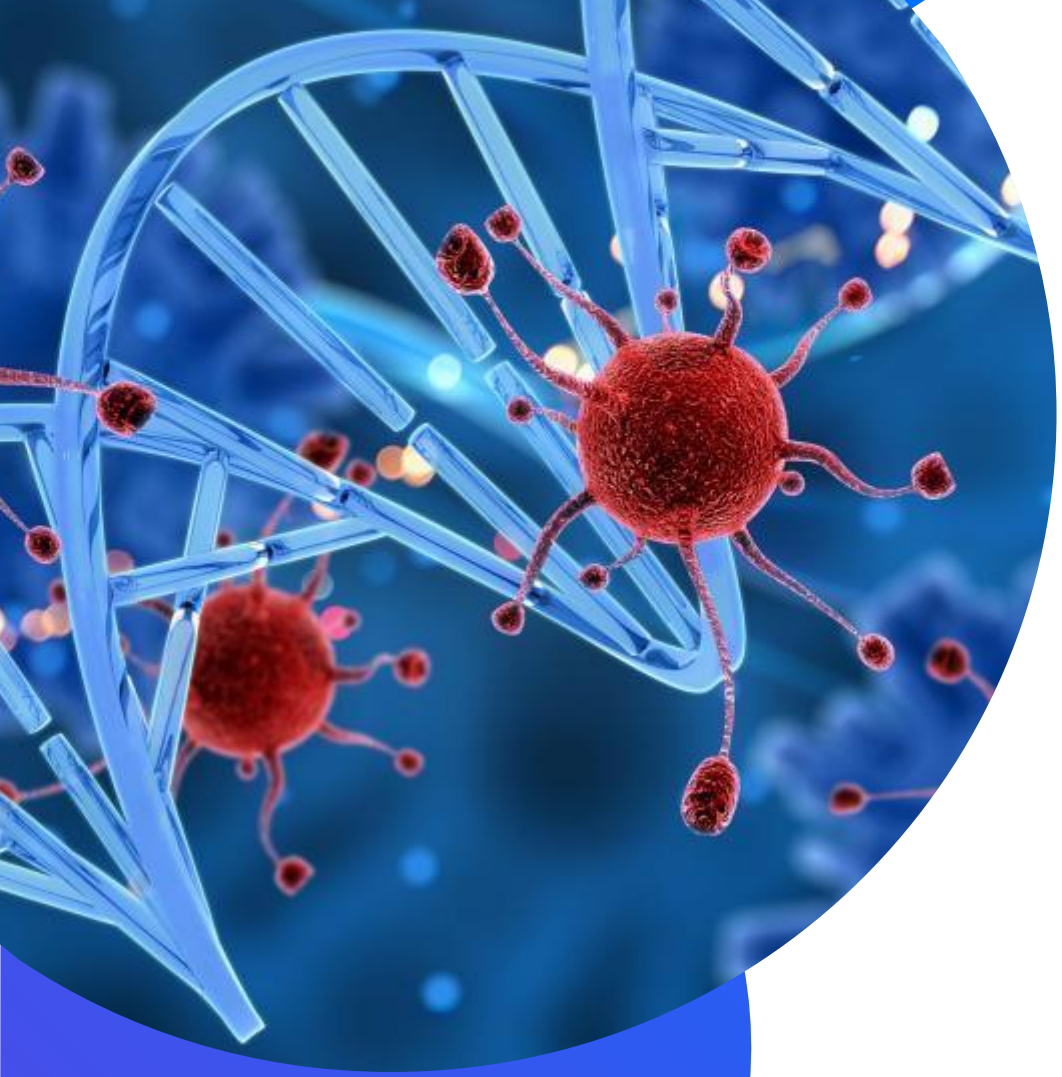

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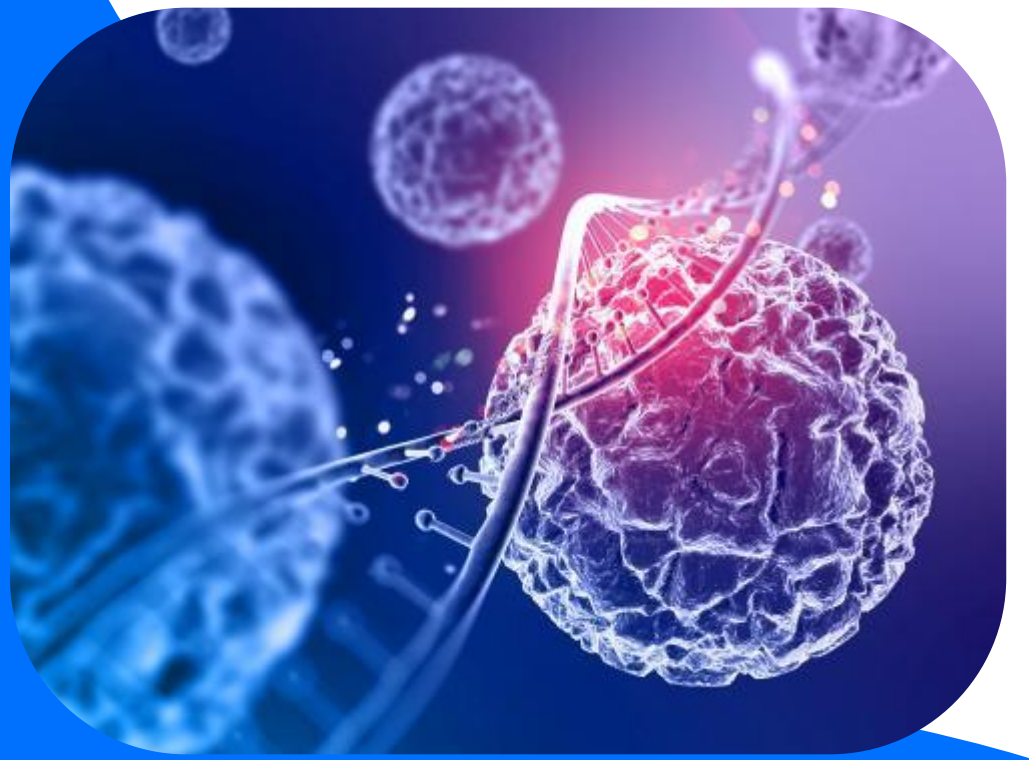
A Case Report of Recurrent Opportunistic Infections in a Child with Severe Combined Immunodeficiency (SCID)

Dr GUELLATI Imane
Medical Microbiolgy Specialist

CHU DE SETIF

Contents

Introduction



Introduction

Severe combined immunodeficiency (SCID) is a primary genetic immunodeficiency disorder that typically manifests in early childhood.

