newsLETTER

Vol. 11, No. 1, Jan - March 2017

Pakistan Society of Haematology

www.psh.org.pk

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Pakistan Society of Haematology

President's Column

Our Dear Colleagues:
Assalam-o-Alaikum,

First of all I must thank you all for the participation in Haemcon2017, Lahore and the trust which you expressed in electing me as the unanimous president of your own society. I request you to pray to Almighty Allah to give me courage and strength to honor this huge obligation.

I am also lucky for having Gen. Pervaiz Ahmed as President Elect and very able, energetic Executive Committee and Secretary/ Treasurer Dr. SaimaFarhan. I am very much confident that with this team, together with your cooperation and blessings, we will achieve all the set targets.

Our first and most important target is to net the present and future budding haematologists in the PSH family. Let us all strive for that. Our website www.psh.org.pk is in a process of being updated. All our activities are uploaded on website, so visit the site and give your valuable suggestions to improve activity.

Our second target is establishment of different working groups (WG) of Society to formulate guidelines for various haematological disease in Pakistani perspective. Continuing Medical Education (CME) is also our main goal. In different institutions of Pakistan workshops, seminars, symposium and public awareness program should be promoted for dissemination of knowledge and skills under the umbrella of PSH.

Our third target is collaboration of PSH with various national professional societies and international societies of blood, bone marrow transplant, transfusion medicine, haemophilia, thalassemia, molecular haematology, cytogenetics, lab haematology, Paediatric haematology for access of academic material, journals, combined annual sessions, exchange of professionals and research collaboration. InshaAllah we are going to start journal of PSH in this year.

Last but not the least, my dear friends the strength of every organization lies in its unity. Let us remain united in achieving our objectives be under the flagship of PSH. Because this society is our family be on active, so part of your own family.

I think I should stop here and rest will be discussed in Up-coming Newsletter. I humbly request you all to strengthen our hands and also pray for us to meet our obligation to you with honor I wish you all great success and Allah blessing in your future deliberations

With Thanks,

Prof. Dr. Nisar Ahmed,
President, Pakistan Society of Haematology.

About PSH

Pakistan Society of Haematology was formed in 1996 with the aim of promoting advancement of haematology, BMT and transfusion medicine in the Country. Presently it has more than 300 members and we all should make efforts to enroll every haematologist in the country. We request all our members to take special interest in extending the membership to all those haematologist around you who have not yet registered with PSH. Pakistan Society of Haematology (PSH) website was launched and has been very active in recent past. We are trying to rejuvenate the website "http://www.psh.org.pk. The website would be interactive and provide on line forum for sharing views with other haematologist, and case discussion with the experts. Other features will be facility to download online membership from, newsletter, list and addresses of the members. Hopefully the website will be more operational within this month InshaAllah.

PSH Activities

PSH Monthly Meeting (Lahore Chapter) at University of Health Sciences, Lahoreon 18th April, 2017.



PSH Monthly Meeting (Lahore Chapter) at Shaikh Zayed Hospital, Lahore on 16th May, 2017



1st PSH Monthly Meeting (Peshawar Chapter) at Rehman Medical Institute, Peshawar on 18th May, 2017



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SCHEDULE OF PSH MONTHLY MEETING

City	Coordinator Name	Date	Time
Lahore	Dr. Muneeza Junaid	2nd Tuesday of the Month	09:00am to 10:00am
Karachi	Dr. Bushra Moiz	Last Friday of the Month	08:00am to 09:00am
Quetta	Prof. Nadeem Samad Shaikh	Last Friday of the Month	09:00am to 10:00am
Rawalpindi/ Islamabad	Brig. Ch. Altaf Hussain	Last Thursday of the month	03:00pm to 05:00pm
Peshawar	Dr. Shahtaj Khan	3rd Thursday of the month	1200pm to 01:00pm

NEW EXECUTIVE COMMITTEE

New Executive committee was elected during 19th Annual Conference Pakistan Society of Haematology held at Lahore from 16th-18th February 2017.Following are the office bearers of executive committee.

PRESIDENT
Prof. Dr. Nisar Ahmed
0300-4330196
dr_nisarahmed@hotmail.com

PRESIDENT ELECT
Maj. Gen. Pervez Ahmed
0300-8561288
parvez101@yahoo.com

SECRETARY/TREASURER
Dr. Saima Farhan
0300-2408440
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MEMBERS

ARMED FORCES
Brig. Ch. Altaf Hussain
Brig. Maqbool Alam
Brig. Saqib Qayyum

ISLAMABAD
Prof. Dr. Ayesha Junaid

PUNJAB
Dr. Muneeza Junaid
Dr. Manzoor Hussain
Prof. Dr. Arif Hussain

SINDH
Prof. Dr. Muhammad Irfan
Prof. Dr. Salman Naseem Adil
Dr. Muhammad Nadeem

BALUCHISTAN
Prof. Dr. Chandi Kapoor

KPK
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NATIONAL PSH COORDINATORS

RAWALPINDI/ISLAMABAD	KARACHI	QUETTA
Brig. CH. Altaf Hussain 0300-5464272 altaf444@gmail.comm	Dr. Bushra Moiz 0300-2160765 bushra.moiz@aku.edu	Prof. Dr. Nadeem Samad 0300-8380847 drnadeemsheikh@hotmail.com

