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CASE REPORT

Klippel–Trenaunay syndrome

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Klippel–Trenaunay syndrome (KTS) is a congenital disorder characterized by triad of vascular nevi, venous varicosities and hyperplasia of soft and hard tissues in the affected area. This syndrome usually affects the extremities but occasionally can manifest in the craniofacial region, including the oral cavity. We report a case of KTS and discuss the oro-surgical and dental considerations regarding hemorrhagic tendencies caused by the known local anomalies such as vascular malformations associated with this syndrome as well as systemic abnormalities.
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Keywords: hemifacial hypetrophy; hemorrhagic tendencies; Klippel Trenaunay syndrome; oro-dental features

Introduction

Klippel–Trenaunay syndrome (KTS) is a congenital disorder characterized by triad of vascular nevi, venous varicosities and hyperplasia of soft and hard tissues in the affected area (Terezhalmy *et al*, 2000). KTS is either caused by a paradominant mutation in VG5Q gene (Tian *et al*, 2004) or it can be a result of mesodermal abnormality during the fetal growth, possibly secondary to an intrauterine insult (Terezhalmy *et al*, 2000). The anomalies in this syndrome usually manifest in the extremities but oro-facial localization can also occur (Defraia *et al*, 2004). Lesions in KTS are associated with capillary fragility and tend to bleed easily (Ita *et al*, 2001). In addition to capillary fragility, platelet dysfunction, clotting and fibrinolytic abnormalities can also occur (Ita *et al*, 2001). The purpose of reporting this case is to emphasize the relevance of performing more elaborate preoperative hematological tests in patients with KTS to avoid possible postoperative bleeding problems.

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Case report

An 18-year-old boy reported at our hospital with a complaint of an asymptomatic swelling on the right side of his face from childhood and nasal bleeding since last 3 months.

His parents had noticed the presence of a bluish-red discolored patch on his right cheek at the time of his birth. At 3 months of age, a swelling appeared on his right cheek, which gradually progressed to involve the right side of the face till the age of one. The swelling was asymptomatic and his prenatal history was uneventful. The patient underwent surgery for the swelling when he was 11/2 years old, the records of which were unavailable.

The patient was apparently asymptomatic after the treatment but he felt that right side of his face was growing faster than his left side. The swelling progressively enlarged in size but as the patient was asymptomatic he did not seek medical advice. Two years earlier, he had reported the swelling at a different hospital. An atrial septal defect was detected and corrected by surgery (records of which were unavailable) but treatment for the facial swelling was deferred. He reported at our hospital for consultation of nasal bleeding that started 3 months earlier.

The patient was well built and nourished with vital signs within normal limits. On general examination it was observed that he had six digits on each foot (Figure 1).

On extra-oral examination, a massive swelling was observed on the right side of his face measuring 8×10 cm, extending from the lower eyelid to the inferior border of the mandible. Anteriorly, the swelling crossed the midline with the involvement of lips and nose, extending posteriorly to the ear (Figure 2).

The swelling was non-tender with local rise in temperature. The skin over the swelling was dark and smooth with no scar marks.