Common symptoms: diarrhea, pneumonia, otitis media, sepsis, and skin infections.

Early recurrence of opportunistic infections with lymphopenia requires immunological investigation.

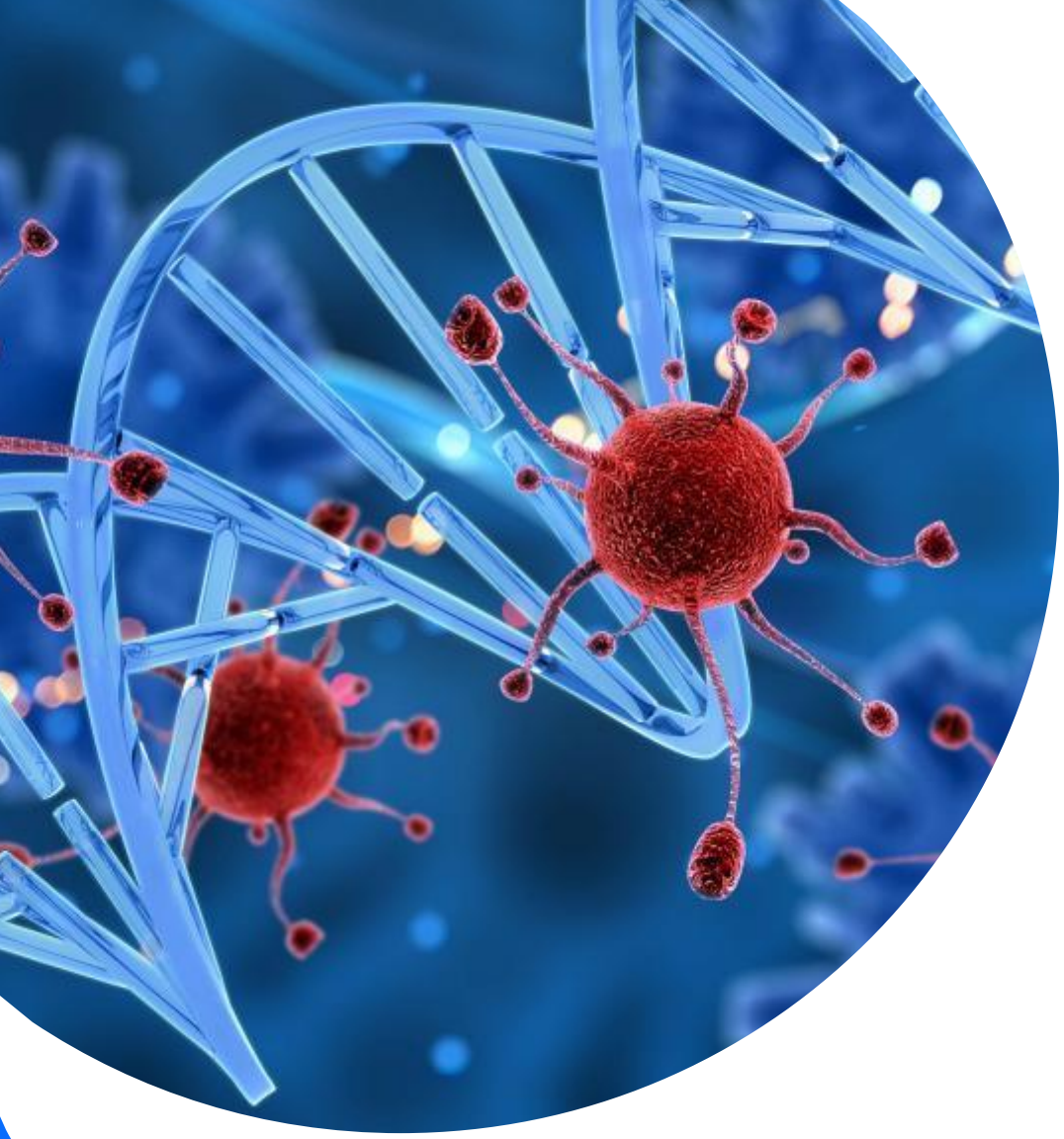
Opportunistic Pathogens

Bacterial infections in SCID patients can include pneumonia caused by encapsulated organisms.

Viral infections such as cytomegalovirus (CMV) are common due to the lack of T-cell mediated immunity.

Fungal infections: Fungal pathogens like Pneumocystis jirovecii can cause severe pneumonia in these patients.

Protozoal infections: Infections such as toxoplasmosis can also occur in patients with SCID.



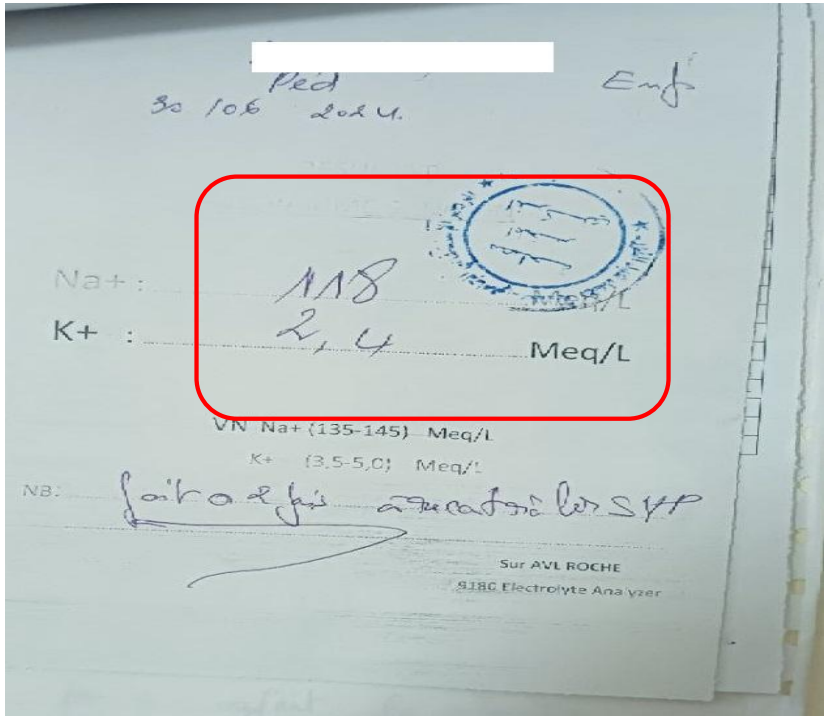
OBJECTIVES:

Consider an underlying cause of recurrent infections in infants and investigate immunodeficiency if any subtle indicators are present.