PESHAWAR	LAHORE
Dr. Shahtaj Masood 0300-9249027 shahtajmasood@yahoo.com	Dr. Muneeza Junaid 0333-8029028 dr.mjunaid@gmail.com

PSH HISTORY

Gen Masood Anwar

1. Pakistan Society of Haematology (PSH) was raised as "Pakistan Society of Haematology/Transfusion Medicine (PASHT)" in 1991. A meeting was held at 5 pm Friday Nov 22, 1991. Professor Dr Mohammad Khurshid, Brig (later Lt Gen) Muhammad Saleem, Dr Khalid Zafar Hashmi, Dr Nasim Siddiqui, and Dr Abdul Hayee attended the meeting as members in presence of Prof A. V Hoffbrand. In this meeting Dr Khurshid presented a brief outlay of the necessity to create such a society. He also pointed out that Dr. Abdul Hayee, Dr. Khurshid, Dr KZ Hashmi and Brig Saleem had met at Bahalpur and agreed on the general principles that the first meeting would be held along with the International conference of Pathology.
2. Though initial work was comprehensive, governing body and meetings of PASHT were not held regularly. In Sept 1994 it was proposed by Gen Muhammad Saleem to meet all PASHT members during Pakistan Association of Pathology(PAP) conference at Quetta. Dr Muhammad Khurshid in consultation with Gen Saleem, Prof Abdul Hayee, Dr Khalid ZafarHashmiproposed a provisional constitution of PASHT for the discussion in meeting
3. Haematologists from all over the country met on Saturday 9th March 1996 at Hotel Pearl Continental Rawalpindi in order to form a society. It was unanimously agreed that official name of society will be "Pakistan Society of Haematology" with official abbreviation of "PSH". It was also decided that until elections for office bearers the society matters will be looked after by a committee as under
    a. Dr. Muhammad Khurshid
    b. Dr. Ehsan-ul-Allah
    c. Dr. Abdul Hayee
    d. Dr. Khalid Zafar Hashmi
    e. Dr. Khalid Hassan
    f. Dr. Masood Anwar will act as Co-ordinator
4. A general body meeting of PSH was held at Peshawar on 2nd and 3rd Nov 1996. Election for office bearers were carried out as follow
    a. Lt. Gen. Muhammad Saleem President
    b. Prof. Muhammad Khurshid as Vice President
    c. Dr. Khalid Hassan as Secretary/treasurer

Later in Oct 1997 appointment of vice president was renamed as president elect.

List of past presidents includes

1. Prof. Dr. Abdul Hayee
2. Prof. Dr. Abdul Khaliq
3. Prof. Dr. Muhammad Khurshid
4. Prof. Dr. Khalid Zafar Hashmi
5. Maj. Gen. Masood Anwer
6. Prof. Dr. Khalid Hassan
7. Maj. Gen. Suhaib Ahmed
8. Prof. Dr. Samina Naeem
9. Gen. Muhammad Ayyub

List of past secretaries includes

1. Dr. Khalid Hassan
2. Maj. Gen. Massod Anwar
3. Prof. Fazle-e-Raziq
4. Dr. Salman Naseem Adil
5. Dr. Shaheena Kauser
6. Brig. Nadir Ali
7. Maj. Gen. Pervez Ahmed
8. Dr. Nadeem Ikram
9. Dr. Humera Rafiq
10. Brig. Tariq Mehmood Satti

5.PSH was registered with Govt of Pakistan on 8th August 1998(RS/ICT/298 dated 8 Aug 1998 as non political and non sectarian body to promote advancement of haematology including transfusion medicine through encouragement of research, teaching and technical methods. The body will also organize scientific meetings, publication of scientific material, and affiliation with other National and international organizations. Members of Governing body included

a. Lt. Gen. Muhammad Saleem as President
b. Dr. Khalid Hassan as General secretary
c. Dr. Birgees Mazhar Qazi as member
d. Dr. Waseem Iqbal as member
e. Dr. Hassan Abbas Zaheeras member
f. Dr. Mobina Ahsan Dhodhyas member
g. Dr. Farah Yasin as member
h. Col. Masood Anwar as member

It was also decided that First National conference will be held on 4th Oct 1998. Since then Annual conference is held regularly in all capital cities of Pakistan. The society is publishing a quarterly newsletter and providing a forum to the haematologists all over the country contributing as advisors in haematology, consultants, researchers and mentorship. Currently the Governing body includes

- Prof. Dr. Nisar Ahmed as president
- Gen. Parvez Ahmed as President elect
- Dr. Saima Farhan as Secretary

PSH National Advisory and Steering Committee

- Gen. Muhammad Saleem
- Prof. Abdul Hayee
- Prof. Muhammad Khurshid
- Prof. Abdul Khaliq
- Prof. Khalid Zafar Hashmi
- Gen. Masood Anwar
- Prof. Khalid Hassan
- Prof. Yasmin Lodhi
- Prof. Fozia Butt
- Gen. Suhaib Ahmad
- Prof. Samina Naeem
- Gen. Muhammad Ayub
- Prof. Fazle Raziq
- Prof. Javed Asif
- Brig. Muhammad Amin
- Col. Farooq Khatak
- Brig. Ehsan Alvi
- Brig. Zahoor ur Rehman
- Prof. Luqman Butt
- Brig. Farhat Abbas Bhatti
- Brig. Nadir Ali
- Brig. Muhammad Ashraf
- Prof. Tahira Zafar
- Prof. Zeba Aziz

