left nasal cavity impeding airflow and expanding externally from the nasal vestibule. **b)** MRI, Sagittal cut showing the lipoma superior to the corpus callosum, displacing the pericallosal artery.

Surgery was planned for the nasal mass. The procedure was explained to the family, and informed consent was duly obtained. The mass protruding from the left nasal vestibule was endoscopically excised under general anesthesia. During an endoscopic evaluation, a lesion was found to be creating a bulge over the anterior septal region extending to anterior border of the middle concha. The septum had a normal appearance from the anterior border of the middle concha until choana. Initially, the part of the mass protruding from the nasal vestibule was excised through sharp dissection, with bleeding controlled with bipolar cautery. Afterwards, the septal cartilage was identified at the site of the sharp dissection and the septal mucosa overlaying the perichondrium was elevated. The tissue causing the bulge was removed with a microdebrider, after which, the openness of nasal passage was ensured endoscopically. After the transseptal sutures were made, Telfa tampons were inserted bilaterally. Surgery was finalized without complication, and a postoperative histopathologic examination confirmed a diagnosis of "fibromatous hamartoma".

DISCUSSION

Clinical findings of Pai syndrome, in addition to nasal polyps, include superior alveolar process polyps, a median cleft of upper lip, intracranial (pericallosal) lipomas and cutaneous polyps.[1] Although the etiology of this syndrome remains unknown, it has been hypothesized that its mode of inheritance is autosomal dominant.[2-4] Differential diagnoses include Loeys-Dietz syndrome, Oculocerebrocutaneous syndrome, frontonasal dysplasia and Goldenhar syndrome, along with chromosomal anomalies.[5]

PS presents at birth as a phenotype ranging from mild facial dysmorphism to severe anomalies resembling frontonasal dysplasia. Advanced cases may present as hypertelorism or bifid nose. A midline cleft lip with a midline nasal and facial polyp usually appears as a bifid uvula and a high-arched palate. Lipomas of skin in the frontal region may have cartilaginous content.[2-4]

Polyps are either situated in the nasal septum or extend into the nostril in addition to the septum. These anomalies may cause respiratory insufficiency, a greater risk of respiratory infection, speech disorders or feeding difficulties.[3]

Congenital nasal masses are rarely encountered, although encephalocele, meningocele, glioma, dermoid cyst, hemangioma and lipoma should be kept in mind when making a differential diagnosis. For the differential diagnosis of these masses in the midline, invasive procedures such as biopsy should not be performed without MRI. Lipomas are the most common soft tissue tumors in the human body, being benign, slow-growing masses composed of mature fat cells. Although lipomas may form in all parts of the body, they are less frequent in the nasopharynx, nasal cavity or paranasal sinuses when compared to other parts, owing to the low fat content in these regions.[4]

To the best of our knowledge, the first nasal lipoma case reported in an adult patient was that of a 21-year-old male patient, whose lipoma originated from the posterior septum and which was excised endoscopically. A further case report detailed a 34-year-old male patient with a subcutaneous mass originating from the dome of the right vestibule that appeared to be a lipoma.[5] In another case report, a lipoma was described presenting with nasal fullness and a 2 cm mass originating from the anterior septum.[6] Only two cases of lipomas deriving from paranasal sinuses have been reported to date.[7,8] Carranza-Romero et al. reported on a 15 mm congenital lipoma on the frontal medial line in a male newborn, in whom an MRI revealed the complete agenesis of the corpus callosum. Despite some controversial findings related to frontal lipomas, the corpus callosum and frontonasal dysplasia lipomas, changes in these disorders are thought to be a result of the same underlying pathophysiologic mechanism. For this reason, researchers tend to suggest central nervous system (CNS) imaging in neonates with median line craniofacial congenital lipomas.[9]

CNS lipomas are rare, accounting for less than 0.1 percent of all intracranial lesions. The majority of CNS lipomas tend to emerge from the corpus callosum, and are identified as low-density areas with peripheral calcification. Few of the cases of PS reported in literature, including the present case, presented with neurologic disorders. Furthermore, Pascual-Castroviejo et al. noted that none of the eight patients with frontonasal dysplasia and corpus callosum lipomas in their study presented with headaches or convulsive episodes.[10] Likewise, the neurologic development of our patient was normal, regardless of the presence of dysplasia of corpus callosum and pericallosal lipoma evidence by imaging.

A variation of expression as a result of a common genetic defect during mesodermal differentiation has been proposed after a patient was described to have *de novo* reciprocal translocation, 46,X,t(X;16)(q28;q11.2), although the mode of inheritance is not clear.[11] Autosomal dominant (AD) inheritance is suggested, on account of a male child having similar features to his father.[12] Twin siblings with PS were presented in one study. Based on the above information, the risk of a first PS case or a second case is considered low in families with no family history. Our patient had no family history of PS.

Feeding and respiratory difficulties may occur in neonates that should be corrected as early as possible, and multi-stage craniofacial surgery may be necessary in many cases. The restoration of orbicularis oris muscle continuity and excisions of cutaneous lipomas may be carried out during early childhood, although corrections of the nasal pyramid should be postponed until after puberty. The cosmetic and functional restoration of buccal and nasal anomalies usually have very good outcomes. In our case, the nasal polypoid lesion was endoscopically excised as it was causing respiratory as well as psychological problems. Corneal or cataract surgery can bring about improvement of vision for some patients presenting with ocular anomalies, while an optical iridectomy may be necessary for cases presenting with corneal leukoma. Patients should be followed up regularly for any increase in intraocular pressure, and such follow ups should be carried out in cooperation with other disciplines if anomalies of other systems are present concomitantly.[13,14]

The aim in this case study is to increase awareness of PS among otolaryngologists, and to aid in the diagnosis of such disorders, since most of the criteria are encountered in the head and neck area. A close relationship between midline congenital masses (e.g. lipoma, dermoid cyst) and CNS deficits has been established in literature. We recommend CNS imaging for all neonates presenting with midline congenital masses so as to detect any accompanying CNS involvement.

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