We report the case of a 4-year-old boy who presented to the pediatric department with recurrent infections, but had an underlying SCID.

Case Report

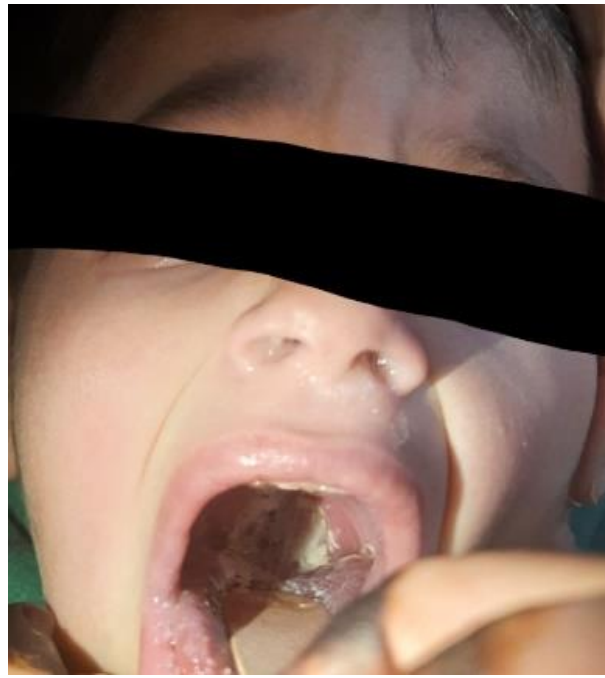
Case Study



A A : 4-year-old boy, the third child of a second-degree consanguineous couple

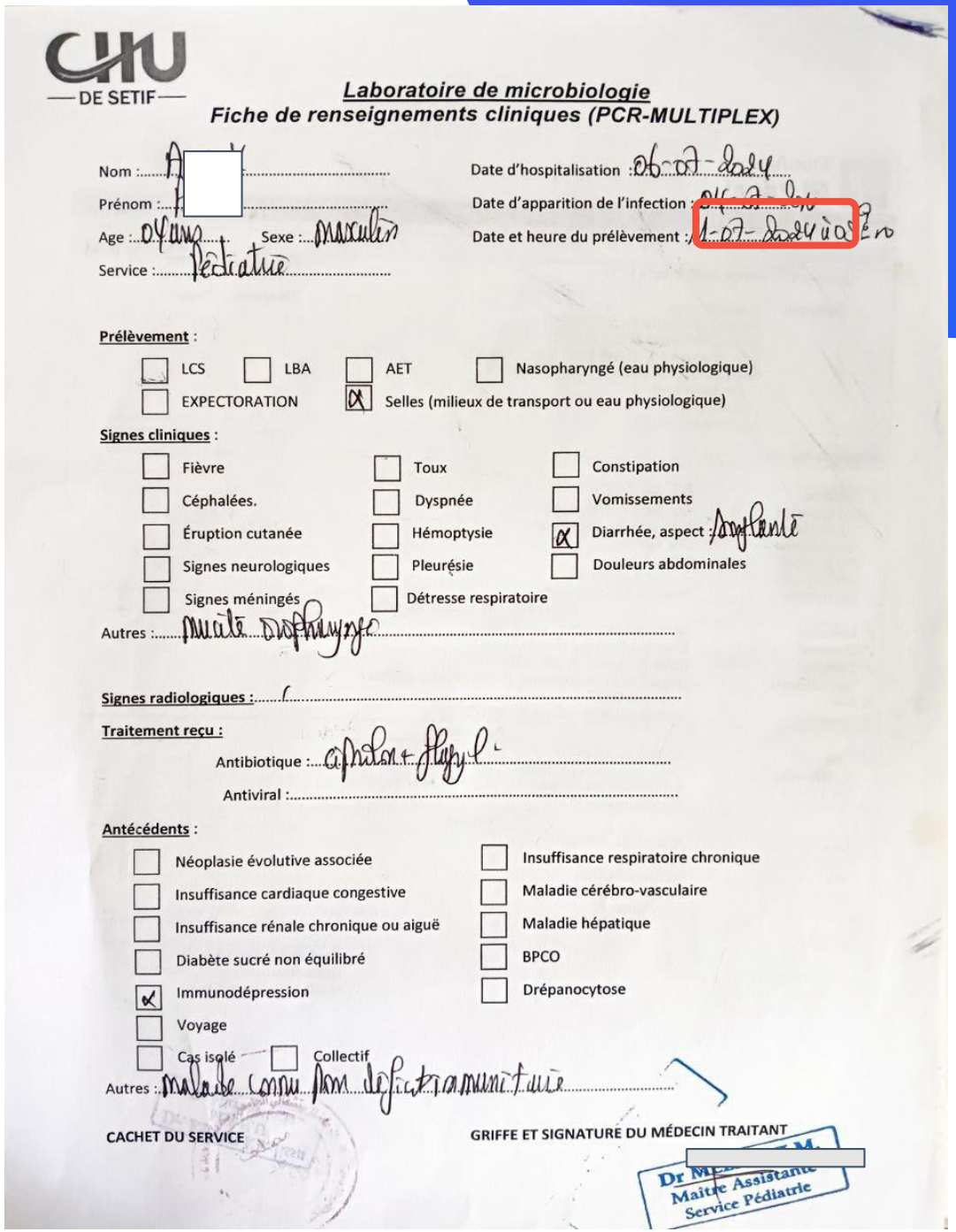
Presented with:

- Severe malnutrition
- Mucositis
- Bloody diarrhea.