- Prof. Tahir Jameel Ghazi
- Maj. Qaiser Husnain
- Col. Ghulam Rasool
- Prof. Tahira Tasneem
- Prof. Farzana Amjad
- Prof. Nouman Malik
- Dr. Barjees Mazhar Qazi
- Prof. Saeed Ahmed Malik
- Prof. Nighat Yasmin Ashraf
- Brig. Jalil Anwar
- Prof. Waseem Iqbal
- Dr. Syed Iftikhar Abdi
- Dr. Madoodul Manan
- Prof. Muhammad Hirani
- Prof. Zahoorul Latif
- Dr. Mian Muhammad Sharif
- Prof. Mussarat Niazi
- Prof. Muhammad Saeed Talpur

HAEMCON 2017, LAHORE

The 19th Annual PSH Meeting and International Haematology Symposium was held at Avari Hotel, Lahore from 16th- 18th February, 2017.
This annual event, held under auspice of Pakistan Society of Haematology, was attended by a large audience. It was unique platform for young Haematolgists to learn from their respected senior faculty and to benefit from their rich professional experiences.

The theme of this year HAEMCON was "Haematology, Challenges in Pakistan". It was aptly addressed to in the annual meeting and diverse, valuable advice in this regard was received from all the participating consultant Haematologists. The advancing field of haematology has many limitation in our country, and steps were proposed that can be implemented in keeping haematology standards in Pakistan at par with the international fraternity.
Haemcon2017, Lahore was fortunate to be honored by the presence of several distinguished international speakers. Amongst the luminaries were Prof. Dr. Catherine P. Hayward (President ISLH and Professor of Pathology and Molecular Medicine at McMaster University, Ontario, Canada), Prof. Dr. Timothy P Hughes (Haed of Haematology at Royal Adelaide Hospital), Dr. Robert McKenne (Professor Emeritus, Department of Lab Medicine and Pathology at University of Minnesota), Dr. Tariq Shafi (Consultant Haemato-Oncologist at Darent Valley Hospital, Kent, UK), Dr. Shahrukh Hashmi (Consultant Haematology and Stem Cell Transplant, Oncology Center, KFSHRC, Riyadh, Saudi Arabia), Dr. WaseemNagi (Consultant Haematologist at Broomfield Hospital, Chelmsford, UK), Dr. Muhammad Faisal Khanani (Consultant Paediatric Haematology/ Oncology), Dr. IrfanMaghfoor (Consultant Medical Oncologist/ Haematologists at KFSHRC, Riyadh, Saudi Arabia) and Dr. GhulamNabiKakepoto (Consultant Haematologist, University Hospitals of North Midlands, UK), Prof. Dr. Jean-Pierre Allain (University of Cambridge, UK) and Prof. Dr. Naeem Arshad Chaudhry (Professor, College of Medicine, Alfaisal University, Director, Research Unit, Oncology Centre, Consultant, Adult Hematology/HSCT, King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia).

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This year's Ibn-e-Sina Lecture was delivered by Maj. Gen(R). Masood Anwar. He shared his invaluable experience regarding history of Haematology in Pakistan and steps to move forward in this regard.

The scientific sessions covered all the diverse aspects of Haematology and included session on Leukemia, Lymphomas/ Plasma Cell Dyscrasias, Red Cell Disorders, Thalassemia and Haemoglobinopathies, Transfusion Medicine, Coagulation, Platelet Disorders, MDS and MPN and Stem Cell Transplant. Each session was addressed by a multitude of experts in their respective fields.

Senior Haematologists from all over Pakistan, including Prof. Dr. Moin-ud-Din, Maj. Gen. Pervez Ahmed, Prof. Dr. Shahid Pervez, Maj. Gen(R). Sohaib Ahmed, Prof. Dr. Tahir Shamsi, Dr. Bushra Moiz, Dr. Saba Jamal gave memorable talks in all the sessions. Other speakers included Dr. Naeem Chaudhry, Prof. Dr. Hassan Abbas Zaheer, Brig. Nuzhat Mushahid, Prof. Dr. Ayesha Junaid, Dr. Sana Jamil, Maj. Qaiser Husnain, Maj. Gen. Tariq Mehmood Satti, Prof. Dr. Abid Sohail Taj, Gen. Saleem Ahmed Khan, Gen. Naeem Naqi, Col. Muhammad Naeem, Prof. Dr. Atifa Shoaib, Brig. Ch. Altaf Hussain, Brig. Nadir Ali, Dr. Saqib Ansari and Dr. Adil Akhtar. Junior haematologists were also provided an opportunity to present their research as Poster and Free Papers. The three best papers and posters were awarded monetary prizes as source of encouragement. The list of recipient of best paper and poster are as follows.