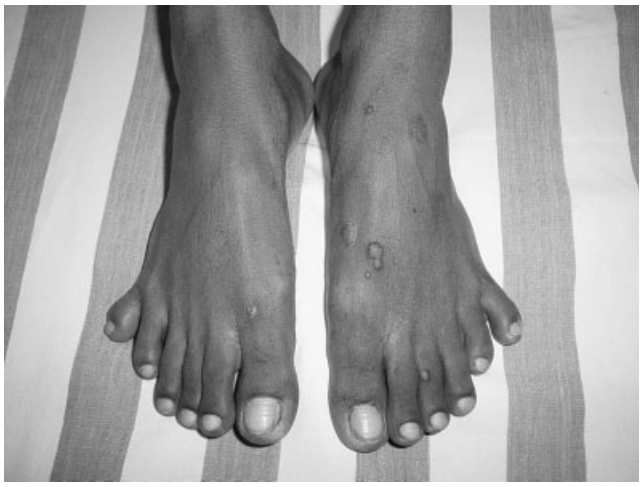

Figure 1 Photograph of the foot showing six digits on each foot toe

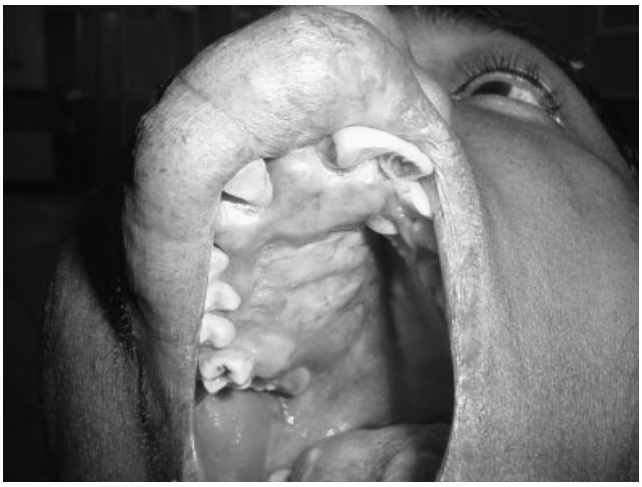

Figure 3 Intra oral photograph showing palatal swelling crossing the midline

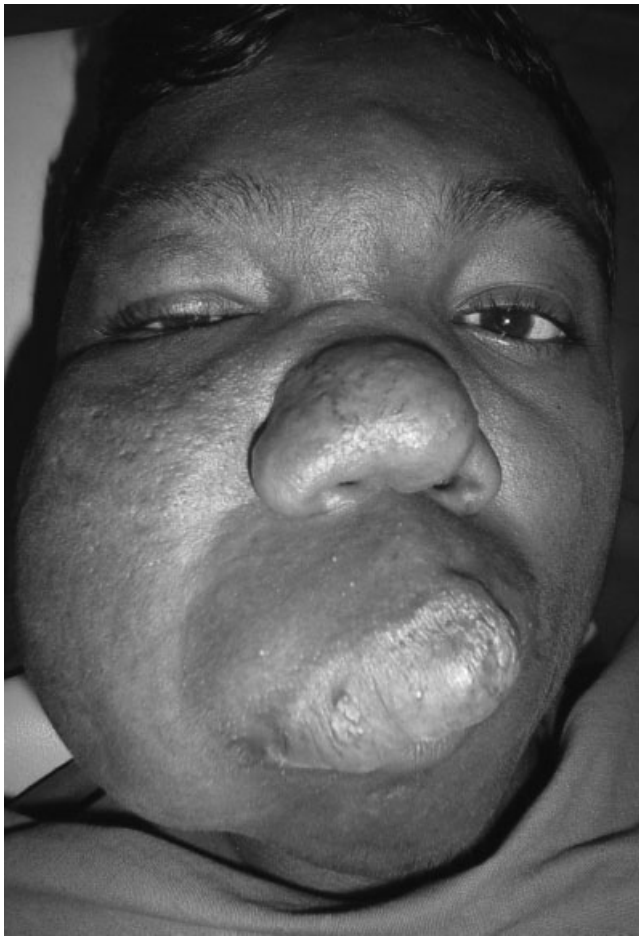

Figure 2 Extra oral photograph showing massive unilateral swelling on the right side

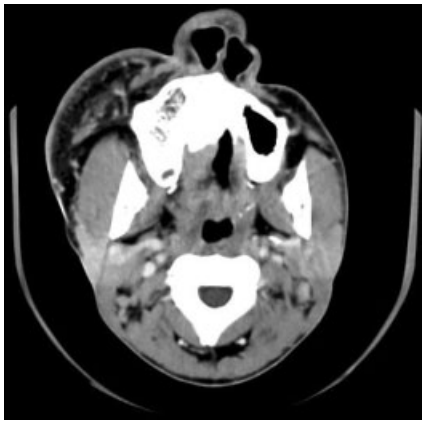

Figure 4 Axial CT showing unilateral hypertrophy of soft and hard tissues

Intra-oral examination revealed a swelling of 5×4 cm in the right palate with diffuse margins and crossing the midline. The swelling was hard, with erythematous overlying mucosa and dilated superficial veins (Figure 3). Spacing between the teeth with labial tilting of the incisors was observed and also his upper right first molar had supra erupted into the edentulous area of the missing lower right first molar.

A provisional diagnosis of a vascular malformation was considered. A CT scan was advised which revealed unilateral hyperplasia of both the bony and soft tissue components on the right side of the face (Figure 4). Subsequently, hematological investigations were ordered which were within normal limits. HIV and HBs Ag tests (routinely carried out for surgical patients in our hospital) were negative.