Standard culture: Negative

Multiplex PCR (GI Panel):



CHU DE SETIF

Laboratoire de microbiologie

Fiche de renseignements cliniques (PCR-MULTIPLEX)

Nom : [redacted]

Prénom : [redacted]

Age : 04 ans Sexe : masculin

Service : Pédiatrie

Date d'hospitalisation : 06-07-2024

Date d'apparition de l'infection : 06-07-2024

Date et heure du prélèvement : 1-07-2024 à 05h

Prélèvement :

- [ ] LCS
- [ ] LBA
- [ ] AET
- [ ] Nasopharyngé (eau physiologique)
- [ ] EXPECTORATION
- [x] Selles (milieux de transport ou eau physiologique)

Signes cliniques :

- [ ] Fièvre
- [ ] Toux
- [ ] Constipation
- [ ] Céphalées.
- [ ] Dyspnée
- [ ] Vomissements
- [ ] Éruption cutanée
- [ ] Hémoptysie
- [x] Diarrhée, aspect : Inflammé
- [ ] Signes neurologiques
- [ ] Pleurésie
- [ ] Douleurs abdominales
- [ ] Signes méningés
- [ ] Détresse respiratoire

Autres : Raideur douloureuse

Signes radiologiques : /

Traitement reçu :

Antibiotique : Ceftriaxone + Flagyl

Antiviral :

Antécédents :

- [ ] Néoplasie évolutive associée
- [ ] Insuffisance respiratoire chronique
- [ ] Insuffisance cardiaque congestive
- [ ] Maladie cérébro-vasculaire
- [ ] Insuffisance rénale chronique ou aiguë
- [ ] Maladie hépatique
- [ ] Diabète sucré non équilibré
- [ ] BPCO
- [x] Immunodépression
- [ ] Drépanocytose
- [ ] Voyage
- [ ] Cas isolé
- [ ] Collectif

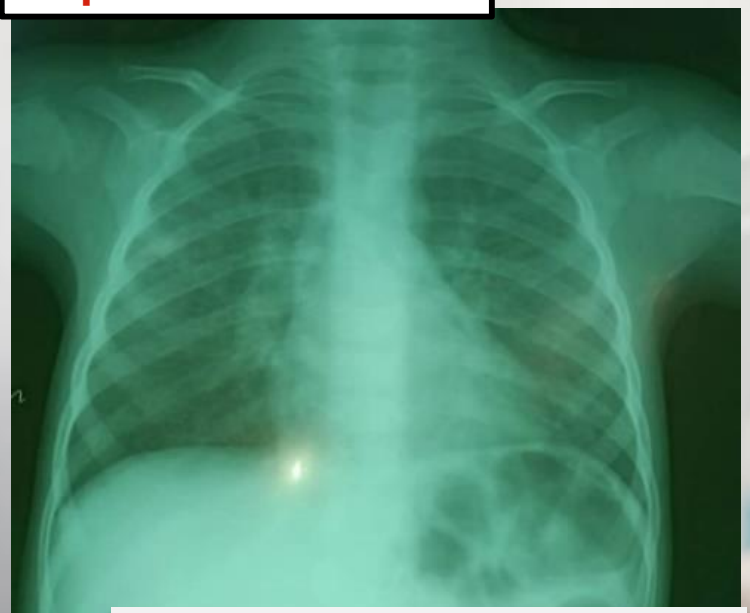
Autres : Malade connu porteur déficit immunitaire

CACHET DU SERVICE

GRIFFE ET SIGNATURE DU MÉDECIN TRAITANT

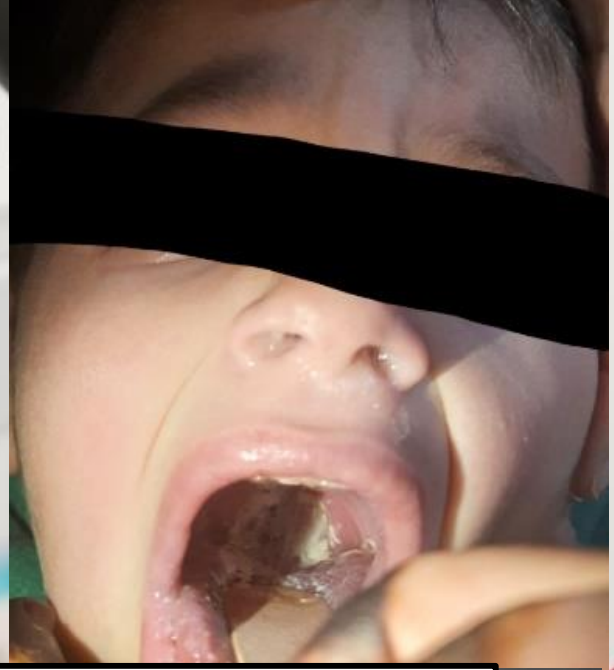
Dr [redacted]
Maître Assistante
Service Pédiatrie

September 2020

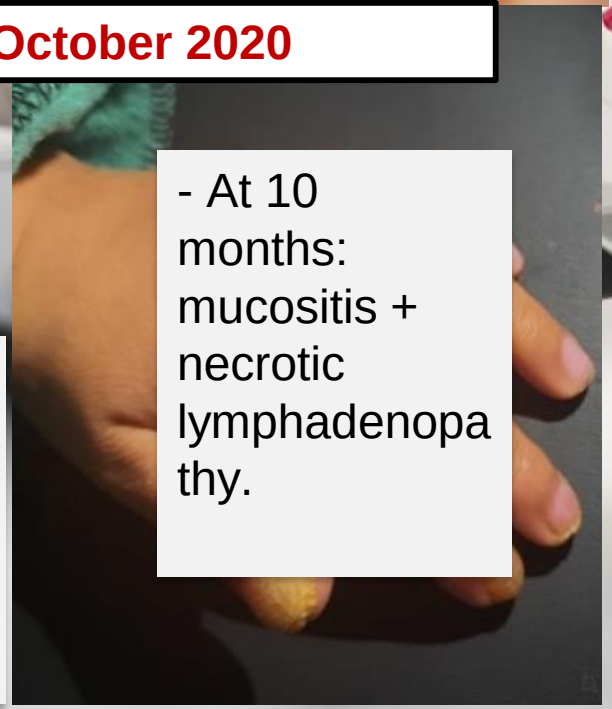


- At 9 months: severe respiratory distress, fever, rhinopharyngitis, oral thrush.