Poster Winners:

1st Prize	2nd Prize	2nd Prize
Dr. Naveena Fatima from NIBD, Karachi	**Dr. Rumana Imtiaz** The Children's Hospital, Lahore	**Miss. Nasira** Punjab University, Lahore

3rd Prize	3rd Prize
Dr. Muhammad Noorulamin Rawalpindi Institute of Cardiology, Rawalpindi	**Dr. Shamila Tahir** University of Health Sciences Lahore

Oral Presentation Winners:

1st Prize	2nd Prize	2nd Prize	3rd Prize
Dr. Maheen Rana University of health sciences, Lahore	**Dr. Maria Khan** Armed Forces Institute of Pathology Rawalpindi	**Dr. Sadia** Punjab University, Lahore	**Ayesha Chaudhry** Punjab University Lahore




Haemcon 2017 was also a stage where lifelong dedication and commitment to the field of haematology were appreciated in the form of Lifetime Achievement Award. The recipients included renowned haematologists of Pakistan. Who have given tremendous contributions to the establishment and advancement of Haemtaology in Pakistan. The distinguished haematologist were Lt. Gen(R). Muhammad Saleem, Maj. Gen(R). Masood Anwar, Prof. Dr. Muhammad Khursheed, Prof. Dr. Abdul Hayee, Prof. Dr. Khalid Zafar Hashmi, Prof. Dr. Moin-ud-Din and Prof. Dr. Khalid Hassan.

The Gala Dinner at Haemcon2017 was a memorable affair. Apart from Lifetime Achievement Awards, there were two book launching ceremonies. "PSH book of Haematology" Launched by Pakistan Society of Haematology, and "How We Manage Blood Disorders with Limited Resources" by National Institute of Blood Diseases, Karachi are two valuable additions to the library of Haematology textbooks.

The Pre-Conference and Post-Conference Workshops as part of Haemcon2017, Lahore were generously attended by a large number of residents as well as senior haematologists. They covered a wide range of practical Haematology, from Immuno haematology to Morphology, haemostasis/ Thrombosis to haemoglobinopathies and the role of haematologists in managing their respective disorders in systemic diseases. A workshop for medical lab technologists as well as workshops on Medical Audit and Medical Writing completed a diverse workshop program in Haemcon2017, Lahore. A tremendous positive feedback from the attendees was received and it is hoped that these workshops would go a long way in improving the practical skills of our haematologists.




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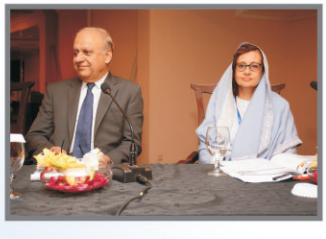









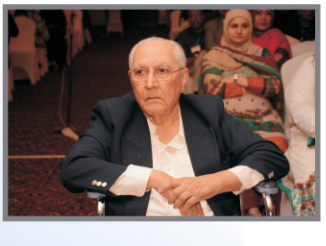


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JUVENILE MYELOMONOCYTIC LEUKEMIA ; A CASE REPORT.

Tooba Fateen, Saima Farhan, Nisar Ahmed
CH & ICH, Lahore

Abstract:

Juvenile Myelomonocytic leukemia belongs to a group, myelodysplastic – myeloproliferative disease. This is a disease of early childhood. It is difficult to distinguish from other myeloproliferative syndrome specially from chronic myeloid leukemia (CML) .They have similar presentation and bone marrow findings but JMML differ from it due to presence of absolute monocytosis with dysplasia and absence of Philadelphia chromosome or BCR-ABL fusion protein along with other coexisting features.Here we report a patient with JMML, who had typical clinical and laboratory findings and discuss further the usual presentation and course of this important childhood entity.

Key words: Juvenile myelomonocytic leukemia, chronic myeloid leukemia, monocytosis

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Introduction:

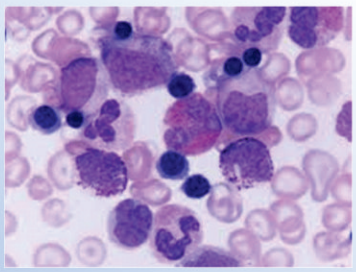
Juvenile myelomonocyticleukaemia (JMML) is characterized by excessive growth of exclusively myelomonocytic cells in both mature and immature forms. Patients with JMML usually present before the age of 2 years with hepatosplenomegaly, lymphadenopathy, infection and skin disease. JMML incidence approaches 1.2/million persons in the United States. [1,5]The diagnosis requires the absence of the Philadelphia chromosome or BCR- ABL fusion protein, monocytosis of more than 1 x 10^9/l on peripheral blood and bone marrow blast count of less than 20%.

Cytogenetic abnormalities have been detected in patients with JMML of which monosomy 7 is the most frequent abnormality[3]

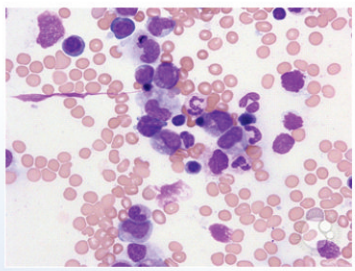
Case Report:

Patient named ABC S/O DEF, two and half years old , resident of Lahore had referred to Hematology, Transfusion medicine and bone marrow transplant department of The Children hospital & Institute of child health Lahore on 15thFeb,2017. He had fever which was low grade, on and off for the past one and half month, episodes of sore throat and diarrhea intermittently and then developed bilateral propotosis for the past one month. There was history of one PRBCs transfusion in last month. The child was product of consanginous marriage. Mother had one miscarriage before him and child had no significant past medical history.On examination he was pale child with splenomegaly and bilateral proptosis was there. CBC count showed Leucocytosis with Thrombocytopenia RBC count was 2.24x10^6/ul, Hb was 6.2 g/dl, and total leucocytes were 98 x10^3/ul with differential of neutrophils: 31%, Lymphocytes: 11%, monocytes. 18%Eosinophils: 4%, Myelocytes: 2%, Metamyelocytes: 31%,Blasts: 3% and 22 NRBCs/100wbcs. Platelets were 124x10^3/ul.Peripheral smear examination revealed anisocytosis with mild hypochromic/micrcocytic blood picture. Leucocytosis with leucoerythroblastic blood picture along with absolute monocytosis was present. Dysplastic monocytes and neutrophils were striking. (Figure-01)CRP was normal. Serum LDH markedly raised (1240 u/L). HPLC showed Hb A 92 %, Hb F 5%, Hb A2 3%.i.e raised Hb F.

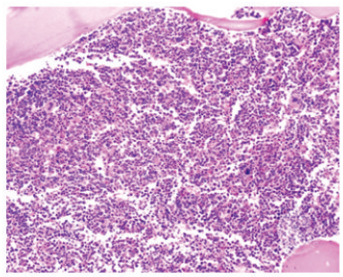
Bone marrow examination revealed hypercellular bone marrow aspirate showing relatively reduced erythropoiesis and hyperplastic leucopoiesis with differential of Polys: 30%, monocytes: 15%, Eosinophils: 3%, Myelocytes: 18%, Metamyelocytes: 10%, blasts: 9% Erythropoiesis: 15%. Dysmyelopoiesis and dysmegakaryospoiesis was observed. (Figure-02a) Trephine biopsy was adequatelenghth showed 95% cellularity. Trilineagehemapoiesis seen and 12% cellularity is replaced with atypical mononuclear cells. (Figure-02b)Karyotyping for chromosomal defects turned out to b negative. Molecular studies for BCR-ABL1 done, which was negative. The peripheral smear findings, Bone marrow examination along with molecular studies was suggestive of Juvenile Myelomonocytic Leukemia.



(Figure-01)



(Figure-02a)



(Figure-02b)

Discussion:

JMML belongs to WHO group Myelodysplastic-myeloproliferative neoplasms and characterized by overproduction of monocytic and granulocytic cells that infiltrate different organs, including the spleen, liver, lung, and gastrointestinal tract.Morphologic evaluation of peripheral blood smear is the most important step in establishing the diagnosis. Immature monocytes, along with myelocytes, metamyelocytes, and erythroblasts, are usually found.[1,2,4.] Almost all cases show striking monocytosis, with dysplastic cells and an absolute monocyte count $>1 \times 10^9$/L is required for diagnosis of JMML.[4,5]. Further more white cell count of more than 10×10^9/l, myeloid precursors on peripheral blood, hypergammaglobulinaemia is also present in majority of cases.[1,4]A remarkable feature of many JMML cases with normal karyotype is a markedly increased synthesis of fetal hemoglobin (HbF).[4]

Other pathological findings include infiltration of various non-haemopoietic organs (skin, lungs, intestines) with leukaemicmonocytic cells like proptosis was seen in our indexed case scenario.Monosomy 7 as well as neurofibromatosis type 1 abnormalities are also reported in association with JMML[3]

Chromosomal studies of leukemic cells show incidence of monosomy 7 in approximately 25% of patients with JMML and other abnormalities incidence is in 10% of children. The majority of cases i.eabout 65% have a normal karyotype.[6,7].Most of the patients in the study by Azma RZ, zarina A L et all had normal karyotype as well as in our reported case.[1]The clinical picture of early phase of JMML can be mimicked by a number of human herpesvirus infections, leukocyte-adhesion deficiency, infantile malignant osteopetrosis, hemophagocyticlymphohistiocytosis, and Wiskott-Aldrich syndrome.[1,8]

The spectrum of mutations described thus far in JMML occur in genes that encode proteins that signal through the Ras/mitogen-activated protein kinase (MAPK) pathways which lead to uncontrolled proliferation of white cells. These include NF1, NRAS, KRAS, PTPN11, and most recently CBL is discovered.[9]Thisopen the door for new opportunities related to both diagnosis and therapy

Allogeneic HSCT is the ultimate cure for most children with JMML. It can result in long-term survival of many patients[9,10].JMML with NF-1, somatic PTPN-11, K-RAS mutations and for the vast majority of patients withsomatic N-RAS mutations, HSCT is the best choice.Children with germline CBL mutations and JMML are reported to have spontaneous regression of their disease.[11]Morbidity and mortality often occur due to bleeding, infection or non-haematopoietic organ failure due to monocytic infiltration. Age less than 2 years, with a low platelet count and a high fetal haemoglobin level are the comonly reported indicators of poor prognosis.[1,2,5]

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PRESIDENT ACTIVITIES

SEMINAR ON DIAGNOSIS OF HEMOLYTIC ANEMIA

Seminar on "An approach for the diagnosis of Hemolytic Anemias" was held on 20th April, 2017 @ Independent University Hospital, Faisalabad. It was first of its kind effort by Pakistan Society of Hematology in collaboration with Pathology department, Independent Medical College, Faisalabad. It was attended by a large gathering of hospital faculty of all departments and students of MBBS.

