Title of the Manuscript: Melkersson-Rosenthal Syndrome (MRS): An Unusual Case of An 8 Years Old Child

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Received: 20 May, 2016
Accepted: 25 May, 2016
Published: 01 Aug., 2016

Abstract Melkersson-Rosenthal syndrome (MRS) is a clinical entity which is characterized by the classic triad of facial palsy. Miescher’s cheilitis granulomatosa (CG) and lingua plicata. It is an intricate neuro-muco-cutaneous disorder and triad of this disorder is very rarely seen. Majority of the patients show facial palsy and cheilitis granulomatosa (CG) and sometimes, lingua plicata. Diagnosis of cheilitis granulomatosa is based on histopathological outlook. Hereewith, we are presenting a case report of an 8 years old, pediatric patient presenting with the classic triad of Melkersson-Rosenthal syndrome.

Keywords Melkersson-Rosenthal syndrome (MRS); Miescher’s cheilitis granulomatosa (CG); facial palsy; lingua plicata

1 Introduction
Melkersson first described the findings of oro-facial edema and facial paralysis in 1928; therefore, initially, the name Melkersson syndrome was given. In 1930, Rosenthal added the finding of lingua plicata (fissured or furrowed tongue); thereby, completing the triad which defines the syndrome. Since then, this triad is identified as Melkersson-Rosenthal syndrome (MRS) (Gürkan et al., 2015). Miescher in 1945, described cheilitis granulomatosa, in patients with Melkersson-Rosenthal syndrome (MRS). Complete expression of the 3 signs, although it is rarely reported and most often, a partial expression is seen (Agarwal et al., 2011). Melkersson-Rosenthal syndrome is an uncommon neuro-muco-cutaneous disorder. The diagnosis is based largely on clinical and characteristic histopathological findings like non-caseating epitheloid cell granulomas, multinucleated giant cells (Langerhan’s giant cells), chronic inflammatory cell infiltrates and significant lymphoedema (Ozgursoy et al., 2009). The exact etiology and pathogenesis of Melkersson-Rosenthal syndrome, however is unknown. It is usually seen in 2nd and 3rd decades of life. Herewith, we are presenting a case report of an 8 years old, pediatric patient presenting with the classic triad of Melkersson-Rosenthal syndrome.

1.1 Case Report
An 8 years old male child reported with a chief complaint of swelling in relation to lower lip since 15 days. The swelling was smaller in size initially and had gradually progressed to the present size. There was no history of trauma or infection or any drug intake in the past for similar reason. On general physical examination, the patient was moderately built and all the vital signs were found to be within normal limits. On cranial nerve examination, facial palsy was noted in relation to left side of the face. Patient was unable to close eye on left side (Figure1), and also on smiling, his left corner of mouth showed a characteristic drooping of the left corner of mouth. Extra-oral examination showed diffuse swelling in relation to both the lips, (Figure 2) which was soft, non-tender and non-fluctuant. Intra-oral examination revealed plications over the tongue. (Figure 3) On the basis of characteristic
clinical findings, the diagnosis of Melkersson-Rosenthal syndrome (MRS), which presents with the classic triad of facial palsy, lingua plicata and cheilitis granulomatosa, was given. Panoramic radiograph did not reveal any significant findings. Complete blood count was normal. HIV/HBV tests were negative. The patient was advised incisional biopsy on lower lip. (Figure 4) On histopathological examination, aggregates of non-caseating epitheloid cell granulomas with multinucleated Langerhan’s giant cells and chronic inflammatory cell infiltrates comprising chiefly of lymphocytes were seen. (Figure 5) Based on characteristic clinical and histopathological findings, the diagnosis of Melkersson-Rosenthal syndrome was confirmed.

Figure 1 Facial palsy in relation to left side of face with the patient being unable to close eye on left side

Figure 2 Extra-oral examination revealing diffuse swelling in relation to both the lips

Figure 3 Intra-oral examination revealing plications over the tongue
2 Discussion