→ Admitted to ICU for 28 days.
→ Sputum: Klebsiella pneumoniae, Enterococcus sp.



October 2020



- At 10 months: mucositis + necrotic lymphadenopathy.

Dosage pondéral des immunoglobulines : 15/10/2020 (Technique : néphélémétrie laser)

IgG	1.22g/l	4.6-8.6 g/l
Ig A	0.10g/l	0.19-0.55 g/l
IgM	0.34 g/l	0.31-0.77 g/l

Measurement of immunoglobulin levels

Analyse par cytométrie en flux :

Phénotypage lymphocytaire T-B-NK :			
Cellules	%	VALEUR ABSOLUE	NORMES/AGE
T-CD3+	42.5%	3520	1900-5900
T-CD4+	31.5%	2609	1400-4300
T-CD8+	9%	745	500-1700
NK	1%	83	160-950
Leucocytes	/	25100	6400-13000
p.Neutrophiles	64%	16064	2300-6400
Lymphocytes	33%	8283	3400-9000
Monocytes	3%	753	300-2000
Rapport CD4+/CD8+		3.5	1.5-2.9
LB CD19+	56.5%	4680	610-2600

lymphocyte phenotyping

→ Immunodeficiency workup confirmed SCID.

Outcome

Recurrent infections continued..

08/12/2020
To
15/12/2020

Respiratory distress

04/07/2021
To
07/07/2021

Malnutrition due to acute gastroenteritis

02/01/2023
To 11/01/2023

Widespread thrush with feeding difficulty

Outcome

Recurrent infections continued (**Respiratory distress**, mucositis, onychomycosis…)

01/03/2024
To 28/03/2024

Fortum: 200 mg/kg/day
Colistin: 100 mg/kg/day
Gentamicin: 5 mg/kg/day
Favorable outcome

FilmArray® Pneumonia Panel *plus* - IVD

BIOFIRE by bioMérieux
www.BioFireDx.com

Run Information

Sample ID	[redacted] ped	Run Date	14 Mar 2024 7:51 PM
Protocol	SPUTUM v3.3	Serial No.	
Pouch Type	Pneumo*plus* v2.0	Lot No.	
Controls	Passed	Operator	
Run Status	Completed	Instrument	

Detection Summary

Bacteria

	Bin (copies/mL)		10^4	10^5	10^6	≥10^7
Detected:	10^6	*Streptococcus pneumoniae*				
	10^5	*Escherichia coli*				
	10^5	*Haemophilus influenzae*				
	10^4	*Acinetobacter calcoaceticus-baumannii* complex				
	10^4	*Enterobacter cloacae* complex				
	10^4	*Klebsiella oxytoca*				
	10^4	*Klebsiella pneumoniae* group				
	10^4	*Pseudomonas aeruginosa*				
	10^4	*Staphylococcus aureus*				

Note: Dete[illegible] indicate the causative agent of pneumonia. Semi-quantitative Bin (copies/mL) results generated by the FilmArray Pneumonia Panel *plus* are not equivalent to CFU/mL and do not consistently correlate with the quantity of bacterial analytes compared to CFU/mL. For specimens with multiple bacteria detected, the relative abundance of nucleic acids (copies/mL) may not correlate with the relative abundance of bacteria as determined by culture (CFU/mL). Clinical correlation is advised to determine significance of semi-quantitative Bin (copies/mL) for clinical management.

Antimicrobial Resistance Genes

Detected: ✓ *mecA/C* and MREJ

Note: Antimicrobial resistance can occur via multiple mechanisms. A Not Detected result for a genetic marker of antimicrobial resistance does not indicate susceptibility to associated antimicrobial drugs or drug classes. A Detected result for a genetic marker of antimicrobial resistance cannot be definitively linked to the microorganism(s) detected. Culture is required to obtain isolates for antimicrobial susceptibility testing and FilmArray Pneumonia Panel *plus* results should be used in conjunction with culture results for the determination of susceptibility or resistance.

Atypical Bacteria

Detected: None

Viruses

Detected:
- ✓ Adenovirus
- ✓ Coronavirus
- ✓ Human Rhinovirus/Enterovirus
- ✓ Parainfluenza Virus
- ✓ Respiratory Syncytial Virus

Outcome

FilmArray® GI Panel — BIOFIRE — www.BioFireDx.com

Run Summary

Sample ID:	4ans PED	**Run Date:**	11 jul 2024 1:21 PM
Detected:	*Campylobacter* Enteroaggregative *E. coli* (EAEC) Enteropathogenic *E. coli* (EPEC) Enterotoxigenic *E. coli* (ETEC) *lt/st* *Shigella*/Enteroinvasive *E. coli* (EIEC) *Cryptosporidium* *Giardia lamblia* Adenovirus F 40/41	**Controls:**	Passed

Result Summary

Bacteria	
✓ Detected	*Campylobacter*
Not Detected	*Clostridium difficile* toxin A/B
Not Detected	*Plesiomonas shigelloides*
Not Detected	*Salmonella*
Not Detected	*Vibrio*
Not Detected	*Vibrio cholerae*
Not Detected	*Yersinia enterocolitica*
Diarrheagenic *E. coli/Shig*	
✓ Detected	Enteroaggregative *E. coli* (EAEC)
✓ Detected	Enteropathogenic *E. coli* (EPEC)
✓ Detected	Enterotoxigenic *E. coli* (ETEC) *lt/st*
Not Detected	Shiga-like toxin-producing *E. coli* (STEC) *stx*
⊘ N/A	*E. coli* O157
✓ Detected	*Shigella*/Enteroinvasive *E. coli* (EIEC)
Parasites	
✓ Detected	*Cryptosporidium*
Not Detected	*Cyclospora cayetanensis*
Not Detected	*Entamoeba histolytica*
✓ Detected	*Giardia lamblia*
Viruses	
✓ Detected	Adenovirus F 40/41
Not Detected	Astrovirus
Not Detected	Norovirus GI/GII
Not Detected	Rotavirus A
Not Detected	Sapovirus

Run Details

Pouch:	GI Panel v2.1	**Protocol:**	
Run Status:	Completed	**Operator:**	
Serial No.:		**Instrument:**	
Lot No.:			

Amoxicilline, Voriconazole, oliclinomel, polyvitamines..