Prof. Dr. Nisar Ahmed, President PSH, delivered a lecture covering different aspects of Hemolytic Anemias followed by actively participated question and answer session.

Dr. Muhammad Usman, FCPS Hematology, Associate Prof of Pathology, Independent Medical College, Faisalabad thanked and appreciated Prof. Nisar Ahmed for coming Faisalabad and asked his help and guidance for

regular seminars in Faisalabad. He also discussed the prospect of holding PSH conference in Faisalabad, to make young doctors and undergraduates more aware about Clinical Hematology.

جنگ
ہیلتھ اینڈ فٹنس

16 اپریل
سنڈے میگزین 2017

ہیموفیلیا.....متاثرہ لڑکیوں، عورتوں کی آوازیں سنو

ہیموفیلک بچّے کی ناف کاٹتے ہوئے خون نہیں رُکے گا، جو مرض کی واضح علامت ہے

90 فی صد مریضوں کو علاج کی سہولت میسّر نہیں، شادی سے قبل خون کا ٹیسٹ لازمی ہونا چاہیے

عالمی یوم کے موقعے پر، چلڈرن اسپتال، لاہور کے شعبۂ ہیموٹولوجی کے سربراہ، پروفیسر ڈاکٹر نثار احمد سے بات چیت

newsLETTER
Vol. 11, No. 1, Jan, March 2017
Pakistan Society of Haematology

UPCOMING EVENTS

NATIONAL

- 11th FCPS Haematology Intensive Course.
  Armed Forces Institute of Pathology, Rawalpindi.
  Dated: 27th – 30th July, 2017.
  For Contact: Brig. Ch. Altaf Hussain, Cell: 0300-5464272,
  Email:altaf444@gmail.com.

- 1st PSH National Symposium,
  Serena Hotel Quetta 12th August, 2017
  For Contact: Prof. Dr. Nadeem Samad Shaikh, Cell: 0300-8380847,
  Email:drnadeemsheikh@hotmail.com

INTERNATIONAL:

- International Society of Blood Transfusion (ISBT).
  27th Regional Congress of ISBT, Copenhagen, Denmark. 17th – 21st June, 2017.

- European Haematology Association (EHA).
  22nd Congress of EHA, Madrid, Spain, 22nd – 25th June, 2017.

- International Society of Thrombosis and Haemostasis (ISTH).
  26thBiennial Congress and 63rd Annual Scientific and Standardization Committee Conference at Berlin, Germany 8th – 13th July, 2017.

Large Granulocytic Leukemia- A Case Repot

Aysha Khan*, Altaf Chaudhry*, Sara Waqar Khan*, Mukarram Bashir*, Pervaiz Ahmed*, Hamid Saeed*
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Abstract

Large Granulocytic leukemia (LGL), previously known as T cell chronic lymphocytic leukemia (T CLL), is a rare disorder as it represents only about 2-3% of all Lymphoproliferative disorders.Most of the patients with this disorder run an indolent course with vague symptoms and are incidentally diagnosed when they seek doctor's help for some other complaint. These patients are easily missed as their blood counts are well maintained and have only mild lymphocytosis which goes unnoticed. In country like Pakistan only 3-4 cases have been previously reported and its exact incidence in Pakistan is still unknown.

Key words: Large granulocytic leukemia (LGL) previously known as T cell chronic lymphocytic leukemia (T CLL)

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Case report .

We report a case of 59 years old man who works at a medical store, is married and has four children. He had complaints of generalized body aches, lethargy and fever on and off for last six months. His fever wasassociated with upper respiratory tract infections,which responded to antibiotics. He also had shortness of breath and weight loss. Patient had a fall in hemoglobin (Hb) 5 months back to 4g/dl for which he received transfusion of 4 units of red cell concentrates (RCCs). He also gives history of steroid intake for 15-20 days only, but no document was available. No significant finding was present on examination. He had no lymphadenopathy or organomegaly.

Figure 1. Picture taken with consent of the patient

His peripheral blood film showed: white blood cell (WBC) count of $10.22X10^{9}$/L, Hb 9.4 g/dl, Mean corpuscular volume (MCV) 99 fl, platelets $247X10^{9}$/L with differential count of neutrophils 16 %(absolute neutrophilic count 1.6) and lymphocytes 75% (absolute lymphocyte count 7.5) as shown in fig 2. In peripheral blood picture, typical large granulocytic lymphocytes with abundant cytoplasm and large granules,were only 5% of the total lymphocytes. Restall were mature looking lymphocytes.

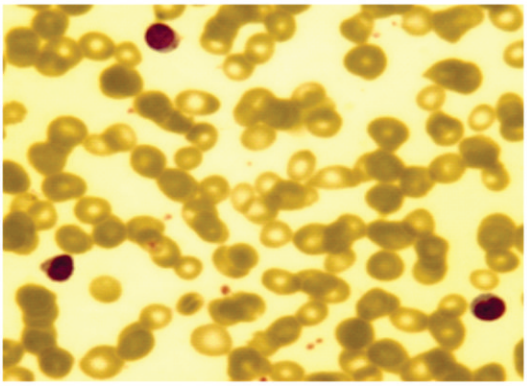
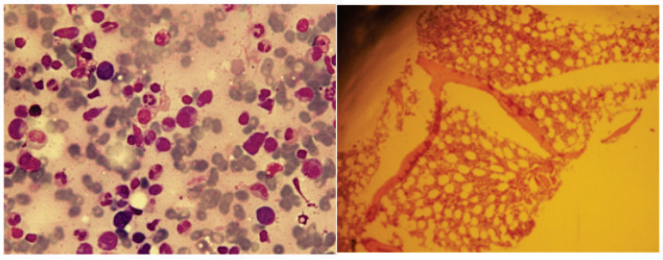


