Indian J Hematol Blood Transfus (Apr-June 2019) 35(2):364–366
https://doi.org/10.1007/s12288-019-01086-w

CORRESPONDENCE

Rare Presentations of Acute Lymphoblastic Leukemia

Kamal Kant Sahu[1] · Susan V. George[1] · Ahmad Daniyal Siddiqui[2]

Received: 24 December 2018 / Accepted: 21 January 2019 / Published online: 29 January 2019

Dear Editor,

Mishra et al. [1] recently reported a rare dermatological presentation of acute lymphoblastic leukemia (ALL). With regards to rare presentations, we hereby present a short review on unusual manifestations and dermatological presentations of ALL.

Fever, shortness of breath, lethargy and night sweats are the common presenting symptoms of ALL. Recently, there have been reports on rare and unusual presentations of ALL like calf pain, retinal detachment, nephromegaly etc. Recently, researchers have also shown interest in studying the dermatological manifestations in association with leukemia [2–7]. Maheshwari et al. [2] retrospectively reviewed their 12-year institutional data of 317 relapsed ALL patients and reported nine unusual presentations. Similarly, Shakibazad et al. [3] did a systematic literature review of 41 published studies on unusual presentations of ALL in children. They found musculoskeletal symptoms (34.2%) as the most common unusual initial presentation of ALL in children. The reported musculoskeletal complaints were nonspecific such as bone pain, fractures, osteoporosis, osteomyelitis and calf pain. Renal involvement (14.6%), neurological impairment (14.6%), orbital manifestations (12.2%) and pericardial involvement (4.9%) were the other unusual initial presentations in this study (3).

✉ Kamal Kant Sahu
drkksahu85@gmail.com

[1] Department of Medicine, Saint Vincent Hospital, 123 Summer Street, Worcester, MA 01608, USA

[2] Division of Hematology and Medical Oncology, Saint Vincent Cancer and Wellness Center, 1 Eaton Place, Worcester, MA 01608, USA

Usually, the dermatological features are not the presenting symptoms in acute leukemia. The skin is the most visible, exposed and the largest organ of the body. Hence if involved, it has the potential of providing essential clues to the ongoing disease process and potential complications [8, 9]. As mentioned by Mishra et al., leukemia cutis, thrombocytopenic purpura and superadded skin infections are the well known dermatological menifestations in acute leukemia. Millot et al. [4] studied the "dermatological manifestations at diagnosis" in 1359 children suffering with either ALL or lymphoblastic lymphoma (LBL). They found that only 24 patients (15 ALL and nine LBL) had dermatological features at the time of diagnosis. Importantly, in 15 of these 24 cases, dermatological features appeared almost six weeks (range, few days to eight months) in advance to hematological presentation. This observation signifies the importance of dedicated dermatological examination while evaluating the suspected cases of ALL.

Just like ALL, other leukemias can also have dermatological manifestations at presentation or during follow up [6, 7]. Aggarwal et al. did a prospective study on Asian cohort of leukemic patients (Table 1). Out of 196 patients with newly diagnosed leukemias (ALL, CLL, CML, CLL), Aggarwal et al. [6] found 87 reports of mucocutaneous involvement, most common being infection related (69%), followed by reactive dermatosis (24%) and leukemia cutis (7%). On follow up, they also re-examined the same patient cohort with regards to the therapy related cutaneous adversities [7]. Alopecia (51%) and abnormal pigmentation (15%) were the most common findings while radiation dermatitis (2%) and phlebitis (1%) were the least common in their follow up study (7).

In conclusion, it is imperative for the clinicians to be aware of dermatological manifestations of leukemia. This is important especially in children in whom diseases like

Table 1 Review on studies conducted on unusual and dermatological presentations in ALL