Ciprofloxacin, Flagyl, Fluconazole, (NA,K) Correction ..

FilmArray® GI Panel — BIOFIRE — www.BioFireDx.com

Run Summary

Sample ID:	4ans PED	**Run Date:**	24 jul 2024 3:00 PM
Detected:	*Cryptosporidium* *Giardia lamblia* Adenovirus F 40/41	**Controls:**	Passed

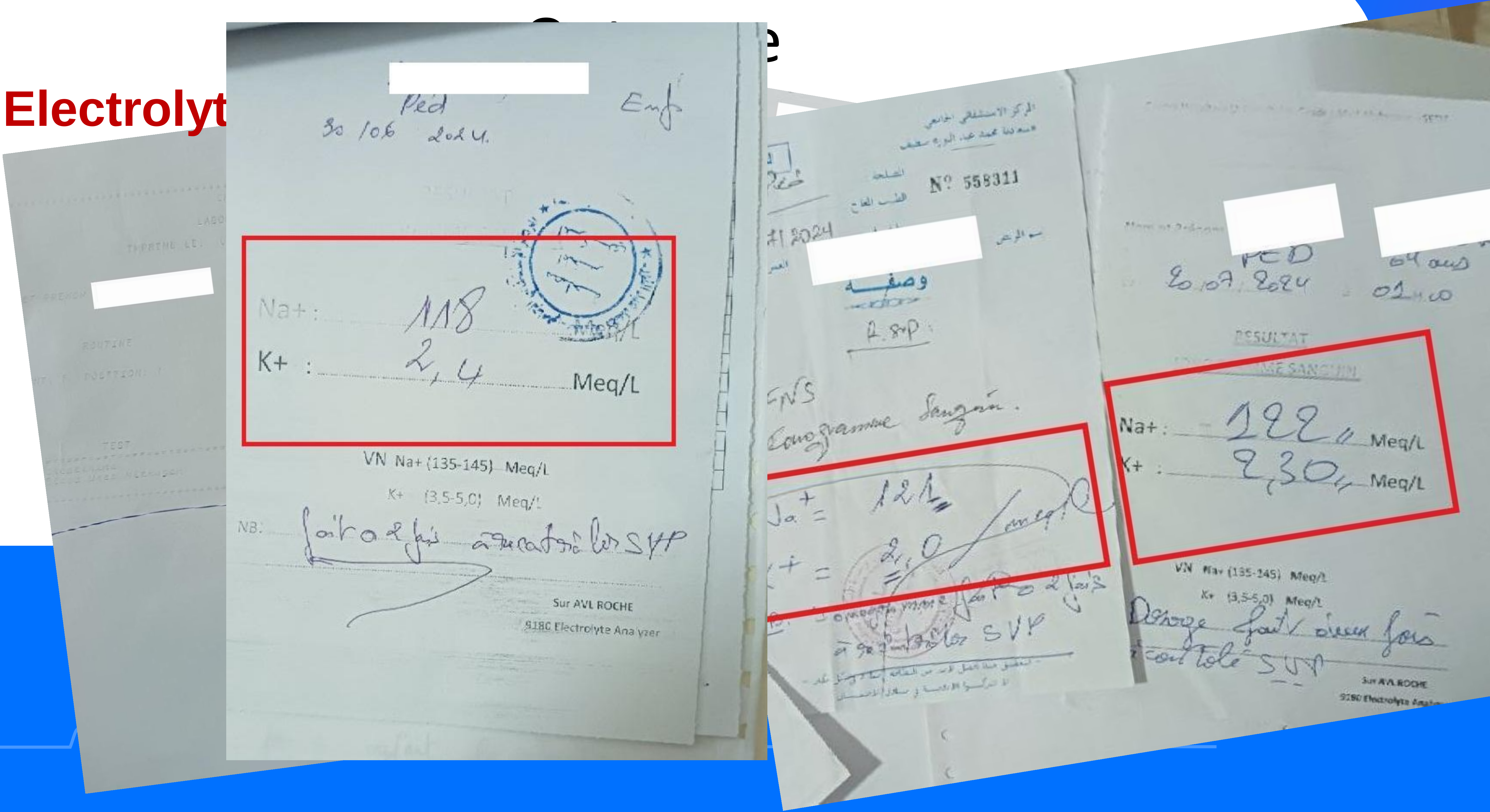
Result Summary

Bacteria	
Not Detected	*Campylobacter*
Not Detected	*Clostridium difficile* toxin A/B
Not Detected	*Plesiomonas shigelloides*
Not Detected	*Salmonella*
Not Detected	*Vibrio*
Not Detected	*Vibrio cholerae*
	Yersinia enterocolitica
Diarrheagenic *E. coli/Shigella*	
	Enteroaggregative *E. coli* (EAEC)
	Enteropathogenic *E. coli* (EPEC)
	Enterotoxigenic *E. coli* (ETEC) *lt/st*
	Shiga-like toxin-producing *E. coli* (STEC) *stx1/stx2*
	E. coli O157
	Shigella/Enteroinvasive *E. coli* (EIEC)
Parasites	
	Cryptosporidium
Not Detected	*Cyclospora cayetanensis*
Not Detected	*Entamoeba histolytica*
	Giardia lamblia
Viruses	
	Adenovirus F 40/41
	Astrovirus
	ovirus GI/GII
	irus A
	us

