NEWSPID

NEWSLETTER from IS**PID**
Indian Society of Primary Immune Deficiency

JAN-FEB 2017

Message from Editor

Dear colleagues,

Hope you have had a great beginning to the year and wish you a fantastic 2017.

On behalf of the Indian Society of Primary Immune Deficiency, I welcome you to the revamped edition of our bimonthly newsletter. Since its inception in 2011, ISPID has been striving to sensitize colleagues regarding the existence of primary immune deficiencies, to develop facilities for PID testing and treatment in India and to encourage scientific collaboration with the international community.

This newsletter aims at highlighting one case of PID in every issue. In this issue, we will discuss the clinical and laboratory aspects of a case of SCID with the treating center that managed the case. We also bring to you upcoming events, interesting journal articles, clinical and laboratory images and updates on our website. We look forward to your continued support.

Hope you enjoy this newsletter.

Nita

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Indian Society for Primary Immune Deficiency

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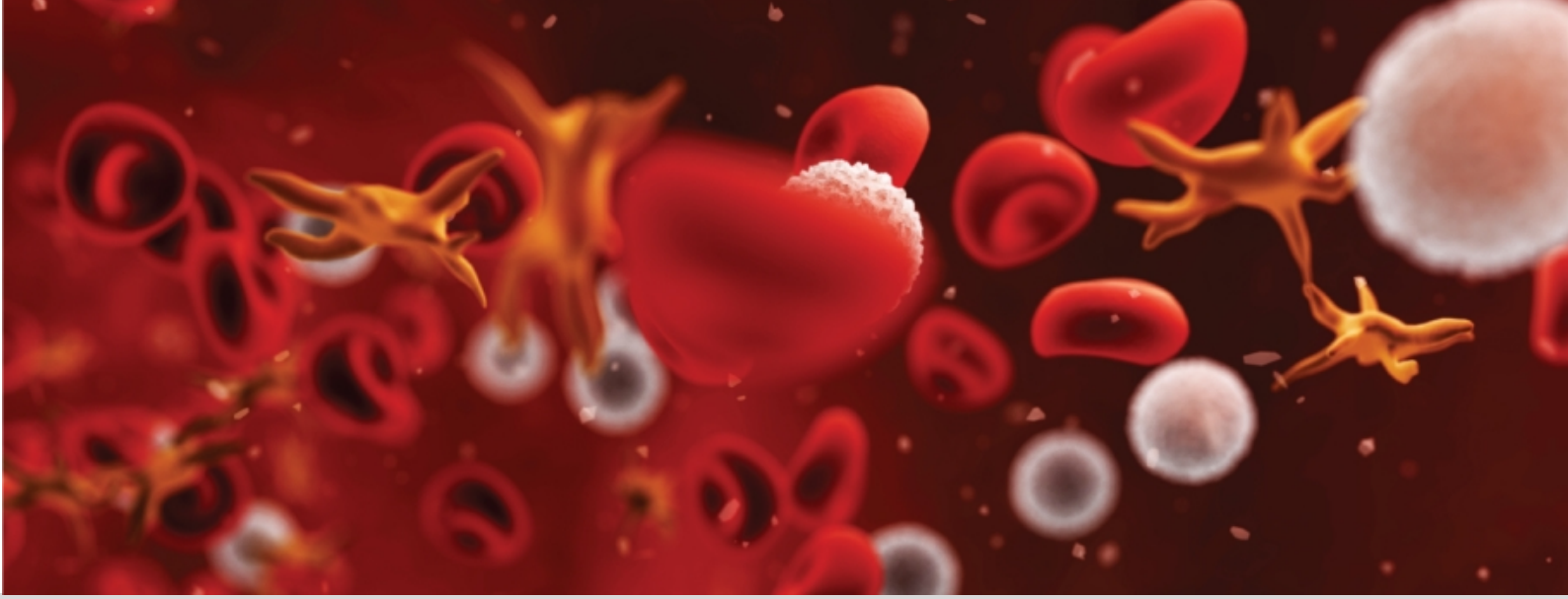

Case of the month

Clinical discussants
Dr. Dinesh Kaul
Dr. Nita Radhakrishnan

Laboratory discussant
Dr. Sabina Langer

Center
Sir Ganga Ram Hospital
Delhi

A 4-month-old boy, 2nd born to non consanguineous parents, full term, birth weight 2.8kg with no neonatal issues, presented to us with complaints of intermittent fever and cough for 3 weeks. Parents also noticed a swelling below left axilla and some hyper-pigmented spots on the skin for last 2 weeks. There was history of recurrent cough since neonatal period and the child was admitted twice for respiratory infection at another center prior to this. Child has been vaccinated for age (BCG, OPV, Hepatitis B, Hib, DPT) and is being exclusively breast-fed, with no significant family and antenatal history.

