LETTER TO THE EDITOR

Unusual Manifestations of Childhood ALL: Isolated Parotid Involvement at Presentation

Dear Sir

We read with interest the article by Biswas et al (2009). The authors have clearly highlighted the uncommon clinicalfeatures at presentation in childhood leukemia and describe a sole case of parotid involvement. In this communiqué we describe additional 4 cases of parotid involvement at presentation in childhood acute lymphoblastic leukemia (ALL) from 762 patients managed at our institute over 16 years from 1990-2006 (Kulkarni, 2009).

The salient clinical and laboratory features of these patients are summarized in Table 1. All patients had fever and/or pallor at presentation to our institute. None had bone pain or overt bleeding manifestations. The mean age at presentation was 5 years (range: 3-8 years) while the male:female ratio was 3:1. All had lymphadenopathy with massive hepatosplenomegaly suggestive of bulky disease. TLC was >50.0_109/L in 2. Thrombocytopenia was present in all 4. Case 2, in addition, had mediastinal adenopathy and proptosis. Parotid swelling was bilateral in case 4.

Diagnosis of ALL was confirmed by bone marrow (BM) examination. Cytochemistry was performed on all BM aspirate/touch smear specimen using myeloperoxidase and Sudan black stains. Central nervous system disease (CNS) was ruled out by cerebrospinal fluid examination (cytospin and cell count). In addition, none of these patients had features of overt CNS disease. All had ALL L1 while none had facial nerve involvement. Case 3 and 4 were treated according to modified United Kingdom Acute Lymphoblastic Leukemia (UKALL) protocol. The parotid swelling subsided rapidly after initiation of therapy. The outcome, however, was dismal. 2 patients refused therapy while death and relapse were observed in the other 2. Small numbers precluded comparative analysis with other ALL patients managed at our institute.

Authors have described parotid involvement along with mental palsy and/or submandibular gland involvement (Hiraki et al 1997). Relapse of disease or secondary malignancy in the parotid/salivary glands after treatment for ALL or AML has also been described (Naithani and Mahapatra, 2007). However, ALL presenting with parotid infiltration is exceedingly rare. To the best of our knowledge this is the first and largest series of childhood ALL patients with parotid gland involvement at presentation with 3 cases of unilateral gland involvement which is a distinct rarity, from India. Occurrence of 2 extramedullary masses in case 2, akin to chloromas in acute myeloid leukemia (AML) is noteworthy.

Parotid involvement in these patients at initial presentation could be a part of bulky extramedullary disease. The significance of parotid infiltration by lymphoblasts is unclear. Whether this rare instance modifies risk category or acts as a sanctuary site remains open to speculation. Both the patients in our series who opted for therapy had an adverse survival outcome, possibly related to the bulk and biology of their disease. Off note case 3 had a combined BM and CNS relapse.

Authors have described facial nerve involvement could co-exist with parotid involvement in AML (Naithani and Mahapatra, 2007). However, parotid gland involvement in ALL along with facial palsy has not yet been reported. Theoretically, lymphoblasts from parotid mass could infiltrate it and cause palsy. We too did not observe facial palsy in any of our patients despite advanced and bulky disease. The implications of these observations and whether some blasts from parotids could penetrate the facial nerve and escape the cytotoxic agents thereby contributing to future CNS relapse; are still unclear.

Patients are often misdiagnosed as mumps and receive symptomatic therapy. They result in late referrals and diagnostic delays. 3 of the 4 patients in our series had a symptom diagnosis interval longer than 1 month (range: 45-120 days). It underscores the importance of detailed clinical examination with a high index of suspicion to look for non-infectious causes of parotid swelling, especially if persistent, and that of subtle changes in blood count which could aid early diagnosis and referral by primary care physicians and pediatricians.

Table 1. Salient Characteristics of ALL Patients Presenting with Parotid Involvement

Case	Age (years)	Gender	SDI (days)	Hepatomegaly (>5cm below RCM/LCM)	Splenomegaly	Hemoglobin Gm/dL	TLC x10^9/L	Platelet count	Outcome
1	5	Male	120	+	+	8.0	9.8	65.0	Refused therapy
2	3	Female	45	+	+	5.3	59.0	36.0	Refused therapy
3	8	Male	90	+	+	5.7	78.0	32.0	Defaulted therapy/12 months
4	4	Male	20	+	+	7.4	9.7	27.0	BM+CNS relapse/18 months

SDI, Symptom diagnosis interval; LCM, left costal margin; RCM, right costal margin

Inclusion of ALL in the differential diagnoses of a parotid swelling, especially in the presence of abnormal blood count (especially thrombocytopenia and elevated leukocyte count) is imperative. Further studies including cytogenetic and molecular characterization of ALL presenting with parotid involvement would be necessary to delineate its clinic-pathological basis and prognostic significance.

References

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