Run Details

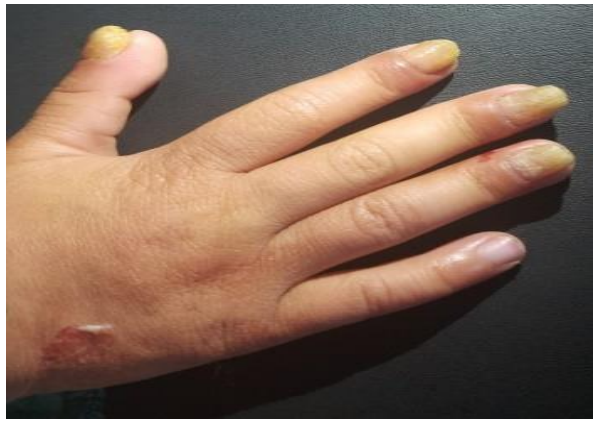
		Protocol:	Stool FA v3.4
		Operator:	
		Instrument:	

Electrolyt

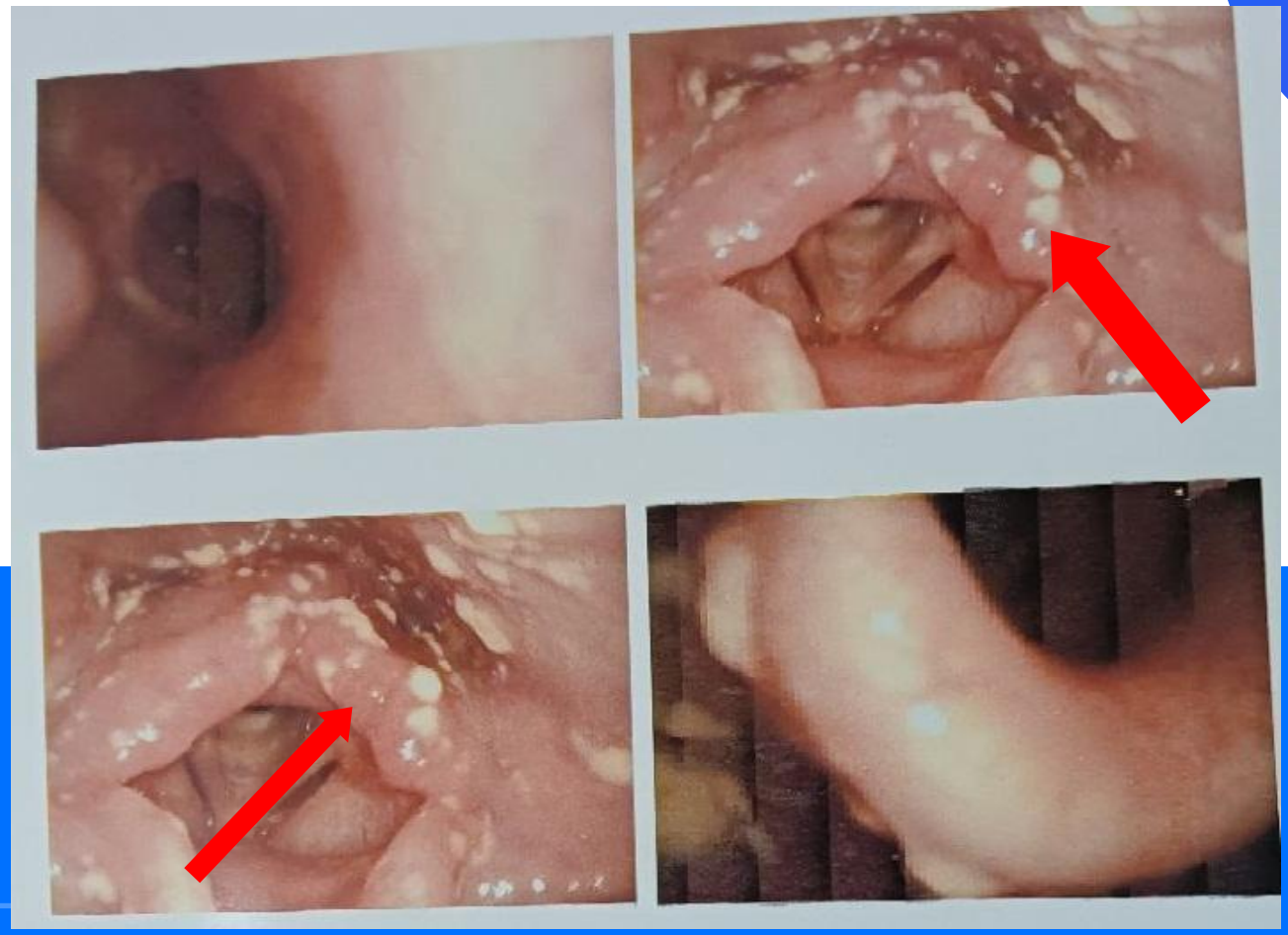

Na+ : 118
K+ : 2,4 Meq/L
VN Na+ (135-145) Meq/L
K+ (3,5-5,0) Meq/L
NB:
Sur AVL ROCHE
9180 Electrolyte Analyzer
N° 558311
RESULTAT
Na+ : 122 Meq/L
K+ : 2,30 Meq/L
VN Na+ (135-145) Meq/L
K+ (3,5-5,0) Meq/L
Sur AVL ROCHE

Outcome

Recurrent infections continued (Respiratory distress, **mucositis**, **onychomycosis…**)



Nasopharyngoscopy: Oropharyngeal mucositis



Outcome

Despite antibiotics and IVIG, due to malnutrition and poor response…

.

the child passed away..

Discussion

Discussion

SCID is a rare disorder with severe T, B, NK cell deficiency.

Asymptomatic at birth, symptoms in early infancy.

Case Report

A case report of severe combined immunodeficiency: Masquerading as sepsis

Subhranshu Sekhar Dhal[1], Hiremath Sagar[2], Rajiv Aggarwal[3], Anil Kumar Sapare[4], Minal Kekatpure[5]

From [1]Resident, [2]Pediatric Intensivist, [3]Head, [4]Pediatric Pulmonologist, [5]Pediatric Neurologist, Department of Pediatrics, NH Health City, Bengaluru, Karnataka, India

Severe combined immunodeficiency (SCID) is usually an autosomally recessive inherited primary immunodeficiency disease which typically occurs in infancy [1]. However, 80% of cases are sporadic in occurrence [2]. Infants with SCID are highly susceptible to severe infections [3]. Diarrhea, pneumonia, otitis media, sepsis, and cutaneous infections are the common manifestation. Opportunistic infections such as pneumocystis carinii, candida, and cytomegalovirus are potential threats. It is a true pediatric emergency as death usually occurs by 2 years if untreated. Hematopoietic stem cell transplant and gene therapy are life-saving [4]. A newborn screening test helps to find out the disease even before the symptoms appear ensuring the affected infants receive life-saving treatments [5]. Here, we report a 5-month-old boy who presented with sepsis but had underlying SCID.