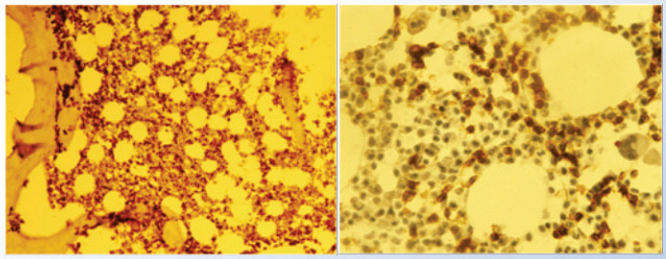
Figure 2. Peripheral blood film showing LGLs and lymphocytes

His bone marrow examination was within normal limits with normal erythroid precursors. Trephine biopsy showed diffuse increase in lymphocytes.

The result of immunohistochemistry showed these cells were negative for CD20 but positive for CD3.CD3 was diffusely positive showing their T cell nature. CD4 was negative and CD8 showed diffuse positivity showing its clonal nature. We also applied CD56 to know aggressiveness of disease which was negative. This is shown in fig 3and 4.

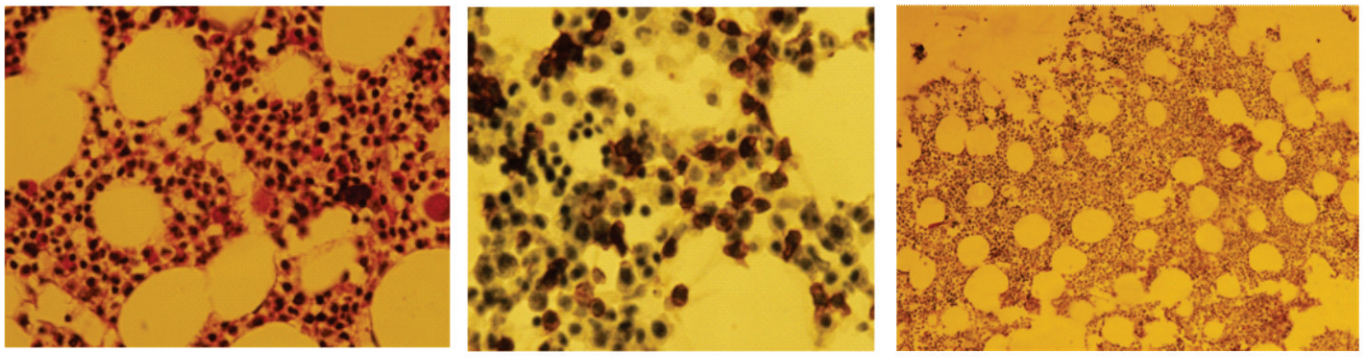


Bone marrow aspirate Trephine biopsy



CD3 diffusely positive CD3 diffusely positive

Figure 3. Bone marrow aspirate and trephine biopsy



CD56 absent | CD8 Positivity | CD 4 Negative

Figure. 4 Immunohistochemistry results

Flowcytometry was also performed on patient's bone marrow sample which showed the following results: CD45(99%),CD5(97%),CD3(98%),CD20+CD3(0%),CD19(0%),CD22(0%),HLADR(0%),CD10(0%),CD11c(0%),CD8(90%),CD4 (7%).

HLA typing was also carried out and patient was found to be positive for HLA DR4 which has a strong association with LGL.

These results again support the findings of immunohistochemistry. On the basis of these results he was diagnosed as a case of LGLor previously T-CLL.

We also carried out further tests to find out its association with other diseases. His liver function tests, renal function tests, viral screening, C reactive protein (CRP), RA factor, immunoglobulins levels and autoimmune profile, all turned out to be normal.

Patient was given tablet folic acid and was on regular follow up. A month later he again developedanemia and his Hb dropped to 7g/dl. He was given blood transfusion and he was started with oral Methotrexate at the dose of 10mg per week for a month. His dose was increased to 15mg per week for another month. But follow up of patient again showed decreased hemoglobin after two months. Packed red cells were transfused as and when required. Patient was then switched to tablet Deltacortil 60 mg/ day which continued for a month. InjectionsEpogen (synthetic EPO) sub cutaneous were also given. After eight months of diagnosis and a total 20 transfusions, patient is much better clinically and has not required transfusion for last ninety days. His recent Hb is 13.9g/dl. Patient is under close surveillance.

Discussion

LGL leukemia was first diagnosed around 3 decades back as T-CLL by Mc Kenna et al in 1977. It has been called with different names such as T-gamma lymphoproliferative disorder,T-suppressor cell chronic lymphocytic leukemia,T-cell lymphocytosis with neutropenia till 1993, when Loughran suggested the term large granulocytic leukemia (LGL). [1]

LGL represents 2% of the cases of monoclonal proliferation of B cells, T cells and natural killer cells as mature lymphocytic leukemia in Western countries .The male: female ratio of the reported cases is approximately one.Majority of cases occur in the age range of 38-72 years. [1] Our described patient also belongs to the same age group.