Melkerson-Rosenthal syndrome (MRS) is a rare neuro-muco-cutaneous disorder presenting with the classic triad of Miescher’s cheilitis granulomatosa (CG), facial palsy and lingua plicata (Gürkan et al., 2015; Agarwal et al., 2011; Talabi O.A., 2011). The exact etiology and pathogenesis of this syndrome is still unclear, however, certain factors such as herpes simplex infection, Epstein Barr virus infection, cytomegalovirus infection, bacterial infection, allergic reaction, immune-mediated phenomena, genetic factors etc., which have been considered etiological but not yet proven (Ozgursoy et al., 2011; Hathiram et al., 2000). Some studies reported an autosomal dominant inheritance pattern with the responsible gene mapping to chromosome 9 pH (Rose et al., 2011). In majority of the MRS patients, most common finding is lip edema. In about 40% of cases, cheilitis granulomatosa is the presenting sign of MRS, which consequently progresses to neurologic signs (Vibhute et al., 2013). It may involve upper or lower lip or both the lips (Critchlow and Chang, 2014). In our case, both the lips were involved. The diagnosis of cheilitis granulomatosa is made by histopathologic findings of non-caseating granulomas. The second most common sign of MRS which is seen rarely is the facial palsy. Facial palsy may be partial or complete and may be unilateral or bilateral. It may be due to the compression of nerve by tissue edema or may be due to granulomatous infiltration of the nerve and nerve sheath (Agarwal et al., 2011). The advanced radiological investigations such as computed tomography and magnetic resonance imaging are advised to rule-out any underlying pathology causing facial nerve paralysis. Facial nerve paralysis is seen in 10% to 20% of the cases reported (Vibhute et al., 2013). The third uncommon sign is fissured or furrowed tongue or lingua plicata. It is most commonly seen as a congenital anomaly in general population. But in our case, classic triad MRS was
present, which is rarely seen. It is most commonly seen in 2nd and 3rd decade of life. Only 30 cases of childhood age group are reported in the literature till date (Gürkan et al., 2015). Literature shows a male to female ratio of 1:3. In the present case, an 8 years old male patient reported with the classic triad of MRS, which is again rare. Cases reported till date in the literature did not show all the features of the triad. They either showed facial palsy, facial edema without lingua plicata or facial edema and lingua plicata without facial palsy or facial palsy and lingua plicata without facial edema. There is no standardized protocol in literature regarding the treatment of MRS patients. Systemic corticosteroids, 1mg/kg/day, have been found to be effective in many cases (Gürkan et al., 2015). Intra-lesional glucocorticoids, triamcinolone acetonide, 40 mg once a week for 3 weeks, for lip edema has also been found to be effective (Crichtlow and Chang, 2014). Metronidazole, clofazimine, roxithromycin, combination of dapsone and triamcinolone are effective in cases of cheilitis granulomatosa. If cheilitis granulomatosa is not responding to the conservative treatment, surgery followed by intra-lesional steroids for 2 to 6 months, found to be effective (Agarwal et al., 2011). For cosmetic purpose, reconstructive surgery of lip is indicated. For facial palsy not responding to medical treatment, surgical decompression of the nerve throughout its bony canal is indicated (Ozgursoy et al., 2011). In patients complaining of burning sensation with fissured tongue, symptomatic treatment with topical steroids is indicated. With the treatment including topical, systemic or intra-lesional steroids, 60% to 80% regression of the disease is noted although recurrence is still noted in 60% to 75% of the cases (Agarwal et al., 2011). In our patient, intra-lesional injections of 0.1% triamcinolone acetonide were given at multiple sites for a period of 10 weeks in lower lip. For facial palsy and lingua plicata, no treatment was indicated as the patient was more concerned for the lip swelling

Conclusion
The diagnosis of facial palsy is often challenging in patients of Melkersson-Rosenthal syndrome where in, in most of the cases, it is often misdiagnosed. A detailed history and clinical examination are often necessary for an accurate diagnosis of Melkersson-Rosenthal syndrome. A close follow-up is also mandatory as it has a high recurrence rate.

Acknowledgment
The research grant for this study was provided by the National Commission for Science, Technology and Innovation, Kenya, awarded to Muthumbi A., Khia C.M., and Okondo J. Institutional support and laboratory facilities provided by Nairobi and Egerton universities, Kenya Marine and Fisheries Institute are appreciated. Members of the Mida Creek Conservation Community, especially Mwamure J., assisted in introduction to fishers. Nthiga A. and Njuguna V. (Msc Students University of Nairobi students), participated in both field and laboratory work. Ngatia J., Muhamed S., and Abutrika M. (University of Nairobi Bsc students), participated in fieldwork. Discussions on commerce and economics with Drs. Thronjo E., (JKUAT), M Kariuki M., (EU) and Wagoki J. (JKUAT), provided useful guidelines. The contributions and suggestions made by the reviewers are also appreciated.

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