Discussion

According to a study by Aluri et al. (2017)

Aluri J, Italia K, Gupta M, Dalvi A, Bavdekar A, Madkaikar M. Low T cell receptor excision circles (TRECs) in a case of ZAP 70 deficient severe combined immunodeficiency (SCID) with a novel mutation from India. Blood Cells Mol Dis 2017;65:95-6.

In a study by Aluri *et al.* [16], the majority of patients of SCID presented at 6 months of age similar to our patient. However, in their study recurrent pneumonia (66%), failure to thrive (60%), chronic diarrhea (35%), gastrointestinal infection (21%), and oral candidiasis (21%) were the common presentations, while the

Discussion

Antibiotic prophylaxis aims to prevent the onset of specific opportunistic infections

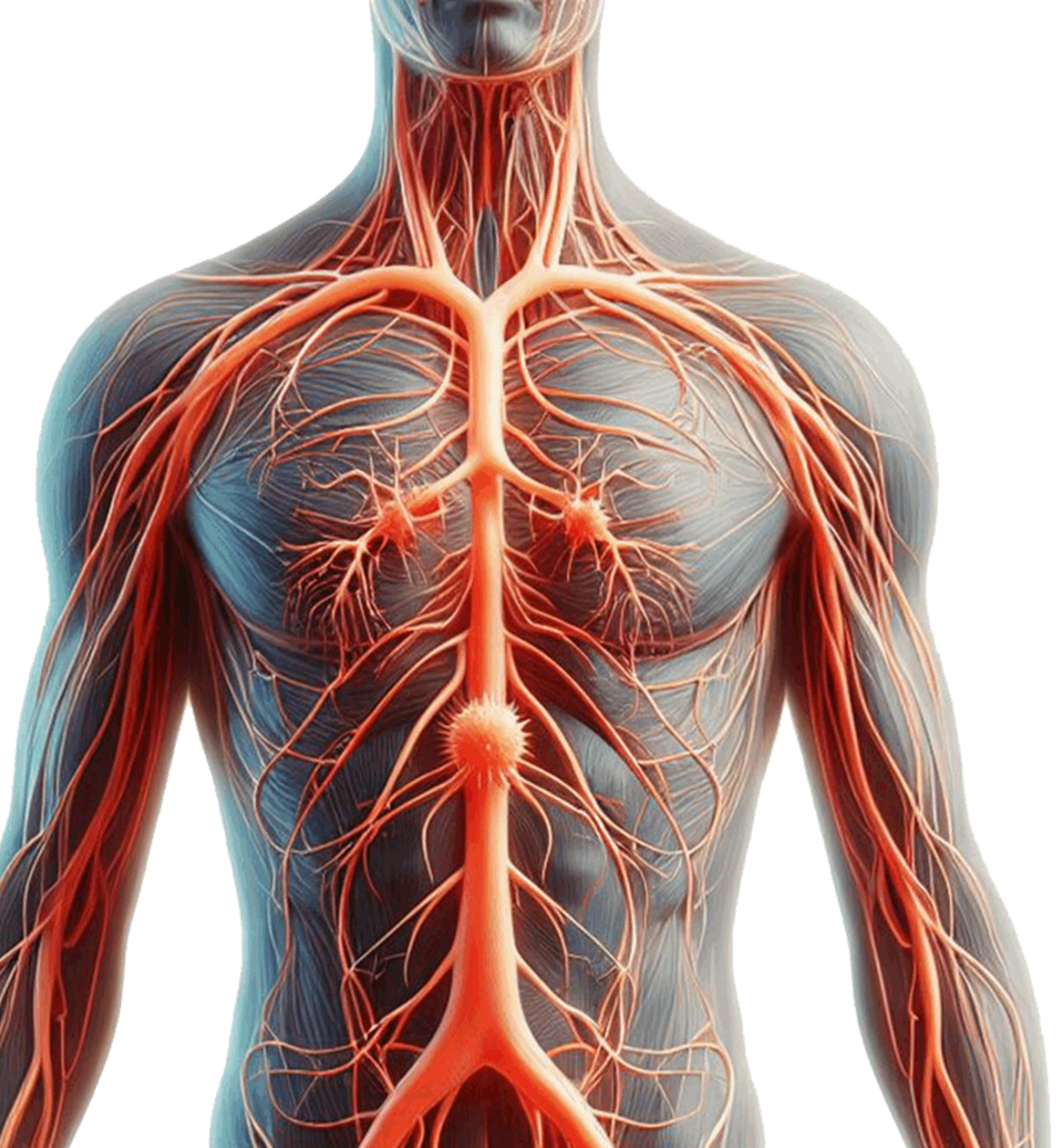
Stem cell transplantation remains the only curative treatment available. Gene therapy is considered if stem cell transplantation is not possible.

Mousa H, Al-Dakheel G, Jabr A, Elbadaoui F, Abouelhoda M, Baig M, *et al*. High incidence of severe combined immunodeficiency disease in saudi arabia detected through combined T cell receptor excision circle and next generation sequencing of newborn dried blood spots. Front Immunol 2018;9:782.

The best treatment for SCID is stem cell transplantation from the matched related donor and it should be done by 3 months of age. Aggressive treatment of infections is very essential to prevent mortality. Gene therapy if a bone marrow transplant is not possible. Transplantation of stem cells is the only cure currently [14].

Conclusion

- Early diagnosis and timely interventions can improve outcomes.
- Monitoring and individualized antibiotic therapy are crucial.
- Molecular diagnostics=fast and accurate pathogen identification, guiding optimal therpy.
- Stem cell transplantation is the only curative option.



Thank You!

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guellatiimene67@gmail.com