At admission, weight: 4 kg (<3rd centile), length 55 cms (<3rd centile), head circumference 40.5 cms (50th centile). Hyperpigmented macules noted on the trunk. Child was afebrile and had left axillary lymphadenopathy (1.5x1cm). Liver was enlarged 4 cms below right subcostal margin and spleen 3 cms along its axis. Cardiovascular system, respiratory system and central nervous system were normal on examination. Child was admitted for evaluation of fever with lymphadenopathy, hepatosplenomegaly and failure to thrive.

Investigations

CBC: Hb: 12.6gm/dl, WBC count: 8400 cells/µL (N81%, L3%), Platelet count: 5,07000/µL

X-ray chest: normal lung fields, thymic shadow absent

TORCH (IgM) negative, Blood culture and urine culture sterile.

HIV antibody test (mother): negative

FNAC of lymph node: inflammatory cells comprising of polymorphs and macrophages. Numerous acid-fast bacilli seen.

GeneXpert/RIF for MTB: positive

Bone marrow aspiration study: Marked lymphopenia, cellular marrow, with features of hemophagocytosis.

Immunoglobulin profile

IgA:	< 2.00 (8-90mg/dl)
IgG:	16.70 (200-1200mg/dl)
IgM:	5.40 (10-90mg/dl)
IgE:	0.11(.08-6.12 IU/ml)

Lymphocyte subset analysis Absolute lymphocyte count: 259/µL			Age adjusted normal 0-11 months	
	%	Absolute number (cells/µL)	Normal %	Per µL
CD 3	43.7%	118	58-85%	2170-6500
CD 19	3.7%	10	11-45%	430-3300
CD 56	32.6%	88	3-19%	80-340

Diagnosis

Severe Combined Immunodeficiency T-B-NK+ subtype

Q1. How did you suspect primary immunodeficiency in this patient?

DK: Infant presenting with recurrent pneumonia needed hospital admission for IV antibiotics with failure to thrive and evidence of BCG lymphadenitis.

Q2. What are the infections that you would screen for in sick infants with suspected combined immunodeficiency?

DK: Essentially any infection is possible in patients with severe combined immunodeficiency. We would evaluate for TORCH group of infections including CMV, Pneumocystis jiroveci, fungal infections and bacterial infections. In patients with combined immunodeficiencies, serological investigations are nor reliable in view of poor B cell function. We would rely on PCR or direct microbiological detection pf pathogens whenever possible.

Q3. What are the differentials you would consider for axillary lymphadenopathy in a child with suspected SCID?

DK: BCG infection is a strong possibility as the child has received BCG at birth. However we would still look for fungal and bacterial infections. FNAC or lymph node biopsy should be sent to microbiology laboratory in addition to cyto/histopathology.

Q4. How will you manage BCG adenitis in an immunocompromised child?

DK: The infant needs to be started on 4-5 drug antitubercular treatment like rifampicin, isoniazid, pyrazinamide, ethambutol and ofloxacin. The anti tubercular drugs can be modified later according to drug sensitivity reports.

Q5. What are severe combined immunodeficiencies? Severe combined immunodeficiencies (SCID) are potentially fatal disorders with absence of T and B lymphocyte function. There are several genetic variants of SCID all of which predispose to infections.

Q6. What are the immunological investigations done in patients with suspected combined immunodeficiency?

SL: Basic immunological assessment should include assessment of total lymphocyte count, lymphocyte subpopulations (T cells, B cells and NK cells) as well as serum immunoglobulins. Results of these investigations should be interpreted alongside age specific normal values. Many patients would require more specialized immunological investigations like T lymphocyte function, T cell repertoire and extended immunophenotyping.

Q7. What would you keep in mind while interpreting lymphocyte subsets?

SL: Age appropriate normal values should be used. During acute illness absolute lymphocyte count might be falsely low giving erroneous reports. In such cases, repeating the sample after the period of acute illness is important.

Q8. In pediatric practice, what precautions will you take while handling babies with suspected SCID?

NR: Any patient with suspected SCID should undergo urgent investigations and needs to be referred to a higher center with expertise as early as possible. They would require barrier nursing, prophylaxis and quick evaluation. Also, live vaccines are contraindicated and ATT may be started in those who have received BCG at birth. All cellular blood products should be irradiated.

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Diagnosis

Severe Combined Immunodeficiency T-B-NK+ subtype

Q9. How will you treat this newly diagnosed case of SCID?