Pathogenesis of LGL is not very well understood. However it is postulated that constant antigenic stimulation leads to proliferation of these oligoclonal cells, finally leading to LGL. It is also suggested that this leukemia is a disorder of dysregulation of apoptosis through abnormalities of Fas/Fas ligand pathway. [2]

T-LGL usually expresses CD3, CD8, and T-cell receptor (TCR) α/β. [3] T-LGL typically has cytotoxic granular proteins. [4] Immunohistochemical analysis of bone marrow (BM) biopsies with antibodies to these antigens and CD8 can be used to confirm a diagnosis of T-LGL. [5]

The classic immunophenotyping of T-LGL is CD3+/CD4-/CD8+/CD16+/CD57+. [6, 7] CD5 and/or CD7 are variably expressed and are often aberrantly diminished on malignant circulating LGL cells. Occasional case reports have reported CD4+/CD8- T-LGL leukaemias, [8] double-positive CD4+/CD8+ T-LGL leukemia [9] and double-negative CD4-/CD8- cases [10]. CD56 expression is associated with anaggressive clinical course. [11, 12] Expression of NK related antigens CD16 (~80%) and CD57 (approximately 100%) along with granzyme B and TIA-1is usual in T-LGL leukemia. [13, 14]. However expression of CD57, granzyme B, TIA-1 and TCR expression could not be evaluated in this case. In majority of the cases reported in the literature, the TCR is of the □/□ subtype [10] and very rarely of the TCR □/□ subtype. [10, 15] Natural killer cell lymphoproliferative disorder was excluded in this patient on the basis of positivity for surface CD3 (NK cells are negative for CD3) and characteristic morphology of LGLs.

In most of the patients who are CD4 positive,common symptoms are neutropenia, anemia, splenomegaly, rheumatoid arthritis, or other autoimmune diseases, alongwith higher incidence of association with malignant diseases. [16]

The most common presentation of LGL patients is persistent lymphocytosis, with an LGL count ranging from 7.8×10^9/L to 20×10^9/L. [17] But our patient presented with absolute lymphocyte count of 7.8×10^9/L and LGL count of only 0.39×10^9/L in peripheral blood. No lower limit of large granulocytes has been defined for diagnosis of LGL; however it is usually above 0.2×10^9/L.Bone marrow aspirate may be required to confirm the diagnosis, especially in those with low absolute numbers of circulating LGLs.

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Anemia maybe the presenting feature with vague symptoms of lethargy, shortness of breath on exertion and feeling of being unwell. Our patient only had anemia and no other associated disease. It can occur due to various causes. Pure red cell aplasia is a well-known complication of this disorder as well as Coombs test positive hemolytic anemia. However both of them were not present in our case. Relative Folate and B12 deficiency also contribute to pathogenesis of anemia.

Other important presenting signs are neutropenia and splenomegaly [17] butthere was no clinical or radiological evidence of these two in our patient.

Currently, there is no standard treatment for patients with T-LGL. For asymptomatic T-LGL patients with an indolent course, a wait-and-see approach can be considered [16] Cyclosporin, low dose Cyclophosphamide and Methotrexate are the first line treatment options for symptomatic patients. Steroids are best to be avoided as patients are usually more prone to develop infections and steroid intake further increases chances of infections.

T-LGL clonality could not be confirmed in this case by a T-cell receptor gene rearrangement because our facility lacks this capacity. The clinical features and laboratory findings in our study were similar to that reported in the literature.

Conclusion

It remains unclear whether the incidence of LGL is truly low or the disease has been under diagnosed because most cases are asymptomatic at presentation. This raises the importance of reviewing the peripheral smears and carrying out flowcytometry and immunohistochemistryin asymptomatic patients who have persistent lymphocytosis or neutropenia. It is often difficult to identify phenotypically abnormal

T or NK cells than abnormal mature Bcells by flowcytometry. In addition, the classification of T-cell neoplasms is less well established than that of B-cell neoplasms, and usually requires assimilation of information from multiple sources. Systematic long-term follow-up studies need to be performed.

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OBITUARY:

Prof. Dr. Moin-ud-Din, an eminent haematologist and very respected member of our PSH family passed away on 6th May, 2017.

Dr. Moinwas Professor of Hematology, Dean Faculty of Medicine and Dentistry and Director Institute of Hematology, at Baqai Medical College and University, Karachi. He had done his post-graduation in both laboratory and clinical hematology from Canada. He was the senior member of Pakistan Society of Haematology and Pakistan Association of Pathology. He was highly qualified hematologist who had a vast experience of working in the leading institutions abroad He was also a well-known author of many books.

Please recite Surah-e-Fatiha for the departed soul. We pray that may Allah bless him in the hereafter and grant patience to his family.

Ameen.

Your Views And News

The Pakistan Society of Haematology newsletter is published on a quarterly basis and is a quick guide to all the happenings in the haematology community. To improve the newsletter, your comments and suggestions are welcome. We further encourage you to send us write ups and photographs of any PSH events in your city/province and they would be featured in our upcoming newsletters.

For contact, please refer to our corresponding address. We hope to hear from you on a regular basis.

This news letter was designed and edited by :

Dr. Anum Wasim

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