References	Study design	Study period	Study sample size	Unusual presentation reported
Maheswari et al. [2]	Institutional review of relapsed ALL patients	2000–2012 (12-year data)	317 cases of relapsed ALL	*Nine cases*
				Parotid gland involvement
				Maxillary sinus
				Retinal detachment
				B/L facial nerve palsies
				B/L bone involvement of both upper and lower limbs
				4th metacarpal bone
				Massive splenomegaly
				Testicular torsion
Shakibazad et al. [3]	Systematic literature review of reported cases	1986–2016 (30-year data)	41 studies	*With decreasing frequency*
				Musculoskeletal symptoms including hypercalcemia (34.2%)
				Renal involvement (14.6%)
				Neurologic signs (14.6%)
				Orbital manifestations (12.2%)
				Pericardial involvement (4.9%)
Millot et al. [4]	Patients enrolled in multicentric trial (EORTC 58881)	1989–1995 (6 years data)	1359 children with ALL and LBL	*15 cases of ALL with dermatological features*
				Most common location noted was head
Pulido diaz et al. [5]	Institutional prospective study	2009–2010 (1 year data)	52 ALL cases	*28 dermatological descriptions in 52 cases were reported*
				11 non-specific (39%)
				10 drug-related (36%)
				7 infectious (25%)
Aggarwal et al. [6]	Institutional prospective study	July 2010–Dec 2011 (1.5-year data)	196 newly diagnosed leukemia cases (ALL, AML, CML, CLL)	*87 mucocutanesous descriptions noted in 79 cases of leukemia*
				60 infections
				Bacterial (33%)
				Viral (30%)
				Fungal (28%)
				Parasitic (8%)
				21 reactive dermatosis
				Neutrophilic dermatosis (23%)
				Drug rash (33%)
				Insect bite hypersensitivity (4%)
				Others (40%)
				6 leukemia cutis

Table 1 continued

References	Study design	Study period	Study sample size	Unusual presentation reported
Aggarwal et al. [7]	Institutional prospective study	July 2010–Dec 2011 (1.5-year data)	196 leukemia cases (ALL, AML, CML, CLL) who were followed up for therapy related cutaneous adversities	*154 cutaneous adversities noted in 115 cases of leukemia* 79 alopecia (51%) 23 pigmentary skin changes (15%) 16 stomatitis (10%) 14 nail changes (10%) 12 acneiform eruptions (8%) 6 imatinib induced (3%) 3 radiation dermatitis (2%) 1 phlebitis (1%)

ALL hold a favourable prognosis if they are diagnosed and treated in a timely fashion.

Compliance with Ethical Standards

Conflict of interest Authors have no conflicts of interest to declare.

Ethical Statement The article doesn't contain participation of any human being and animal.

References

1. Mishra K, Jandial A, Sandal R, Lad D, Prakash G, Khadwal A et al (2018) Haemorrhagic bulla: a rare presentation of acute lymphoblastic leukemia. Indian J Hematol Blood Transfus. 1:1. https://doi.org/10.1007/s12288-018-1060-8
2. Maheshwari G (2018) Unusual presentations of acute lymphoblastic leukemia in children: a study of 9 patients. J Glob Oncol 4(Supplement 2):87s
3. Shakibazad N, Haghpanah S, Shahriari M (2016) International conference on leukemia and hematologic oncology. J Hematol Thrombo Dis 4(Suppl 5):37
4. Millot F, Robert A, Bertrand Y, Mechinaud F, Laureys G, Ferster A et al (1997) Cutaneous involvement in children with acute lymphoblastic leukemia or lymphoblastic lymphoma. The Children's Leukemia Cooperative Group of the European Organization of Research and Treatment of Cancer (EORTC). Pediatrics 100(1):60–64
5. Pulido-Díaz N, Medina G, Palomino N, Peralta F (2015) Cutaneous manifestations of leukemia. Rev Med Inst Mex Seguro Soc 53(Suppl 1):S30–S35
6. Aggarwal S, Malhotra P, Dogra S, Vinay K, Kanwar AJ, Saikia UN (2016) Spectrum of mucocutaneous manifestations in an Asian cohort of patients with leukemia. Int J Dermatol 55(8):893–897
7. Aggarwal S, Malhotra P, Dogra S, Vinay K, Kanwar AJ, Saikia UN (2016) Therapy-related cutaneous adverse effects in an Indian cohort of adult leukaemia patients. J Eur Acad Dermatol Venereol 30(12):e202–e204
8. Sahu KK, Mishra A, Chastain I (2018) Novel anticancers and dermatological adversities: old rivals but new challenges. BMJ Case Rep 14:11
9. Mishra AK, Sahu KK, Atem J (2019) Disseminated herpes zoster following treatment with benralizumab. Clin Respir J