An arteriogram was performed which revealed hyperplasia of the right facial and superficial temporal arteries, but there was no evidence of any arteriovenous malformation. Aspiration did not yield any blood and as the screening tests for hemorrhagic tendencies were normal a biopsy was advised.

A biopsy was performed under general anesthesia after infective endocarditis prophylaxis (because of the history of an atrial septal defect). An incisional biopsy from the upper lip and right anterior maxilla was performed and sent for histopathological examination. Following biopsy, the patient had bleeding from the biopsy site; pressure packs were applied but were

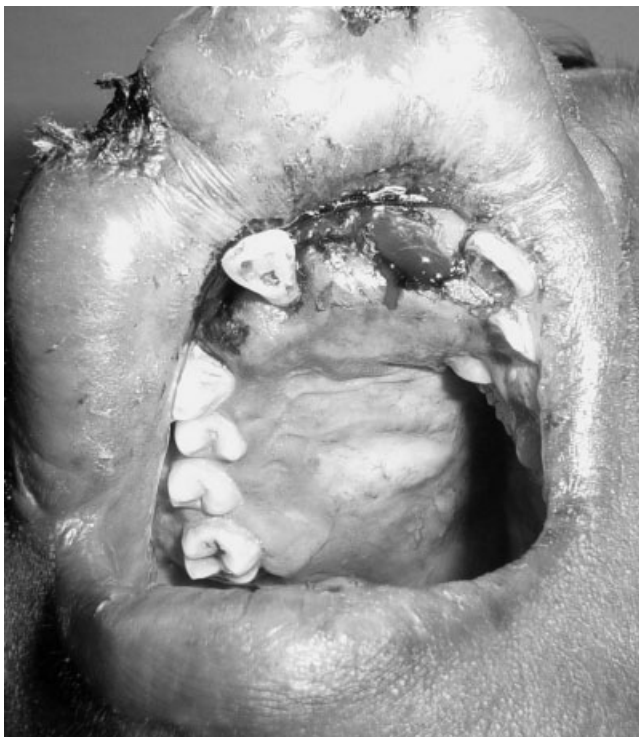

Figure 5 Intra oral bleeding after biopsy

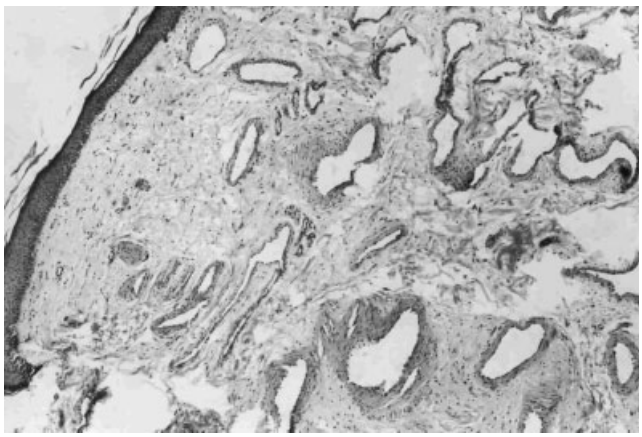

Figure 6 Photomicrograph of the soft tissue showing numerous dilated capillaries

unsuccessful in stopping bleeding (Figure 5). Hemostatic agent ethamsylate was used but only stopped the bleeding temporarily. Bleeding halted completely on application of epsilon-amino caproic acid. The biopsy report of the hard tissue revealed normal tissue but in soft tissue sections numerous dilated capillaries were observed (Figure 6). The patient insisted on discharge against medical advice and was subsequently lost to follow up.

On the basis of classical features of hemi-facial hyperplasia of soft and hard tissues, a cutaneous vascular malformation and associated findings of polydactyly and atrial septal defect, a final diagnosis of KTS was made.

Discussion

Klippel–Trenaunay syndrome was first reported in 1900 by Klippel and Trenaunay (Bathi *et al*, 2002). KTS is characterized by capillary malformations, venous varicosities and bony and soft tissue hyperplasia of the affected area. Diagnosis is based upon the presence of any two of these three features (Terezhalmy *et al*, 2000). In contrast to involvement of the extremities, when the syndrome affects the craniofacial region, varicosities are rarely observed as gravity facilitates venous drainage from the head and neck region (Bathi *et al*, 2002). This explains the absence of venous varicosities in our case.