NR: Co-trimoxazole and fluconazole prophylaxis, ATT, 3-4 Weekly IVIG will be started at diagnosis. CMV status of the infant and mother has to be assessed and treatment given appropriately. HLA typing of patient and siblings will be advised and the family will be counselled for bone marrow transplantation.

In addition, molecular diagnosis will be sought for providing genetic counselling and prenatal diagnosis for next pregnancy.

Q10. How early should bone marrow transplantation done in this child?

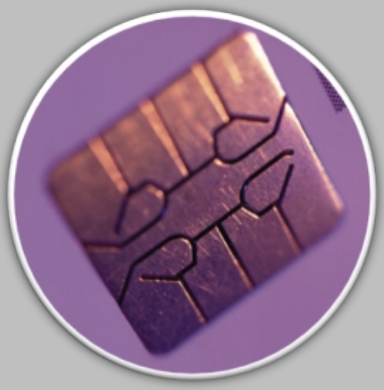
NR: As early as possible would be the right answer. SCID is disease that is universally fatal without stem cell transplantation. Transplanting children early in infancy (either in the pre-symptomatic stage or when diagnosed with minimal infections) has significantly better results. This is the advantage of diagnosing patients though neonatal screening. Unfortunately, we do not have a screening program in place for SCID in India. Absolute lymphocyte count is a cost effective investigation that can help us identify potential SCID patients early.

Q11: How will you select a donor for bone marrow transplantation?

NR: Bone marrow transplant is an emergency for SCID patients. Hence unlike in many other diseases, we do not have much time to wait for an ideal donor. If siblings are not a match, then one would proceed with an unrelated donor or even a haploidentical (parent) donor. The longer one waits, the more are the chances that the child develops infections that make the transplant riskier.

Q12: What are the other treatment options available for such babies?

NR: Gene therapy is offered for few subsets of SCID patients in few research centers.



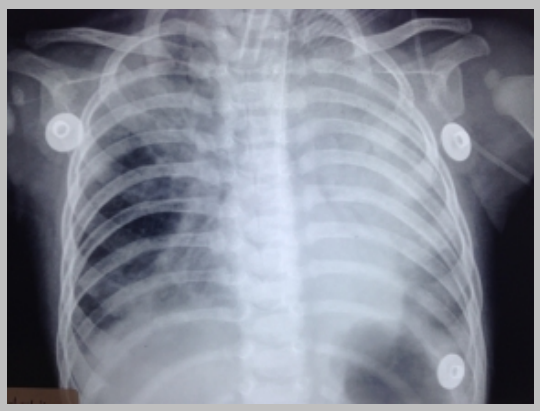
Event Watch

1. 4th International conference on Primary Immunodeficiency diseases (ICPID), 11-13 March 2017, The Leela Palace, Bengaluru. For registrations, contact: icpid2017@gmail.com
2. CME on Primary immunodeficiencies in pediatric practice. 23 Feb 2017, Sir Ganga Ram Hospital, New Delhi For registrations, contact: 011-42251856 or ispidofficial@gmail.com
3. Introductory course on Primary Immunodeficiency Diseases, at Guwahati 15 October, 2017. For registrations contact, Dr Rashna Dass rashnadass@gmail.com
4. ESID 2017
   2017 meeting of the European Society of Immunodeficiencies, 11-14 September 2017
   http://esid2017.kenes.com

Journal Watch

1. Update on the safety and efficacy of retroviral gene therapy for immunodeficiency due to adenosine deaminase deficiency. Blood 2016 128:45-54
2. X-linked Hyper IgM Syndrome Presenting as Pulmonary Alveolar Proteinosis Journal of Clinical Immunology August 2016, Volume 36, Issue 6, pp 564-570
3. Clinical heterogeneity of dominant chronic mucocutaneous candidiasis disease: presenting as treatment-resistant candidiasis and chronic lung disease Clinical Immunology April 2016

Image Watch



Pneumocystis jiroveci pneumonia

Diffuse bilateral infiltrates
Often perihilar in distribution
Perihilar adenopathy rare
Small pneumatocoeles often seen

About ISPID

The Indian Society of Primary Immune Deficiency was founded in 2011 and has currently more than 100 members.

We hope to generate interest in PIDs and help clinicians achieve a diagnosis and guide their management. We organize periodic courses to sensitize pediatric and adult colleagues to primary immunodeficiencies.

Kindly visit our website for further information www.ispid.org.in

We would love to hear from you.

Please send your comments, suggestions and cases/images for discussion to the following address

ispidofficial@gmail.com

Editor, NEWSPID