Oro-facial localization of hyperplasia can occur in KTS (Bathi *et al*, 2002). However there can be some degree of variability regarding the localization and the extent of hyperplasia. In KTS there occurs a characteristic unilateral increase in dimensions of both hard and soft tissues, particularly involving the lips, cheeks, tongue and teeth. Also reported are ipsilateral hyperplasia of maxilla and mandible with increase in volume of the tongue and palatal vault (Ita *et al*, 2001). In our patient, the majority of these features were present but the tongue, teeth and mandible were normal.

Klippel–Trenaunay syndrome is characterized by an extreme degree of variability when affecting the craniofacial region, with the majority patients not exhibiting the classical triad of signs. The greatest variability pertains to vascular anomalies, which can range from cutaneous hemangioma to arterio-venous malformations (Ita *et al*, 2001). The hyperplasia can be attributed to increased vascularity resulting from abnormal vascular development (Ita *et al*, 2001). In our case also the vascular malformation and hyperplasia were observed on the same side. Vascular malformations occur unilaterally (Hallet *et al*, 1995) as observed in our case. These vascular malformations are attributed to intrauterine disturbances between third and sixth week of intrauterine life (Ita *et al*, 2001). Our patient had a cutaneous hemangioma but no arteriovenous malformation, which explains the absence of blood on aspiration.

In addition to the classical features of KTS, associated additional findings like abdominal hemangioma, heart defects, syndactyly, polydactyly, oligodactyly and macrodactyly are also reported in the literature (Steiner *et al*, 1987; Bathi *et al*, 2002). Our patient had polydactyly as he had six toes (Figure 1) and an atrial septal defect, which was surgically corrected.

Maxillary enlargement with marked displacement of teeth on the affected side leading to malocclusion is not uncommon in KTS(Hallet *et al* (1995) and was also observed in our case. The development of features in KTS during the pubertal phase is rapid and the changes do not progress after puberty (Bathi *et al*, 2002). Our patient was a teenager who had recently undergone a pubertal growth spurt, which explains the rapid progression of the swelling.

Only 5% of cases of KTS involve the head and neck region (Bathi *et al*, 2002). It is difficult to explain the reason for the segmental involvement of the face in KTS

with unilateral enlargement of the maxilla and dentoalveolar region with normal growth of contralateral components (Ita *et al*, 2001) as observed in our patient.

Prolonged bleeding in our case was attributed to local vascular anomalies. In addition to the local anomalies, systemic causes of bleeding have also been reported like (i) functional abnormality of blood vessels (Mhaiskar *et al*, 1980; Adams and Cunliffe, 1982), (ii) factor XIII deficiency, (iii) platelet dysfunction (iv) cryofibrinogenemia (Endo *et al*, 1983) and (v) increased fibrin degradation products (FDP) levels (Ita *et al*, 2001). The association of systemic causes of bleeding in these reported cases could be either coincidental or a variant of expression of KTS. Specific preoperative laboratory investigations like FDP, anti-thrombin III and specific factor XIII assay should therefore be performed in patients with KTS. In our case, we attributed bleeding to the local anomaly. Only on a detailed survey of the literature following surgery we became aware of these systemic abnormalities by which time unfortunately the patient was discharged from the hospital, so the tests to rule out these bleeding abnormalities were not performed. Therefore, the possibility of a systemic cause of prolonged bleeding in addition to the local anomaly could not be completely excluded in our patient. Hence we emphasize the value of detailed preoperative hematological investigations in all patients with KTS prior to performing any oral surgical procedures.

Klippel–Trenaunay syndrome should be distinguished from other congenital vascular anomalies like Parkes Weber syndrome, which has similar features in addition to arterio-venous fistula (Cohen, 2000; Bathi *et al*, 2002). In Sturge Weber syndrome there are hemangiomas along the distribution of the trigeminal nerve with focal seizures, sensory and motor paralysis, calcifications of vessel walls and visual field defects (Bathi *et al*, 2002). Our patient had none of these features.

The facial asymmetry and esthetics are the main concerns of the patient who requires an interdisciplinary team approach between a dentist, an oral maxillofacial surgeon, plastic surgeon and an orthodontist who have to formulate a coordinated plan in the management of such patients. In all patients with KTS, even without craniofacial involvement, a dentist must advise detailed hematological investigations prior to any oro-surgical procedure to prevent a possible postoperative bleeding problem.

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